ISSN 0125-1252

วชิรเวชสาร
และวารสารเวชศาสตร์เขตเมือง

VAJIRA MEDICAL JOURNAL:
Journal of Urban Medicine

ปีที่ 64 ฉบับที่ 4 กรกฎาคม - สิงหาคม พ.ศ. 2563

Vol. 64 No. 4 July - August 2020

วชิรเวชสาร
และวารสารเวชศาสตร์เขตเมือง
Vajira Medical Journal:
Journal of Urban Medicine

วชิรเวชสาร
และวารสารเวชศาสตร์เขตเมือง
Vajira Medical Journal:
Journal of Urban Medicine

วชิรเวชสาร
และวารสารเวชศาสตร์เขตเมือง
Vajira Medical Journal:
Journal of Urban Medicine

วชิรเวชสาร
และวารสารเวชศาสตร์เขตเมือง
Vajira Medical Journal:
Journal of Urban Medicine

คำชี้แจงการส่งบทความ

วชิรเวชสารเป็นวารสารการแพทย์ของคณะแพทยศาสตร์-วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช เริ่มพิมพ์ครั้งแรกในปีพ.ศ. 2500 และพิมพ์เผยแพร่อย่างสม่ำเสมอ ปีละ 6 ฉบับ ทุก 2 เดือน (มกราคม-กุมภาพันธ์, มีนาคม-เมษายน, พฤษภาคม-มิถุนายน, กรกฎาคม-สิงหาคม, กันยายน-ตุลาคม และพฤศจิกายน-ธันวาคม) และมีฉบับเพิ่มเติมปีละ 1 เล่ม เพื่อตีพิมพ์ผลงานที่นำเสนอในงานประชุมวิชาการของมหาวิทยาลัยหรือของคณะ โดยมีวัตถุประสงค์เพื่อเผยแพร่ผลงานวิจัยในรูปแบบของนิพนธ์ต้นฉบับ รายงานผู้ป่วยและบทความวิชาการทางการแพทย์ รวมทั้งผลงานวิชาการด้านแพทยศาสตรศึกษาและวิทยาศาสตร์สุขภาพ

วชิรเวชสารมุ่งเน้นความรู้เกี่ยวกับเวชศาสตร์เขตเมือง ได้แก่ วิทยาศาสตร์พื้นฐานและวิทยาศาสตร์การแพทย์คลินิก รวมถึง ระบาดวิทยา สมุฏฐานวิทยา พยาธิกำเนิด การวินิจฉัย และการดูแลรักษาโรค อันเกี่ยวข้องกับสุขภาพของประชาชนในเขตเมือง

บทความที่ส่งมาตีพิมพ์จะได้รับการกลั่นกรองโดยผู้ทรงคุณวุฒิที่มีความเชี่ยวชาญในสาขานั้น ๆ อย่างน้อย 2 ท่านในแง่ของความเหมาะสมทางจริยธรรม วิธีการดำเนินการวิจัย ความถูกต้อง ความชัดเจนของการบรรยายในการนำเสนอ รายชื่อของผู้นิพนธ์และผู้กลั่นกรองจะได้รับการปกปิดโดยกองบรรณาธิการก่อนส่งเอกสารไปให้ผู้เกี่ยวข้องทั้ง 2 ฝ่าย กองบรรณาธิการขอสงวนสิทธิ์ในการตรวจแก้ไขบทความก่อนพิจารณาตีพิมพ์ ทั้งนี้ข้อความและความคิดเห็นในบทความนั้น ๆ เป็นของเจ้าของบทความโดยตรง

บทความที่ส่งมาต้องไม่เคยพิมพ์ที่ใดมาก่อน และไม่อยู่ระหว่างการพิจารณาเพื่อพิมพ์ที่ใด ๆ ยกเว้นในรูปแบบบทคัดย่อหรือเอกสารบรรยาย กรณีที่บทความได้รับการพิมพ์ในวชิรเวชสารแล้ว ผู้นิพนธ์จะได้รับสำเนาพิมพ์ 30 ฉบับ ภายหลังหนังสือเผยแพร่เรียบร้อยแล้ว และผู้นิพนธ์ไม่สามารถนำบทความดังกล่าวไปนำเสนอหรือพิมพ์ในรูปแบบใด ๆ ที่อื่นได้ ถ้าไม่ได้รับคำอนุญาตจากวชิรเวชสาร

หลักเกณฑ์ทั่วไปในการเตรียมและส่งต้นฉบับ

การส่งต้นฉบับ ให้ส่ง 3 ชุด พร้อม diskette หรือแผ่น CD หรือส่งทางระบบ online (https://tci-thaijo.org/index.php/VMED และ http://thailand.digitaljournals.org/index.php/VMJ/) หรือส่ง ทางระบบ online (https://tci-thaijo.org/index.php/VMED และ http://thailand.digitaljournals.org/index.php/VMJ/) พร้อมรายการตรวจสอบบทความ และจดหมายเพื่อขอพิมพ์ ไปยังกองบรรณาธิการ ซึ่งจดหมายนี้ต้องมีชื่อ ที่อยู่ หมายเลขโทรศัพท์ โทรสาร และ email address ของผู้นิพนธ์ระบุว่า ผู้นิพนธ์ท่านใดเป็นผู้รับผิดชอบหลัก และต้นฉบับนั้นเป็นบทความประเภทใด (นิพนธ์ต้นฉบับ รายงานผู้ป่วย หรือบทความวิชาการ) รวมทั้งต้องมีข้อความว่าผู้นิพนธ์ทุกท่านได้อ่านและเห็นด้วยกับต้นฉบับนั้น และเชื่อว่าต้นฉบับนั้นรายงานผลตรงตามผลการวิจัยที่ได้ศึกษา และต้นฉบับนั้นไม่เคยพิมพ์ที่ใดมาก่อนและไม่อยู่ระหว่างการพิจารณาเพื่อพิมพ์ที่ใด ๆ ในกรณีที่เรื่องนั้นเคยพิมพ์ในรูปบทคัดย่อ หรือวิทยานิพนธ์ หรือเคยนำเสนอในที่ประชุมวิชาการใด ๆ จะต้องแจ้งให้กองบรรณาธิการทราบด้วย สำหรับเรื่องที่ทำการศึกษาในคน จะต้องมีหนังสืออนุญาตจากคณะกรรมการจริยธรรมการศึกษาวิจัยในมนุษย์แนบมาด้วย

ต้นฉบับจะเป็นภาษาไทยหรือภาษาอังกฤษก็ได้ ถ้าเป็นภาษาไทยควรใช้ภาษาไทยให้มากที่สุด ยกเว้นคำภาษาอังกฤษที่ไม่มีคำศัพท์นั้น ๆ ในภาษาไทยหรือแปลแล้วได้ใจความไม่ชัดเจน ภาษาอังกฤษที่ใช้ให้ใช้ตัวพิมพ์เล็กทั้งหมดยกเว้นชื่อเฉพาะที่ให้ใช้ ตัวพิมพ์ใหญ่เฉพาะอักษรต้น ตัวเลขใช้เลขอารบิก เนื้อหาควรมีความกระชับโดยมีความยาวเหมาะสมกับการพิมพ์ การพิมพ์ต้นฉบับให้ใช้ font Cordial New 16 พิมพ์หน้าเดียวบนกระดาษ A4 และพิมพ์บรรทัดเว้นบรรทัด โดยเว้นระยะห่างจากขอบทั้ง 4 ด้านไม่น้อยกว่า 1 นิ้ว โดยไม่ต้องปรับขอบด้านขวาให้ตรงกัน

รายการตรวจสอบบทความ (checklist guideline)

ผู้นิพนธ์ต้องตรวจสอบต้นฉบับที่จัดเตรียมให้ครบถ้วนถูกต้องตรงตามรายการตรวจสอบบทความ และส่งมาพร้อมกับบทความ บทความที่ส่งมาโดยไม่มีใบรายการตรวจสอบบทความ หรือมีไม่ครบ หรือไม่ถูกต้องตามที่กำหนดไว้จะถูกส่งกลับก่อนการดำเนินการใด ๆ ทั้งสิ้น ผู้นิพนธ์สามารถ download รายการตรวจสอบบทความชนิดต่าง ๆ ได้จาก website ของวชิรเวชสาร (http://www.vajira.ac.th/vmj)

คำแนะนำในการเขียนบทความ

การวิจัยแบบสุ่ม การวิจัยเพื่อการวินิจฉัยโรค และการวิจัยเชิงสังเกต ควรจะตรวจสอบความถูกต้องครบถ้วนของเกณฑ์ตามแนวทางของ Consort 2010 checklist, STARD checklist และ STROBE checklist ตามลำดับ ผู้นิพนธ์สามารถอ่านรายละเอียดเพิ่มเติมได้ผ่านทาง website ของวชิรเวชสาร

ผู้นิพนธ์ควรเตรียมบทความตามแนวทางการเขียนบทความทางวิทยาศาสตร์สุขภาพของคณะบรรณาธิการวารสารนานาชาติ (International Committee of Medical Journal Editors) ซึ่งมีรายละเอียดทาง website http://www.icmje.org/recommendations/ ดังจะสรุปไว้เป็นแนวทางดังต่อไปนี้ คือ บทความที่ส่งเพื่อพิจารณาตีพิมพ์ ควรเขียนเรียงตามลำดับดังนี้ ชื่อเรื่องและผู้นิพนธ์ บทคัดย่อ เนื้อหาหลัก กิตติกรรมประกาศ เอกสารอ้างอิง

1. ชื่อเรื่อง (title) ควรตั้งชื่อเรื่องให้กะทัดรัด ได้ใจความชัดเจน ไม่ใช้ตัวย่อใด ๆ ชื่อเรื่องภาษาไทยให้ใช้ภาษาไทยทั้งหมด ภาษาอังกฤษที่มีในชื่อเรื่องให้แปลเป็นไทย ถ้าแปลไม่ได้ให้เขียนทับศัพท์ ถ้าเขียนทับศัพท์ไม่ได้ให้เขียนเป็นภาษาอังกฤษด้วยตัวพิมพ์เล็กยกเว้นชื่อเฉพาะที่ให้ใช้ตัวพิมพ์ใหญ่เฉพาะอักษรต้น ชื่อเรื่องภาษาอังกฤษให้ใช้ตัวพิมพ์ใหญ่ในอักษรต้นตัวแรกของทุกคำ ยกเว้นคำบุพบท

2. ผู้นิพนธ์ (authors) เขียนชื่อ นามสกุล และคุณวุฒิของผู้นิพนธ์ คุณวุฒิภาษาไทย เขียนด้วยตัวย่อตามพจนานุกรม เช่น พ.บ. ว.ว.ศัลยศาสตร์ หรือ วท.บ. กศ.บ. คุณวุฒิภาษาอังกฤษ ให้เขียนตัวย่อโดยไม่ต้องมีจุด เช่น MD, PhD, FICS, FRCST, MRCOG เป็นต้น หลังคุณวุฒิให้ใส่เครื่องหมายเชิงอรรถ (footnotes) กำกับให้รายละเอียดสถานที่ทำงานในบรรทัดล่างของหน้าแรก เชิงอรรถใช้ตัวเลขเรียงจากเลข 1 ขึ้นไป และให้ใส่เครื่องหมายดอกจันหลังคุณวุฒิของชื่อผู้ติดต่อ หรือ corresponding author และให้ e-mail address ของผู้ติดต่อในบรรทัดล่างสุดของหน้าแรกต่อจากรายละเอียดสถานที่ทำงานของผู้นิพนธ์และผู้นิพนธ์ร่วม

3. บทคัดย่อ (abstract) หมายถึง เรื่องย่อของงานวิจัยซึ่งต้องมีทั้งภาษาไทยและภาษาอังกฤษ เนื้อหาต้องมีความสมบูรณ์ในตัวเอง โดยเขียนให้สั้นที่สุดและได้ใจความ บทคัดย่อทั้งภาษาไทยและภาษาอังกฤษต้องมีเนื้อหาเหมือนกัน ไม่ใส่ตารางหรือแผนภูมิใด ๆ ไม่มีการอ้างอิงเอกสาร ไม่ใส่ตัวเลขหรือข้อความที่ไม่ปรากฏในผลการวิจัย สำหรับบทคัดย่อภาษาอังกฤษให้ใช้ past tense เท่านั้น และให้ใส่ keywords ต่อท้าย ไม่เกิน 3-5 คำหรือวลี เพื่อใช้เป็นดัชนี

นิพนธ์ต้นฉบับให้เขียนบทคัดย่อแบบ structured abstract ส่วนรายงานผู้ป่วยและบทความวิชาการให้เขียนบทคัดย่อแบบปกติย่อหน้าเดียว (standard abstract) ซึ่งควรมีจำนวนคำทั้งหมดไม่เกิน 300 คำ structured abstract ให้เขียน 4 หัวข้อหลัก ซึ่งประกอบด้วย วัตถุประสงค์ (objective) วิธีดำเนินการวิจัย (methods) ผลการวิจัย (results) และสรุป (conclusion) โดยวัตถุประสงค์ควรกล่าวถึงจุดมุ่งหมายหลักที่ต้องการศึกษาหรือทฤษฎีที่ต้องการทดสอบ วิธีดำเนินการวิจัยควรรวมถึงรูปแบบการทำวิจัย สถานที่ทำการวิจัย จำนวนและลักษณะของกลุ่มตัวอย่าง วิธีการรักษาหรือทดลอง

ผลการวิจัยหมายถึงผลลัพธ์ส่วนที่สำคัญที่สุดของการศึกษา และสรุปควรเน้นถึงความสำคัญของผลการวิจัย

4. เนื้อหาหลัก ในส่วนของนิพนธ์ต้นฉบับ ควรประกอบด้วย 4 หัวข้อหลัก ได้แก่ บทนำ วิธีดำเนินการวิจัย ผลการวิจัย และวิจารณ์ รายงานผู้ป่วย ควรมี 4 หัวข้อหลัก คือ บทนำ รายงานผู้ป่วย วิจารณ์และสรุป ส่วนบทความวิชาการ ให้ปรับหัวข้อหลักตามความเหมาะสมกับบทความนั้น ๆ

บทนำ ควรกล่าวถึงความเป็นมาของปัญหา เช่น ลักษณะและความสำคัญของปัญหาที่จะนำมาศึกษา มีการเน้นถึงความรู้เดิมของปัญหาโดยอ้างอิงจากเอกสารที่เกี่ยวข้องตามสมควรเพื่อนำผู้อ่านเข้าสู่เรื่องที่จะทำวิจัย รวมทั้งบอกวัตถุประสงค์ในการทำวิจัยอย่างชัดเจน ทั้งนี้บทนำไม่ควรยาวเกินไป ไม่ใส่ข้อมูลผลการวิจัย ตารางหรือแผนภูมิใด ๆ และต้องไม่วิจารณ์หรือสรุปในบทนำ

วิธีดำเนินการวิจัย ควรบอกว่าเป็นรูปแบบการวิจัยชนิดใด กลุ่มตัวอย่างขนาดเท่าใด โดยแสดงวิธีคำนวณขนาดตัวอย่างอย่างสั้น ๆ สุ่มตัวอย่างโดยวิธีใด บอกสถานที่ที่ทำการวิจัย ระยะเวลาที่ศึกษา เกณฑ์การคัดเข้าและเกณฑ์การคัดออก บอกรายละเอียดของการวิจัยว่าดำเนินการอย่างไร เพื่อให้ผู้อื่นสามารถนำไปศึกษาซ้ำได้ หากเป็นวิธีที่ใช้อยู่ทั่วไปอาจบอกเพียงชื่อวิธีการพร้อมเอกสารอ้างอิง แต่ถ้าเป็นวิธีใหม่ ต้องแจงรายละเอียดให้ผู้อ่านเข้าใจ รวมทั้งบอกรายละเอียดของการวิเคราะห์ข้อมูลทางสถิติ ว่าใช้โปรแกรมคอมพิวเตอร์อะไรในการวิเคราะห์ข้อมูล ใช้สถิติอะไร และกำหนดระดับนัยสำคัญเท่าใด

ผลการวิจัย ควรนำเสนอให้เข้าใจง่ายและชัดเจน โดยใช้ตารางและแผนภูมิหรือรูปประกอบ แต่ไม่ใช้ตารางและแผนภูมิในเรื่องเดียวกัน ควรออกแบบให้มีจำนวนตารางและแผนภูมิน้อยที่สุด โดยไม่ควรเกิน 5-7 ตาราง ตารางและแผนภูมิต้องมีเลขที่ และชื่อกำกับ และมีคำอธิบายโดยสรุป เส้นของตารางให้มีเฉพาะเส้นแนวขวาง 3 เส้นที่ด้านบนสุด ด้านล่างสุดของตาราง และเส้นแบ่งหัวข้อตารางกับเนื้อหาเท่านั้น รูปประกอบควรเป็นรูปที่จัดทำขึ้นเอง ถ้าเป็นรูปจากแหล่งอื่นจะต้องระบุที่มา รวมทั้งเอกสารสำเนาลิขสิทธิ์จากสำนักพิมพ์ต้นฉบับด้วย สำหรับรูปผู้ป่วยจะต้องไม่ให้ทราบว่าเป็นบุคคลใดโดยได้รับการปกปิดส่วนที่สามารถระบุถึงบุคคลได้ และอาจจะต้องมีคำยินยอมจากผู้ป่วยด้วย

วิจารณ์ ให้วิจารณ์ผลการวิจัยทั้งหมดที่นำเสนอ สรุปผลการวิจัยสั้น ๆ โดยไม่ต้องลอกข้อความที่เขียนแล้วในผลการวิจัย เปรียบเทียบผลการวิจัยกับการศึกษาอื่น ๆ ให้ความเห็นว่าเหตุใดผลการวิจัยจึงเป็นเช่นนั้น ควรวิจารณ์ข้อจำกัดของการทำวิจัย วิธีดำเนินการวิจัยและความน่าเชื่อถือทางสถิติ รวมทั้งประโยชน์ที่จะนำไปใช้ได้ และการวิจัยที่ควรศึกษาต่อเนื่องต่อไปในอนาคต

5. **Conflict of interest** ให้ระบุว่าผู้นิพนธ์แต่ละท่านมี conflict of interest ใด ๆ หรือไม่ ในจดหมายเพื่อขอพิมพ์

6. **กิตติกรรมประกาศ** แสดงความขอบคุณผู้สนับสนุนการทำวิจัย เช่น ผู้ให้การสนับสนุนทางด้านเทคนิค เครื่องมือที่ใช้ และทางการเงิน นอกจากนี้ควรขอบคุณหน่วยงานหรือผู้รับผิดชอบข้อมูล และผู้ให้คำแนะนำด้านต่าง ๆ

7. **เอกสารอ้างอิง** ให้ใส่หมายเลข 1,2,3 ไว้ท้ายประโยคโดยพิมพ์ตัวยกสูงโดยไม่ต้องใส่วงเล็บ เอกสารที่อ้างอิงเป็นอันดับแรกให้จัดเป็นหมายเลข 1 และเรียงลำดับก่อนหลังต่อ ๆ ไป หากไม่มีความจำเป็นไม่ควรอ้างอิง abstract, unpublished paper, in press หรือ personal communication นิพนธ์ต้นฉบับควรมีเอกสารอ้างอิงไม่เกิน 30 รายการ และไม่ควรใช้เอกสารอ้างอิงที่เก่าเกินไป เอกสารอ้างอิงทั้งหมด รวมทั้งเอกสารอ้างอิงภาษาไทย ให้เขียนเป็นภาษาอังกฤษ โดยเขียนตาม Vancouver guideline ซึ่งกำหนดโดย International Committee of Medical Journal Editors โดยมีหลักโดยย่อดังนี้

ชื่อผู้เขียน ให้ใช้ชื่อสกุลตามด้วย อักษรแรกของชื่อต้นและชื่อกลางเป็นตัวพิมพ์ใหญ่ ใส่ชื่อผู้เขียนทุกคนคั่นด้วยเครื่องหมายจุลภาค ถ้าเกิน 6 คน ใส่ชื่อ 6 คนแรก ตามด้วย et al

การอ้างอิงวารสาร ให้ใส่ชื่อผู้เขียน. ชื่อเรื่อง. ชื่อย่อวารสารตาม index medicus. ปี ค.ศ.; ปีที่ (volume): หน้าแรกถึงหน้าสุดท้าย. โดยเลขหน้าที่ซ้ำกันไม่ต้องเขียน เช่นหน้า 124 ถึงหน้า 128 ให้เขียน 124-8.

ตัวอย่าง: Tangjitgamol S, Hanprasertpong J, Manusirivithaya S, Wootipoom V, Thavaramara T, Buhachat R. Malignant ovarian germ cell tumors: clinico-pathological presentation and survival outcomes. Acta Obstet Gynecol Scand. 2010; 89: 182-9.

การอ้างอิงหนังสือตำรา ให้เขียน ชื่อผู้เขียน. ชื่อหนังสือ. ครั้งที่พิมพ์ (ถ้าพิมพ์ครั้งแรกไม่ต้องเขียน). ชื่อเมือง (ใช้ชื่อเมืองแรกชื่อเดียว): ชื่อโรงพิมพ์; ค.ศ. p.หน้าแรกถึงหน้าสุดท้าย.

ตัวอย่าง: Straus SE, Richardson WS, Glasziou P, Haynes RB. Evidence based medicine: how to practice and teach EBM. 3rd ed. Edinburgh: Churchill Livingstone; 2005. p.10-5.

การอ้างอิงบทหนึ่งในหนังสือตำรา ให้เขียน ชื่อผู้เขียน. ชื่อเรื่อง. In: ชื่อบรรณาธิการ, editor(s). ชื่อหนังสือ. ครั้งที่พิมพ์ (ถ้าพิมพ์ครั้งแรกไม่ต้องเขียน). ชื่อเมือง: ชื่อโรงพิมพ์; ปี ค.ศ. p. หน้าแรก-หน้าสุดท้าย.

ตัวอย่าง: Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p.93-113.

การอ้างอิงบทคัดย่อจากที่ประชุมวิชาการ (published proceedings paper)

ตัวอย่าง: Berger H, Klemm M. Clinical signs of gastric ulcers and its relation to incidence [abstract]. In: Chuit P, Kuffer A, Montavon S, editors. 8th Congress on Equine Medicine and Surgery; 2003 Dec 16-18; Geneva, Switzerland. Ithaca (NY): International Veterinary Information Service (IVIS); 2003. p. 45.

การอ้างอิงจากวารสาร/ข้อมูลทางอิเล็กทรอนิกส์:

ตัวอย่าง: International Committee of Medical Journal Editors. Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals [Internet]. 2014 [updated 2014 Dec 1; cited 2015 Jan 30] Available from: http://www.icmje.org/icmje-recommendations.pdf.

การอ้างอิงจากวิทยานิพนธ์

ตัวอย่าง: Liu-Ambrose TY. Studies of fall risk and bone morphology in older women with low bone mass [dissertation]. [Vancouver (BC)]: University of British Columbia; 2004. 290 p.

การแก้ไขบทความเพื่อส่งตีพิมพ์

ให้ผู้นิพนธ์แก้ไขบทความ และอธิบายชี้แจงข้อสงสัยตามที่ผู้กลั่นกรอง และกองบรรณาธิการให้ข้อเสนอแนะให้ครบทุกประเด็น และควรเน้นหรือขีดเส้นใต้ส่วนที่ได้แก้ไขในบทความพร้อมทั้งมีจดหมายสั้น ๆ ระบุว่าได้แก้ในประเด็นใดบ้าง รวมทั้งอธิบายประเด็นที่ไม่ได้แก้ไขให้ผู้นิพนธ์ส่งคืนบทความที่แก้ไขแล้ว พร้อมทั้งบทความเดิมที่ได้รับจากกองบรรณาธิการภายใน 4 สัปดาห์หลังได้รับบทความ ถ้าภายใน 12 สัปดาห์ ผู้นิพนธ์ไม่ส่งบทความคืน หรือไม่ได้แก้ไขบทความตามคำแนะนำ ทางกองบรรณาธิการขอสงวนสิทธิ์ในการถอนบทความออกจากการพิจารณาบทความเพื่อตีพิมพ์

Instructions for Authors

Vajira Medical Journal (Vajira Med J) is the official medical journal of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University. The journal was established in 1957 and, since then, has been regularly published 6 issues per year (January-February, March-April, May-June, July-August, September-October and November-December). The aim is to provide medical knowledge, medical education, and other biomedical sciences information in various types of publications: original article, case report, and review article.

A Key focus of Vajira Med J is on basic and clinical science in urban medicine, including but not limited to epidemiology, etiology, pathogenesis, diagnosis and management for a better health of urban population.

Vajira Med J is a peer reviewed journal with an editorial policy of anonymous (when the reviewers' name are unrevealed) and blind review (when the authors' name are removed from the manuscript submitted for review). All submitted manuscripts are promptly assigned, by the Editor-in- Chief, to two or more members of the editorial board members who are expertise in the field to review the content in terms of ethics, methodology, accuracy, and clarity. In the event that the article is accepted, the corresponding author will receive 30 copies of the paper after it is published.

Submission of a manuscript implies that the article or any part of its essential substance, tables, or figures has not been previously published or not under consideration for publication elsewhere. This restriction does not apply to abstract or published proceedings to the scientific meetings, or an academic thesis. If accepted, it will not be published elsewhere in the same form, in Thai, English or in any other languages, without written consent from the Journal. The Editorial Board reserves the right to modify the final submission for editorial purposes. The intellectual content of the paper is the responsibility of the authors. The Editors and the Publisher accept no responsibility for opinions and statements of the authors.

Preparation of manuscripts

General requirements

All manuscripts can be submitted online (https://tci-thaijo.org/index.php/VMED and http://thailand.digitaljournals.org/index.php/VMJ/) or sent to email: sathit@nmu.ac.th 3 copies in print and on electronic data file via CD, diskette or email along with a cover letter and the checklist guideline. A cover letter must include name and title of the first or corresponding author, full address, telephone number, fax number, and e-mail address, title and category of the submitted manuscript: original article, case report, or review articles. The letter should contain the declared statements that the manuscript has been read and approved by all the authors in terms of the content and accuracy, and that the manuscript has not been previously published or is not under consideration for publication elsewhere. Previous publication in the form of abstract, published proceedings in the scientific meetings, or academic thesis is acceptable for a duplication or modification with an information (or declaration) to the editorial board. If applicable, a copy of ethics approval document should be sent along with the manuscript.

The article must be written in clear and concise Thai, or English. If the manuscript is written in Thai, English is allowed only when Thai word/phrase is unable to make the sentence clear. When English is used, lowercase letters are required. The numbers must be typed in Arabic. The text must be typed double-spaced, in single column, with 1 inch unjustified right margin on A4 paper. Cordial New in 16 pt. size is the preferred font style.

Checklist guideline for an author to submit a manuscript

To facilitate the manuscript preparation and submission, the authors must complete the checklist form and send it along with the manuscript. Any submitted manuscript without checklist form, incomplete data, or incorrect format will be returned to the corresponding author before proceeding. Checklist forms for various types of manuscript can be downloaded from Vajira Med J website (http://www.vajira.ac.th/vmj).

Manuscript Preparation

For researches which fit into any of the following study designs: randomized controlled, diagnostic test or observational studies should follow consort 2010 checklist, STARD checklist and STROBE checklist respectively. These checklists can be downloaded through our website.

The author should prepare the manuscript according to the Uniform Requirements for Manuscript Submitted to Biomedical Journals of the International Committee of Medical Journal Editors. (http://www.icmje.org/recommendations/). Briefly, the manuscripts should be structured in the following order: title and authors, abstract, main text, acknowledgments, and references.

1. **Title:** the title should be concise and suitable for indexing purposes. The first letter of each word should be in capital letter except for a preposition and an article.

2. **Authors:** all contributing author(s) with full name, graduate degree, and department and institutional affiliation of each author are required. E-mail address of the corresponding author should also be addressed.

3. **Abstract:** The abstract must be submitted in duplicate, both in Thai and English. Both Thai and English abstract should have similar or parallel contents. It should be concise and stand for the article. Tables, figures, or references are not included in the abstract as well as the figures or results which do not appear in the article. A standard abstract in one paragraph

without subheading is required for case report and review articles and should be limited to 300 words. Below the English abstract list 3-5 keywords for indexing purposes.

A structured abstract is required for original article. It must consist of 4 concise paragraphs under the headings: Objective(s), Methods, Results, and Conclusion(s). The **objective(s)** reflect(s) the purpose of the study, i.e. the hypothesis that is being tested. The **methods** should include the study design, setting of the study, the subjects (number and type), the treatment or intervention. The **results** include the salient outcome(s) of the study. The **conclusion**(s) state(s) the significant results of the study.

4. Main text: The text should be structured with the headings of **introduction, methods, results, and discussion** for original articles, and of **introduction, case report, discussion and conclusion** for case report. Review articles should have heading appropriate for the article.

The **introduction** should state clearly the objective(s) and rationale for the study and cite only the most pertinent references as background. The **methods** should include study design, subjects with inclusion and exclusion criteria, material, methods and procedures utilized with enough details for the study to be repeated, sample size calculation, and the statistical software and methods employed. The **results** should describe the study sample and data analyses to answer the objectives. There should be no more than 5-7 figures and tables (total) per manuscript. For the table, only horizontal lines above and below the heading and at the bottom of the table are made without any column line. The figures used should be original, any modification from other sources should be clearly indicated and state the site of the origin with written permission. If any photographs of the patients are used, they should not be identifiable or the photographs should be accompanied by written permission to use them. The **discussion** should briefly summarize or emphasize the main findings, interpret or explain their findings in comparison with other reports, state any limitation of the study, describe an impact on healthcare if any, and comment on the potential for future research.

5. Conflict of interest: the authors should declare the conflict of interest in the cover letter.

6. Acknowledgments: the authors should include only those who have made a valuable contribution to the work presented but who do not qualify as authors. This may include an involved patient population and any grant support.

7. References: state the references consecutively in the order in which they are first mentioned in the text. Use arabic numerals in superscription without parenthesis for reference in the text. Unpublished data and personal communications is not allowed. Published abstracts can be used as numbers references; however, reference to the complete published article is preferred. The references should be upto- date in that subject and be no more than 30 references for original articles. The 'Vancouver style' of references must be applied. List all authors when there are 6 or fewer, and list the first 6 and add 'et al' when there are 7 or more authors. Please refer to further detail of the reference format in the NEJM or official website of our journal.

Examples:

Journals

Tangjitgamol S, Hanprasertpong J, Manusirivithaya S, Wootipoom V, Thavaramara T, Buhachat R. Malignant ovarian germ cell tumors: clinico-pathological presentation and survival outcomes. Acta Obstet Gynecol Scand. 2010; 89: 182-9.

Books

Straus SE, Richardson WS, Glasziou P, Haynes RB. Evidence based medicine: how to practice and teach EBM. 3rd ed. Edinburgh: Churchill Livingstone; 2005. p.10-5.

Chapter in Books

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p.93-113.

Published proceedings paper

Berger H, Klemm M. Clinical signs of gastric ulcers and its relation to incidence [abstract]. In: Chuit P, Kuffer A, Montavon S, editors. 8th Congress on Equine Medicine and Surgery; 2003 Dec 16-18; Geneva, Switzerland. Ithaca (NY): International Veterinary Information Service (IVIS); 2003. p. 45.

Electronic journals/data

International Committee of Medical Journal Editors. Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals [Internet]. 2014 [updated 2014 Dec 1; cited 2015 Jan 30] Available from: http://www.icmje.org/icmje-recommendations.pdf.

Thesis

Liu-Ambrose TY. Studies of fall risk and bone morphology in older women with low bone mass [dissertation]. [Vancouver (BC)]: University of British Columbia; 2004. 290 p.

Manuscript revision

All comments or queries returned to the authors for a revision or clarification should be thoroughly addressed or revised accordingly. The revised manuscript must be underlined or highlighted for the changes, and re-submitted, preferably, within four weeks to prevent a delay of a final decision. A maximum of 12 weeks is allowed for a revision or the editorial board will take the right to withdraw the manuscript from the submission system. The original manuscript must be returned along with the printed and electronic revised version. An accompanying summarized letter of revision point by point may expedite the re-review.

วชิรเวชสาร
และวารสารเวชศาสตร์เขตเมือง
Vajira Medical Journal:
Journal of Urban Medicine

ปีที่ 64 ฉบับที่ 4 กรกฎาคม - สิงหาคม พ.ศ. 2563 Vol. 64 No. 4 July - August 2020

สารบัญ

หน้า

นิพนธ์ต้นฉบับ (Original Articles)

วชิรเวชสาร
และวารสารเวชศาสตร์เขตเมือง
Vajira Medical Journal:
Journal of Urban Medicine

ปีที่ 64 ฉบับที่ 4 กรกฎาคม - สิงหาคม พ.ศ. 2563 Vol. 64 No. 4 July - August 2020

สารบัญ

หน้า

An Educational Video Intervention to Increase Advance Care Planning in A Geriatric Clinic: A Randomized Controlled Trial

Basmon Manomaipiboon, MD[1*]
Surin Assawawitoontip, MD[1]
Sudsri Kokaewichain, MD[1]
Bhorn-ake Manasvanich, MD[1]

[1] King Chulalongkorn Memorial Hospital, The Thai Red Cross society, Bangkok, Thailand

* Corresponding author, e-mail address : basmon@nmu.ac.th

Vajira Med J. 2020; 64(4) : 235-42
http://dx.doi.org/10.14456/vmj.2020.23

Abstract

Introduction: Advance care planning should ideally be discussed with every geriatric patient in the ambulatory settings. However, only a small percentage of geriatric patients have had the discussion with their providers. We hypothesized that an educational video intervention would better promote interest compared to verbal advice alone.

Objectives: To compare the levels of interest in advance care planning between the educational video interventional group and the control group at the geriatric clinic.

Methods: Older adults aged 60 years and older who visited the clinic between November and December 2018 were enrolled and randomized into 2 groups. The intervention group was shown an 8-min video with verbal advice while the control group received standardized verbal advice. Participants were administered a Likert scale questionnaire after the intervention. The primary outcome was the proportion of participants who expressed interests in completing an advance directive.

Results: Of the 110 enrolled participants [55 in intervention group and 55 in controls: mean age was 67 years, and most of them were female (83%)]. There was no difference in the baseline characteristics between the two groups including age, sex, education, marital status, income, and health status. Ninety eight percent of the participants in video group expressed interests to complete an advance care plan, whereas only 67% of the control group did (P<0.001).

Conclusion: An educational video significantly increased awareness and interests among geriatric clinic patients compared to verbal education alone.

Keywords: elderly, geriatric care, advance care planning, advance directive, video support tool

การใช้สื่อวีดีทัศน์เพื่อเพิ่มการทำหนังสือแสดงเจตนาไม่ประสงค์จะรับบริการสาธารณสุขที่เป็นไปเพียงเพื่อยืดการตายในวาระสุดท้ายของชีวิต หรือเพื่อยุติการทรมานจากการเจ็บปวด ณ คลินิกผู้สูงวัย สุขภาพดีโรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย : การศึกษาเชิงทดลองเปรียบเทียบระหว่างกลุ่มที่ใช้สื่อวีดีทัศน์และกลุ่มที่ได้รับคำแนะนำตามปกติ

บาศมน มโนมัยพิบูลย์ พบ.[1*]
สุรินทร์ อัศววิทูรทิพย์ พบ.[1]
สุทธ์ศรี กอแก้ววิเชียร พบ.[1]
ภรเอก มนัสวานิช พบ.[1]

[1] โรงพยาบาลจุฬาลงกรณ์, สภากาชาดไทย, กรุงเทพมหานคร, ประเทศไทย

* ผู้ติดต่อ, อีเมล: basmon@nmu.ac.th

Vajira Med J. 2020; 64(4) : 235-42
http://dx.doi.org/10.14456/vmj.2020.23

บทคัดย่อ

หลักการและเหตุผล: หนังสือแสดงเจตนาไม่ประสงค์จะรับบริการสาธารณสุขที่เป็นไปเพียงเพื่อยืดการตายในวาระสุดท้ายของชีวิต หรือเพื่อยุติการทรมานจากการเจ็บปวดเป็นเรื่องที่ผู้สูงอายุควรได้รับการให้คำแนะนำตามมาตรฐานการรักษาเพื่อเข้าใจถึงสิทธิในการเลือกวิธีการดูแลรักษาตนเองเมื่อไม่มีสติสัมปชัญญะเพียงพอในการตัดสินใจและแนวทางการรักษาเมื่อเข้าสู่วาระสุดท้ายของชีวิต ในการดูแลทั่วไปมีอุปสรรคหลายอย่างทำให้ผู้สูงอายุที่เข้ารับบริการไม่ได้รับคำแนะนำตามที่ควรได้รับ

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบสัดส่วนของผู้สนใจทำหนังสือแสดงเจตนาฯระหว่างกลุ่มอาสาสมัครที่ได้ดูวีดีทัศน์แนะนำแนวทางการรักษาเมื่อเข้าสู่วาระสุดท้ายของชีวิต และกลุ่มอาสาสมัครที่ได้รับการให้คำปรึกษาตามปกติในผู้เข้ารับบริการคลินิกผู้สูงวัย

วิธีดำเนินการวิจัย: ผู้สูงอายุที่มีอายุตั้งแต่ 60 ปีขึ้นไป ที่ได้เข้ารับบริการในคลินิกผู้สูงวัยสุขภาพดีในระหว่างเดือนพฤศจิกายน ถึง เดือนธันวาคม พ.ศ. 2561 ที่ได้เข้าร่วมโครงการวิจัยจะถูกแบ่งออกเป็น 2 กลุ่ม กลุ่มที่ได้รับการดูวีดีทัศน์จะได้รับชมวีดีทัศน์ความยาว 8 นาที และได้รับการให้คำแนะนำ ในขณะที่กลุ่มควบคุมจะได้รับการให้คำแนะนำตามมาตรฐาน หลังจากได้รับการให้ข้อมูลทั้งสองกลุ่มจะได้รับการประเมินความสนใจด้วยแบบประเมิน Likert scale วัตถุประสงค์หลักเพื่อดูอัตราส่วนความสนใจในการทำหนังสือแสดงเจตนาฯ

ผลการศึกษา: ผู้สูงอายุที่เข้าร่วมการศึกษามีจำนวน 110 คน แบ่งเป็นกลุ่มที่ได้รับการให้คำแนะนำตามปกติ 55 คน (ร้อยละ 50) และกลุ่มที่ได้รับการดูวีดีโอแนะนำ 55 คน (ร้อยละ 50) พบว่าหลังได้รับคำแนะนำกลุ่มที่ได้รับการดูวีดีโอมีความสนใจในการทำหนังสือแสดงเจตนาฯ คิดเป็น 98% และกลุ่มที่ได้รับคำแนะนำตามปกติสนใจทำหนังสือแสดงเจตนาฯ คิดเป็น 67% ซึ่งกลุ่มที่ได้รับการดูวีดีทัศน์มีความสนใจในการทำหนังสือแสดงเจตนาฯ มากกว่ากลุ่มได้รับคำแนะนำตามปกติอย่างมีนัยสำคัญทางสถิติ (อัตราส่วนออด 33.35, 95% ช่วงความเชื่อมั่นที่ร้อยละ 4.33 to 4.69, P<0.05)

สรุป: กลุ่มที่ได้รับการดูวีดีโอมีความสนใจทำหนังสือแสดงเจตนาฯมากกว่ากลุ่มที่ได้รับคำแนะนำตามปกติ ในระยะเวลารับคำแนะนำที่เท่ากัน

คำสำคัญ: ผู้สูงอายุ, พินัยกรรมชีวิต, หนังสือแสดงเจตนาฯ, การให้คำแนะนำ, วีดีโอ

Introduction

The number of older persons is highly increasing globally[1]. Thailand has entered to aging society since 2014 and is predicted to become aged society in this coming future[2]. The important key to serve the elderly is to respect their autonomy even in the end of life[3-4]. Advance directive (AD) is introduced to protect patients' preferences by documented the goals of care before facing the serious health event[6-8]. Advance directive has strong potential benefits in helping medical providers and the family to choose the right way to treat the patient as they wish[5-6].

In Thailand, Patient Self-Determinant Act of 2007 were endorsed the advance care plan and advance directive for all population to decide their own option. Still, end of life care is limit to discuss when patients were already in the emergency stage or at the end of life, and only small number of people know their right to complete advance directive[9-10]. Guidelines for elderly care also suggest the Advance directive during the routine health visit. There still have several limitations such as limitation of time, limitation health care providers, and uncomfortable feeling to discuss the topic[11-13].

Educational visual media is an innovative solution to reduce the barriers and better communication in complex health information[14-16]. The previous study shown the benefit on completing advance care planning about cardiopulmonary resuscitation in progressive pancreas and hepatobiliary cancer patients[16]. We hypothesized that an educational video intervention would better promote interest in Advance Directive compare to verbal communication alone. This randomized controlled trial was done in a comprehensive geriatric clinic.

Methods

Participants were recruited from a comprehensive geriatric clinic in King Chulalongkorn Memorial hospital, The Thai Red Cross Society, Bangkok, Thailand. Recruitment occurred during 1st November 2018 to 31st December 2018. The inclusion criteria were age 60-year-old and older, capable to communicate in Thai and absence of cognitive impairment based on mini-mental standard examination (MMSE) score of ≥24. The exclusion criteria were history of psychiatric problems or neurologic problems. All the participants were informed and obtained the inform consent. A total of 110 participants were enrolled.

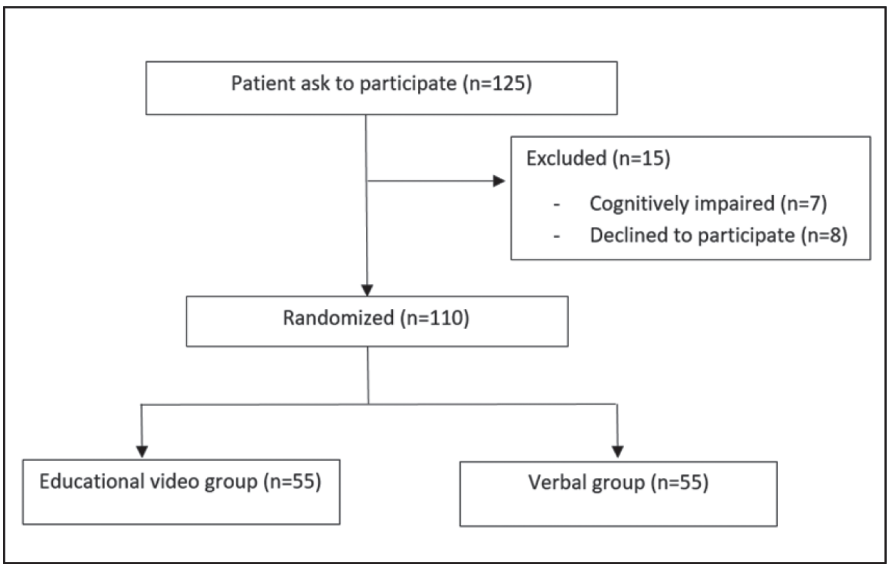

Figure 1: Flow diagram of the study

The participants were randomized into two groups by simple randomization computed by a member of research team. The intervention group watched the educational video before verbal advice and the control group received only standardized verbal communication advice. The educational video was an 8-minute movie consist of a story about *an 80-year-old male patient was in a wheelchair with their family and then was fainted. The man was transferred to an emergency room and was found cardiac arrest. The emergency doctor tried to resuscitate by 30-minute cardiopulmonary resuscitation, endotracheal tube insertion through the cardiac arrest guideline but the patient did not response with the treatment. The doctor talked to his family about the prognosis and treatment option, but the family were too confused to decide anything for this unexpected situation.* The video presented the information about cardiopulmonary resuscitation, endotracheal tube insertion, nasogastric tube insertion, intravenous fluid supplement and also the role of advance directive whereas the standardized verbal communication described the information regard all of those procedure and the role of advance directive. Before filming, we obtained consent from the patient and his family to film the patient and to use the video for research. The video was approved in terms of both standard care and ethical issue by three medical staffs from department of palliative, department of internal medicine and department of family medicine.

The participants were interviewed with blinded research assistant by two questionnaires. Eight-item question for demographic data consisted of age, sex, marital status, education, religion, medical condition, income, and health satisfaction. Three-section for the advance directive data consisted of experience in advance directive, the interest in completing advance directive and the level of interest (five-point likert scale). The member of the research team, who was not blinded to the randomization group, used the demographic data questionnaires to interview participants then participants were received information follow the group randomization. The advance directive questionnaire was collected after receiving the verbal communication or watching the educational video.

The primary outcome was to compare the interest in completing advance directive between the educational video intervention group and standardized verbal communication group (control). The secondary outcome was to find the association between participants factor and the interest in completing advance directive.

Statistical analysis was done by SPSS software version 22. Categorical variable of descriptive data was calculated in percent and compared using Pearson Chi-square. Continuous of descriptive data was calculated in mean (SD). The association factors were calculated in binary logistic regression. The level of interest was calculated in minimum to maximum and median.

Results

Among the 110 participants, baseline characteristic including age, sex, marital status, education, income, health satisfaction, previously known about advance directive and previously completing advance directive were similar between the two groups (P>0.05). (Table 1)

After received the intervention, the video group had greater likelihood of interest in completing advance directive more than the verbal group (OR = 33.35, 95% confident interval 4.33 to 4.69, P=0.001) (Table 2). The level of interest was significantly increase in video group (min to max 3-5, median 5) compare to verbal group (min to max 0-5, median 3). (Table 3)

The association between participants' factor (sex, marital status, education, income, and self-reported health satisfaction) and the interest in completing advance directive had no impact in each factor. (Table 4)

Table 1:

Baseline characteristic of participants

Parameter	Count (%)		p-value
	video intervention group (n = 55)	Control group (n = 55)	
Mean age ± SD	68 ± 5	67 ± 5	0.759
Sex			
Male	7(12)	12(21)	0.207
Female	48(87)	43(78)	
Status			
Single	23(42)	15(27)	0.128
Married	22(40)	22(41)	
Divorced	1(2)	6(11)	
Widowed	10(16)	18(21)	
Education			
Elementary	7(13)	9(16)	0.657
High school	6(11)	3(6)	
College	9(16)	7(13)	
Postgraduate	33(60)	36(65)	
Religion			
Buddhism	55(100%)	55(100%)	-
Income (Bath/month)			
<10,000	24(44)	18(33)	0.657
10,000 - 20,000	8(14)	9(16)	
20,000 - 50,000	22(40)	22(40)	
50,000 - 100,000	1(2)	4(7)	
>100,000	0	2(4)	
Self-reported health satisfaction			
Excellent	3(5)	6(11)	0.616
Very good	22(40)	17(31)	
Good	27(49)	26(47)	
Fair	2(4)	4(8)	
Poor	1(2)	2(4)	

Table 2:

The interest in completing AD after receiving the educational video or verbal counseling

Intervention	Interest in completing AD (%)	Not interest in completing AD (%)	OR (95%CI)	P-value
Educational video intervention group	54(98)	1(2)	33.35	0.001
Control group	34(67)	21(33)	(4.33 to 4.69)	

Table 3:

The level of interest between two groups

Intervention	Level of interest (likert scale) Min to max	Median
Educational video intervention group	3-5	5
Control group	0-5	3

Table 4:

Association between participants' factor and interest in completing advance directive

Variables	Interest in completing AD (%)	No interest in completing AD (%)	OR (95%CI)	P-value
Sex				
Male	13(15)	4(24)	1.712	1.712
Female	76(85)	13(76)	(0.49 to 5.98)	
Status				
Single	34(38)	3(18)	1.589	0.429
Married	35(39)	8(47)	(0.48 to 1.36)	
Widowed	20(23)	6(35)		
Education				
Elementary	10(11)	2(12)	1.305	0.909
High school	6(7)	3(18)	(0.95 to 1.77)	
College	15(17)	1(6)		
Postgraduate	58(65)	11(65)		
Income				
<10,000	34(38)	6(35)	1.09	0.744
10,000 - 20,000	13(15)	3(18)	(0.64 to 1.87)	
20,000 - 50,000	35(39)	8(47)		
50,000 - 100,000	5(6)	0		
>100,000	2(2)	0		
Self-reported health satisfaction				
Excellent	8(9)	1(6)	1.584	0.191
Very good	33(37)	6(35)	(0.79 to 3.16)	
Good	43(48)	9(53)		
Fair	3(3)	1(6)		
Poor	2(2)	0		

Discussion

In Educational video, with the emergency care story were presented to stimulate participants' interest. Then the story informed about the procedures to resuscitate patients and the important role of advance directive to protect patient's preference and to help their family to decide the proper way of treatment. Viewing the video both improve patients' interest and knowledge of end of life care.

The study showed the significantly increase of the interest in completing advance care plan after watching the video (OR = 33.35, 95% confident interval 4.33 to 4.69, P=0.001) and the level of interest was also higher in the video educational group similar to other randomized controlled trial[15-16].

The associated factors had no effect on the interest in completing advance directive. This result was different from the previous published data[17-18] showing that educational level was associated with the higher number of completing advance directive. Participants received over 12-year of education had significantly complete the advance directive. The study was conducted in multiple nursing home and long-term service and support setting with higher number of participants. The participants were from one setting and the number of participants were small. This study has few limitations. First, the educational video can be manipulated to favor the participants' perspective. Second, the participants were all Buddhists. So, our finding might not be generalizable to other groups (such as Christians and Muslims). Third, our study did not compare the functional status and activities daily living.

In summary, elderly patients often face the complex decision-making, and the family have to make unprepared options for stressful emergency situations[19]. Patient and Family should be informed about their planned option, their goals of care, and their preferences during a routine health assessment. Educating the patients by using the video provide more concrete context compared to verbal communication alone and increase the level of the interest. Future studies could extend the completion of advance directive, the patients' preferences, and the effectiveness of advance directive. The study has shown that educational video enhances the interest level, this can be implemented in the ambulatory care setting for educate elderly patients visiting any clinic.

Conflict of interest

The authors declare that there are no conflict of interests.

Acknowledgement and Funding

This study was supported by self fund.

Ethical consideration

Ethic approval was obtained from Institutional review board, faculty of medicine, Chulalongkorn University (COA No. 1011/2018, IRB No. from all participants 404/61). Informed, written consent was obtained.

References

1. World health organization. Department of aging and life course. Integrated care for older people. Guidelines on community-level interventions to manage declines in intrinsic capacity: Geveva. 2017.
2. National Statistical Office Ministry of Digital Economy and Society. The survey of elderly population in Thailand 2017. Bangkok: Text and journal publication; 2017.
3. Emanuel L, Barry MJ, Stoeckle JD, Ettelson LM, Emanuel EJ. Advance directives for medical care—a case for greater use. N Engl J Med. 1991;324(13):889–95.
4. Kohn M, Menon G. Life prolongation: views of elderly outpatients and health care professionals. J Am Geriatr Soc. 1988;36(9):840–44.
5. Gamble ER, McDonald PJ, Lichstein PR. Knowledge, attitudes, and behavior of elderly persons regarding living wills. Arch Intern Med. 1991;151(2):277–80.
6. Emanuel LL, Danis M, Pearlman RA, Singer PA. Advance care planning as a process: structuring the discussions in practice. J Am Geriatr Soc. 1995;43(4):440–46.

7. Sudore RL, Fried TR. Redefining the "planning" in advance care planning: preparing for end-of-life decision making. Ann Intern Med. 2010; 153(4): 256-61.
8. Connors AF, Dawson NV, Desbiens NA, et al. A Controlled Trial to Improve Care for Seriously Ill Hospitalized Patients: The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT). JAMA 1995; 274(20):1591–98.
9. Ting FH, Mok E. Advance directives and life-sustaining treatment: attitudes of Hong Kong Chinese elders with chronic disease. Hong Kong Med J. 2011;17(2):105-11.
10. Doukas DJ, Hardwig J. Using the family covenant in planning end-of-life care: obligations and promises of patients, families, and physicians. *J Am Geriatr Soc*. 2003; 51(8): 1155-58.
11. Ramsaroop SD, Reid MC, Adelman RD. Completing an advance directive in the primary care setting: what do we need for success. *J Am Geriatr Soc*. 2007; 55(2): 277-83.
12. Morrison RS, Morrison EW, Glickman DF. Physician reluctance to discuss advance directives: an empiric investigation of potential barriers. Arch Intern Med. 1994;154(20):2311–18.
13. Silveira MJ, Kim SY, Langa KM. Advanced directives and outcomes of surrogate decision making before death. N Engl J Med 2010; 362(13):1211-18.
14. Detering KM, Hancock AD, Reade MCSilvester W. The impact of advance care planning on end of life care in elderly patients: randomised controlled trial. BMJ. 2010;340:345.
15. Volandes AE, Paasche-Orlow MK, Barry MJ, Gillick MR, Minaker KLChang Y, et al. Video decision support tool for advance care planning in dementia: randomised controlled trial. BMJ. 2009;338:b2159.
16. Epstein AS, Volandes AE, Chen LY, Gary KA, Li YAgre P, et al. A randomized controlled trial of a cardiopulmonary resuscitation video in advance care planning for progressive pancreas and hepatobiliary cancer patients. J Palliat Med. 2013;16(6):623-31.
17. Hirschman KB, Abbott KM, Hanlon AL, Prvu Bettger JNaylor MD. What factors are associated with having an advance directive among older adults new to long-term care services? J Am Med Dir Assoc. 2012; 13(1): 827–38.
18. Alano GJ, Pekmezaris R, Tai JY, Hussain MJ, Jeune JLouis B, et al. Factors influencing older adults to complete advance directives. Palliat Support Care. 2010;8(3):267-75.
19. Garrett JM, Harris RP, Norburn JK, Patrick DLDanis M. Life-sustaining treatments during terminal illness: who wants what. J Gen Intern Med. 1993;8(7):361-68.

Effects of I-Walk Training on Gait Performances in Patients with Chronic Stroke

Nathamon Pansuksawat, B.Sc.[1]

Pinailug Tantilipikorn Earde, Ph.D.[1]

Patcharee Kooncumchoo, Ph.D.[1]

Bunyong Rungroungdouyboon, Ph.D.[2]

Noppol Pramodhyakul, Ph.D.[1*]

[1] Department of Physical Therapy, Faculty of Allied Health Sciences, Thammasat University, Pathumthani, Thailand

2 Excellent center in creative engineering design and development, Department of Mechanical Engineering, Faculty of Engineering, Thammasat University, Pathumthani, Thailand

* Corresponding author, e-mail address : Noppol.p@allied.tu.ac.th

Vajira Med J. 2020; 64(4) : 243-54

http://dx.doi.org/10.14456/vmj.2020.24

Abstract

Objective: To determine the effects of I-Walk (Robotic-assisted gait device) training compared with over-ground walking training on motor impairments assessed by lower extremity scores, lower extremity angles during walking, and gait performances in patients with chronic stroke.

Methods: A single blinded randomized controlled trial was conducted. Twenty four chronic stroke patients were randomly assigned into two groups; experimental group (n=12) and control group (n=12). For gait performances, patients in an experimental group received I-Walk training, while those in a control group received over-ground walking training. The duration of training was 60 min per day, 3 days per week for 8 weeks. The outcome measures included motor impairments assessed by the Fugl-Meyer Assessment of Lower Extremity (FMA-LE) scores, lower extremity angles during walking (hips, knees, ankles), and gait performances (step length, cadence, walking speed, stride length, and step length symmetry ratio). All variables were measured before and after the training period.

Results: There was a statistically significant difference in motor impairments assessed by the FMA-LE scores, lower extremity angles during walking on hips and knees, as well as gait performances, including step length, cadence, and walking speed, between the experimental and the control groups ($p<0.05$). In particular, the statistically significant changes were demonstrated in motor impairments assessed by the FMA-LE scores, lower extremity angles during walking on hips, knees, and ankles, as well as gait performances, including step length, cadence, walking speed, stride length, and step length symmetry ratio, before and after the I-Walk training in the experimental group ($p<0.05$).

Conclusions: The I-Walking training could yield a statistically significant improvement of motor impairments assessed by FMA-LE scores, lower extremity angles during walking, and gait performances in chronic stroke patients. Nonetheless, further studies are recommended to elucidate and ratify the effective outcomes in patients with other stages of stroke, different ranges of lower extremity, and various spatiotemporal parameters.

Keywords: Gait training, Hemiplegia, Physical therapy, Robotic, Task-specific training

ผลของการฝึกด้วยเครื่องไอ-วอล์คต่อสมรรถนะของการเดินในผู้ป่วยโรคหลอดเลือดสมองระยะเรื้อรัง

ณฐมน ปั้นศุขสวัสดิ์ วท.บ.[1]
พินัยลัค ตันติลีปิกร เอิร์ด ปร.ด.[1]
พัชรี คุณค้ำชู ปร.ด.[1]
บรรยงค์ รุ่งเรืองด้วยบุญ ปร.ด.[2]
นพพล ประโมทยกุล ปร.ด.[1*]

[1] ภาควิชากายภาพบำบัด คณะสหเวชศาสตร์ มหาวิทยาลัยธรรมศาสตร์ ปทุมธานี ประเทศไทย

[2] ศูนย์ความเป็นเลิศทางวิชาการด้านการออกแบบและพัฒนาต้นแบบทางวิศวกรรมอย่างสร้างสรรค์ ภาควิชาวิศวกรรมเครื่องกล คณะวิศวกรรมศาสตร์ มหาวิทยาลัยธรรมศาสตร์ ปทุมธานี ประเทศไทย

* ผู้ติดต่อ, อีเมล: Noppol.p@allied.tu.ac.th

Vajira Med J. 2020; 64(4) : 243-54
http://dx.doi.org/10.14456/vmj.2020.24

บทคัดย่อ

วัตถุประสงค์: เพื่อเปรียบเทียบผลของการฝึกด้วยเครื่องไอ-วอล์ค (หุ่นยนต์ฝึกเดิน) และการฝึกเดินบนพื้นราบต่อการทำงานของขา, มุมการเคลื่อนไหวของขาขณะเดิน และสมรรถนะของการเดินในผู้ป่วยโรคหลอดเลือดสมองระยะเรื้อรัง

วิธีดำเนินการวิจัย: เป็นการทดลองแบบสุ่มและมีกลุ่มควบคุม ผู้ป่วยโรคหลอดเลือดสมองระยะเรื้อรังจำนวน 24 คน ได้รับการสุ่มแบ่งกลุ่มเป็น 2 กลุ่มคือ กลุ่มทดลอง (n =12) และกลุ่มควบคุม (n=12) สำหรับการฝึกเดิน กลุ่มทดลองจะได้รับการฝึกด้วยเครื่องไอ-วอล์ค ในขณะที่กลุ่มควบคุมจะได้รับการฝึกเดินบนพื้นราบ ระยะเวลาในการฝึก 60 นาทีต่อวัน 3 วันต่อสัปดาห์ เป็นเวลา 8 สัปดาห์ โดยทำการวัดผลการทำงานของขาด้วยแบบประเมิน Fugl-Meyer Assessment of Lower extremity (FMA-LE), มุมการเคลื่อนไหวของขาขณะเดิน และสมรรถนะของการเดินใน โดยทำการวัดค่าตัวแปรเหล่านี้ก่อนการฝึกและหลังการฝึก

ผลการวิจัย: มีความแตกต่างอย่างมีนัยสำคัญทาสถิติของการทำงานของขา มุมการเคลื่อนไหวข้อสะโพก ข้อเข่า ระยะก้าวขา ความถี่ในการก้าวขา ความเร็วในการเดิน เมื่อเปรียบเทียบระหว่างกลุ่มทดลองและกลุ่มควบคุม ($p<0.05$) และพบว่าคะแนนของ FMA-LE และความสมมาตรของการก้าวขา มีการเปลี่ยนแปลงอย่างมีนัยสำคัญทางสถิติ เมื่อเปรียบเทียบก่อนและหลังการฝึกในกลุ่มทดลอง ($p<0.05$)

สรุป: การฝึกด้วยเครื่องไอ-วอล์ค สามารถเพิ่มการทำงานของขา, มุมการเคลื่อนไหวของขาขณะเดิน และสมรรถนะของการเดินในผู้ป่วยโรคหลอดเลือดสมองระยะเรื้อรังได้ อย่างไรก็ตามในอนาคตคณะผู้วิจัยแนะนำว่าควรมีการศึกษาในผู้ป่วยโรคหลอดเลือดสมองระยะอื่น, ระดับความรุนแรงของขาที่แตกต่างกัน รวมถึงศึกษาในตัวแปร spatiotemporal เพื่อให้เกิดความชัดเจนและช่วยยืนยันผลการศึกษาที่พบได้ดียิ่งขึ้น

คำสำคัญ: การฝึกเดิน, อัมพาตครึ่งซีก, กายภาพบำบัด, หุ่นยนต์, การฝึกแบบ Task-specific training

Introduction

Stroke is a major cause of various impairments in the patients, for example muscle weakness, sensory impairment, poor balance and spasticity [1]. These impairments affect the control of movement of one side of the body that limit ability to perform activities of daily living [2].

Walking is the one of the most common movement problem in patients with chronic stroke [3]. The capacity of walking in a community is required, for example : the ability of walking at speeds to crossing the street, stepping on and off a moving footpath, walking through the doors, walking around furniture, obstacle crossing [4]. Therefore, gait recovery is a major goal in physical therapy rehabilitation for patients with chronic stroke [5].

In the last decade, physical therapy has focused on using robotic-assisted gait device[6]. Goals of the robotic assisted gait a training are to control movement and to design training for rehabilitation exercise that will induce neural plasticity changes associated with task-specific training (active assisting, challenge-based, stimulating normal task) and improving motor recovery[7]. Hesse and colleagues in 2013 concluded that robotic assisted gait training resulted in restoring and improving gait in patients with subacute and chronic stroke. They found significant larger increments in walking speed, walking distance after using robotic assisted gait device than usual physical therapy treatment [8]. Moreover, robotic assisted gait training could improve walking ability in patients with stroke. However, the robotic assisted gait training device in Thailand are still limited due to the high price. Therefore these devices are available only in some medical centers or hospitals.

In Thailand, I-Walk is a new device that designed from the robotic assisted gait training, end-effector type for patients with stroke. I-Walk is less costly. The device is consisted of two systems, body weight support system and gait training system. I-Walk training is more repetitive gait pattern of complex gait cycles than overground walking training. However, Implementations of the I-Walk in stroke individuals to improve gait performance are limited due to the lack of research study. Therefore, the aim of this study was to investigate the effect of I-Walk training to improve motor impairments, lower extremity angles during walking and gait performances in patients with chronic stroke.

Methods

Design

The study design in this research was experimental single-blind randomized controlled trial comparing the effect of I-Walk gait training and overground walking training on gait performances in participants with chronic stroke.

Participants

The experimental protocol was set up at Physical therapy and Hydrotherapy center, Faculty of Allied Health Sciences, Thammasat University and at Bueng Yitho Medical and Rehabilitation Center, Pathumthani, Thailand. The protocol of this study was approved by the Ethics Review Sub-Committee for Research Involving Human Research Subjects of Thammasat University.

Inclusion criteria

1. The participants were inpatients who got stroke attack onset more than six months.
2. Age between 45 and 70 years.
3. Able to walk at least 10 m. with or without walking device.

Exclusion criteria

1. The patients were excluded if they had unstable vital signs.
2. Any symptoms and signs that may affect their participation such as neurogenic pain and pain scale on a visual analog scale more than 5 out of 10.
3. Other neurological or medical disorder that can attribute negative impact on ambulatory ability.

Sample size

The researcher set a confidence level at 95 % and the power of test at 80 %. The $Z_{\alpha/2}$ is 1.96 and the Z_{β} is 0.84. The σ^2 is 0.015 and Δ^2 is 0.01 was derived from the pilot study which was conducted in 20 participants (10 participants/group). With the additional number of 20% drop out, the number of participants in each group was 12 participants.

Description of the outcome measures

The assessor of the study was a physical therapist who had a clinical experience in stroke rehabilitation more than 3 years.

The Fugl-Meyer Assessment of Lower Extremity (FMA-LE)

The FMA-LE reflects a motor recovery in post-stroke. The FMA-LE consisted of lower extremity, co-ordination/speed, and motor function. The motor function scores used to measure lower extremity recovery in stroke patients. The FMA-LE reflects a motor recovery in post stroke. The original scale, consisted of six domains (lower extremity, co-ordination/ speed, motor function, sensation, joint mobility and pain) and scoring is done on 3 ordinal scale ranges from 0 to 2. The lower extremity tested for the reflex activity (flexors and extensors), flexor synergy (hip flexion, knee flexion and dorsiflexion), extensor synergy (hip extension, adduction, knee extension, and plantar flexion), and lower extremity movement combining synergies in sitting and standing position. The scale of lower extremity has 14 items. The score range from 0 to 28. The co-ordination/speed of heel to opposite knee (tremor, dysmetria and speed). The scale of co-ordination/speed has 3 items. The score range from 0 to 6. The FMA-LE, motor function, used to measure lower extremity recovery in stroke patients. The scale has 17 items from the sum of lower extremity and co-ordination/speed. The total score range from 0 (no motor function) to 34 (good motor recovery). FMA-LE, sensation, the scale has 6 items, two for light touch and four for position sense. The patient is asked whether who feels that light touches on leg and the feet. The total score ranges from 0 to 12. FMA-LE, joint motion and pain, the scale has 20 items, ten for joint motion and ten for joint pain. The patient is asked whether who feels that passive joint motion and pain that pain during or at the end of movement on leg and the feet. The total score ranges from 0 to 20 of each.

Lower extremity angles during walking

Prior to the gait analytic test, participants were wearing the body's most compact and black clothing. Then, the markers were attached at anatomical references consisted of acromion process of the scapular, greater trochanter, knee joint line, lateral malleolus, and fifth metatarsal. Participants were assessed their lower extremity angles during walking and gait performance using the Kinovea Software Version 0.8[9]. Participants were recorded for their walking ability using a digital camera with a frame rate of 60 Hz.[10]. Prior to the test, the video recording system was positioned perpendicular to the walkway, at approximately 4 m. from the walkway to capture 4 m. section in the middle of the walkway. An angular of lower extremities was analyzed at heel strike, mid stance, toe-off, push off, and mid-swing of gait cycle[9]. Hip angle was measured at the intercept between the line from the acromion process to the greater trochanter and the line from the greater trochanter to the lateral knee joint line. Knee angle was measured at the intercept between the line from the greater trochanter to the lateral knee joint and from the lateral knee joint to the lateral malleolus. Ankle angle was measured at the intercept between the line from the lateral knee joint to lateral malleolus and from the lateral malleolus to the fifth metatarsal. Three completed gait cycles were selected and parameters of complete gait cycle of each participant were averaged. Participants were assessed their walking performance while walking with preferred and fastest walking speed for 3 trials per condition. Then the average data of each speed were collected. The parameters were analyzed from the frames that best represent each gait phase with visible markers[11].

Gait performances

The step length was measured from the length as the distance between the heels of one foot to the other[10,12]. The stride length was measured from the total distance of the step length of the left and right leg[10,12]. The cadence was determined by the number of steps in the 4 m. moving range in the middle of the walkway[10]. Then the results were converted to a number of steps in 60 s.[10]. Walking speed was measured based on a distance of 4 m.

in the middle of the walkway[9-10]. The step length symmetry ratio was measured from the distance of the legs compared to the distance between the stepping of the paretic side and the non-paretic side. The ratio score that is closer to 1 indicates a more symmetrical gait[13].

Experimental protocol

Participants with stroke who meet the inclusion and exclusion criteria were randomized into experimental group (walking training with I-walk) or control group (walking training with conventional physical therapy) by a random number generator. On the first day, participants were interviewed and assessed for their baseline demographics, stroke characteristics. On the following days, they were trained in the program of allocated group. Participants in both groups received the usual physical therapy program before walking training program. The usual physical therapy program consists of upper extremity training (*grasping* and releasing balls, pinching tongs, using a spray bottle, kneading putty, pinching coins, using a spoon, lifting a heavy can, and wiping a table with a towel) for 15 min. and sit-to-stand training for 15 min. Prior to and after completing the program (24 sessions), participants were assessed lower limbs impairments by the FMA-LE and gait performances by hip angle, knee angle, ankle angle, step length, cadence, walking speed, stride length and step length symmetry ratio.

I-Walk gait training program (experimental group)

I-Walk gait training device consists of two systems: body weight support system and gait training system. The body weight support system consists of harness that used to support and prevent falling during the training. The gait training device represents by two-foot plates connected to a doubled plate. I-Walk generates a human like walking pattern. The end-effectors are represented by two foot plates connected to a double plate. The rear ends of the foot plates move forward and backward. The backward movement of the footplates simulates the stance phase while the forward movement simulates the swing phase. Based on task-specific repetitive training. The device helps initiate the repetitive forward gait motion. Cadence of device was set according to participants' average self-determined walking cadence over three trials before training[14]. The walking cadence can be selected from 0-120 steps per min. Prior to training; participants had to wear the harness of the safety system. The participants were encouraged to hold onto the handrails when they feel unstable (Figure 1). When participants could sustain the greater load in the lower paretic limb without help from the physical therapist. The greater load (I-walk cadence) of 10% of baseline was applied when the participants were able to straight the affected leg and increase weight bearing during the single-leg stance phase and move the affected leg during the swing phase without any compensations, fatigue or increased spasticity [15]. The I-Walking training period was 30 min.

Figure 1: A safety harness on the I-Walk trainer

Over-ground walking training program (control group)

Participants with stroke were allowed to use their walking devices as needed. Over-ground walking program was consisted of forward walking training for 10 minutes, sideway walking training for 10 minutes and obstacle walking training (obstacle height = 8 cm, width = 8 cm) for 10 minutes on the 10 m. walkway with self-selected walking speed. When participants could sustain the greater load in the lower paretic limb without help from the physical therapist without any compensation, fatigue and increased spasticity, the speed and distance of training were increased of their self-determined. The overground walking training period was 30 min.

Statistical analysis

Descriptive statistics were applied to explain the characteristics of the participants and findings of the study and SPSS version 11.5 was used for statistical analysis. The Two Way Mixed ANOVA was used to analyze the differences within the group and compare the differences between groups. The significance level was set at $p< 0.05$.

Results

Characteristics of the participants

Thirteen participants had a left-sided hemiparesis and eleven participants had a right-sided hemiparesis with the average 4.49 years post stroke (range 0.50-30.00, SD = 6.18). The characteristics are shown in Table 1. All baseline characteristics of either group were not significantly different across the groups ($p>0.05$).

Table 1:

Baseline characteristics of the participants

Variables	Experimental group (n=12)	Control group (n =12)
Mean age (years) (SD)	59.83 (6.53)	61.83 (7.24)
Mean height (m) (SD)	1.64 (0.06)	1.62 (0.80)
Mean weight (kg) (SD)	65.58 (8.29)	70.08 (14.37)
Mean BMI (kg/m^2) (SD)	24.38 (3.62)	27.02 (34.37)
Gender (Male:Female)	7 : 5	8 : 4
Mean post-onset time of stroke (years) (SD)	3.59 (2.82)	5.37 (8.37)
Pathology (Infarction:Hemorrhagic)	11 : 1	10 : 2
Affected side (Right:Left)	8 : 4	3 : 9
Mean MMSE (scores) (SD)	21.83 (3.12)	22.08 (3.28)
Mean MAS of lower limb (scores) (SD)	0.41 (0.67)	0.50 (0.52)
Assistive device (non use:use)	4 : 8	3 : 9

Note: BMI = Body Mass Index, MMSE = Mini Mental State Examination Thai version 2002, MAS = Modified Ashworth Scale.

Effects of the interventions

The improvement of lower extremity, co-ordination, motor function scores were statistically significant within the both groups ($p<0.05$). When comparing between groups, lower extremity and motor function scores of experimental group was significantly greater than control group ($p<0.05$) as shown in Table 2. The range of motion of lower extremity had a trend of increment in both groups after gait training. When comparing between groups, hip flexion and knee flexion during mid-swing of gait cycle in the experimental group was significantly greater than control group ($p<0.05$) as shown in Table 3**.** Participants in the I-walk training group had walked in a range of 1,120-1,200 steps per session while those in the over-ground walking training group had walked a range of 259-570 steps per session. After training, gait performance (walking speed, step length, stride length cadence and step symmetry ratio) in preferred and maximal walking speed test of experimental group was significantly improved ($p<0.05$). When comparing between groups, the improvement of step length, cadence and walking speed in the experimental group was significantly greater than those in the control group ($p < 0.05$) as shown in Table 4.

Table 2: The Fugl-Myer assessment of lower extremities before and after the training period

FMA-LE	Experimental group (n=12)			Control group (n=12)			Mean difference		
	Pre-test	Post-test	P-value [a]	Pre-test	Post-test	P-value [a]	Experimental group	Control group	P-value [a]
Mean scores of item E. Lower extremity (SD)	14.25 (3.81)	23.16 (2.88)	<0.001***	15.41 (5.28)	18.50 (4.01)	0.002**	8.91 (4.03)	3.09 (2.61)	0.003**
Mean scores of item F. Co-ordination (SD)	2.25 (1.21)	4.08 (1.37)	0.001**	3.16 (1.26)	3.75 (1.28)	0.012*	1.83 (1.34)	0.59 (0.67)	0.547
Mean scores of total E-F. Motor function (SD)	16.50 (4.05)	27.25 (3.84)	<0.001***	18.58 (6.31)	22.25 (5.04)	0.001**	10.75 (4.52)	3.67 (2.93)	0.012*

Note: [a] P-value from the Two-Way Mixed ANOVA with repeated measures. *Indicates significant difference, P-value <0.05; ** P-value <0.01; *** P-value <0.001.

Table 3:

Lower extremity angles during walking before and after the training period

Variables		Experimental group (n=12)			Control group (n=12)			Mean difference		
		Pre-test	Post-test	P-value [a]	Pre-test	Post-test	P-value [a]	Experimental group	Control group	P- value [a]
Mean degree of hip extension, Push off (SD)	Preferred	-0.88 (1.13)	5.22 (1.95)	0.003**	-2.50 (0.30)	0.30 (0.08)	0.127	6.10 (5.48)	2.80 (5.83)	0.288
	Maximal	0.50 (1.25)	6.83 (3.42)	0.001**	-0.50 (0.13)	1.69 (1.40)	0.233	6.33 (5.35)	2.19 (13.45)	0.323
Mean degree of hip flexion, Mid swing (SD)	Preferred	15.16 (6.03)	24.91 (8.19)	<0.001***	14.75 (5.22)	18.30 (5.14)	0.026*	9.75 (6.91)	3.55 (4.80)	0.027*
	Maximal	17.05 (7.65)	29.91 (8.36)	0.001**	17.38 (6.92)	21.44 (5.97)	0.045*	12.86(10.17)	4.06 (6.20)	0.009**
Mean degree of knee extension, Mid stance(SD)	Preferred	0.22 (5.42)	1.33 (1.67)	0.556	1.97 (2.03)	1.44 (1.66)	0.336	1.11 (1.33)	0.53 (1.82)	0.872
	Maximal	0.91 (5.23)	1.52 (2.23)	0.753	2.00 (2.99)	1.25 (2.18)	0.096	0.61 (1.56)	0.75 (1.43)	0.761
Mean degree of knee flexion, Mid swing (SD)	Preferred	22.11 (7.36)	34.97 (4.74)	<0.001***	23.30 (10.95)	28.91 (8.12)	0.023*	12.86(7.47)	5.61 (7.36)	0.036*
	Maximal	23.61 (9.43)	36.27 (5.83)	0.001**	25.83 (11.74)	30.16 (9.09)	0.021*	12.66(9.60)	4.33 (5.56)	0.063
Mean degree of dorsiflexion, Heel stride(SD)	Preferred	-30.72 (11.78)	-28.13 (11.58)	0.130	-27.05 (15.23)	-26.27(15.30)	0.323	2.59 (5.47)	0.78 (2.60)	0.740
	Maximal	-31.80 (9.71)	-29.25 (10.89)	0.093	-27.58 (15.99)	-28.08(16.04)	0.305	2.55 (4.81)	0.50 (1.61)	0.837
Mean degree of plantar flexion, Toe off (SD)	Preferred	37.30 (14.59)	33.63 (15.20)	0.012*	37.77 (10.13)	34.55(11.25)	0.331	3.67 (4.19)	3.22 (10.97)	0.611
	Maximal	32.86 (14.44)	38.22 (14.95)	0.018*	38.33 (9.02)	39.30 (9.79)	0.398	5.36 (6.70)	0.97 (10.94)	0.610
Mean degree of dorsiflexion, Mid swing (SD)	Preferred	-34.30 (19.18)	-27.34 (11.11)	0.072	-35.22 (12.80)	-26.47(15.43)	0.193	6.96 (12.13)	8.75 (21.83)	0.877
	Maximal	-35.42 (19.16)	-25.31 (10.99)	0.016*	-35.11(12.34)	-25.89(14.86)	0.161	10.11(12.29)	9.22 (21.24)	0.914

Note: [a] P-value from the Two-Way Mixed ANOVA with repeated measures. *Indicates significant difference, P-value <0.05; ** P-value <0.01; *** P-value <0.001.

Table 4:

Gait performances before and after the training period

Variables		Experimental group (n=12)			Control group (n=12)			Mean difference		
		Pre-test	Post-test	P-value [a]	Pre-test	Post-test	P-value [a]	Experimental group	Control group	P-value [a]
Mean step length of paretic side (m) (SD)	Preferred	0.35 (0.10)	0.45 (0.11)	<0.001***	0.33 (0.09)	0.36 (0.08)	0.007**	0.10 (0.07)	0.03 (0.03)	0.047*
	Maximal	0.38 (0.12)	0.47 (0.10)	0.004**	0.34 (0.10)	0.37 (0.10)	0.005**	0.09 (0.08)	0.03 (0.03)	0.024*
Mean step length of non-paretic side (m) (SD)	Preferred	0.28 (0.09)	0.33 (0.11)	0.001**	0.28 (0.11)	0.29(0.15)	0.009**	0.05 (0.03)	0.01(0.03)	0.038*
	Maximal	0.33 (0.11)	0.35 (0.11)	0.007**	0.29 (0.12)	0.33(0.13)	0.005**	0.02 (0.05)	0.04 (0.06)	0.046*
Mean cadence (step/min) (SD)	Preferred	63.05 (18.97)	84.56 (16.78)	<0.001***	51.78 (27.55)	58.59 (29.81)	0.136	21.51 (13.73)	6.81 (14.65)	0.017*
	Maximal	71.10 (18.30)	92.47 (15.49)	<0.001***	62.47 (28.16)	68.80 (29.63)	0.328	21.37 (12.88)	6.33 (12.41)	0.007**
Mean walking speed (m/s) (SD)	Preferred	0.27 (0.11)	0.60 (0.17)	<0.001***	0.24 (0.21)	0.30 (0.02)	0.029*	0.33 (0.15)	0.06 (0.08)	0.001**
	Maximal	0.37 (0.20)	0.74 (0.18)	<0.001***	0.29 (0.21)	0.36 (0.23)	0.035*	0.37 (0.16)	0.07 (0.09)	0.001**
Mean stride length (m) (SD)	Preferred	0.62 (0.18)	0.79 (0.23)	0.009**	0.61 (0.18)	0.65 (0.19)	0.014*	0.17 (0.18)	0.04 (0.05)	0.127
	Maximal	0.71 (0.22)	0.83 (0.23)	0.013*	0.64 (0.22)	0.74 (0.21)	0.005**	0.12 (0.12)	0.10 (0.06)	0.210
Mean step symmetry ratio (ratio) (SD)	Preferred	1.43 (0.58)	1.33 (1.18)	0.692	1.35 (0.39)	1.32 (0.31)	0.980	0.10 (0.25)	0.03 (0.30)	0.160
	Maximal	1.25 (0.38)	1.05(1.31)	0.297	1.56 (0.94)	1.34 (0.45)	0.265	0.20 (0.30)	0.22 (0.40)	0.320

Note: [a] P-value from the Two-Way Mixed ANOVA with repeated measures. *Indicates significant difference, P-value <0.05; ** P-value <0.01; *** P-value <0.001.

Discussion

This study was the first determining the effects of I-Walk (Robotic-assisted gait device) training compared with overground walking training. In our study found that participants in I-Walk training group walked more than 1,000 steps per session compare with over-ground walking training group walked less than 1,000 steps per session which similarly found in previous study. Hesse and Werner in 2003 reported that up to 1,000 steps which could be performed in a 20-minute treadmill training session, compared with 50 to 100 steps during a 20-minute session of conventional physical therapy. Their study suggested that approximately 1,000 steps per session are required to improve gait performance in patients with stroke [16]. The patients with chronic stroke in I-Walk training group had a significant motor recovery which might be due to brain plasticity [17]. The advantage of walk more than 1,000 steps per session is the ability of walking at speeds to crossing the street in the country of the previous study but maybe not sustable in Thailand.

The I-Walk training could improve volitional movements in patients with chronic stroke. As presented in the results, the participants with stroke in the experimental group demonstrated a greater improvement in score of FMA-LE than those in control group. The characteristic of I-Walk training similar with BWSTT and robotic assisted gait training that were task-specific training or task-oriented training [5,18]. Task-specific training focused on improvement of performance in functional tasks through repetition, progressive and intensity. Previous studies suggested that the task-specific training in a natural gait circuit and extend period of time available in a training session can influence the brain to adaptive, create a new neural network and brain activation patterns that can facilitate the motor recovery process[19]. The walking pattern on the I-walk is similar to walking with elliptical trainers. The movement patterns and muscle demands of the elliptical training related with walking up and down stairs climbing. Previous study reported that walking on the stairs is a movement that requires greater lower-limb strength and balance than walking on the ground[20].

The improvement of volitional movements of the participants in the I walk training group might effect on ankle movement during walking. As presented in the result that the range of motion of ankle plantar flexion during toe-off was improved in participants who were trained with I-Walk device. Previous study reported that the ability to perform ankle plantar flexion of the paretic ankle was strongly related to maximum walking speed and a reduction in plantar flexion was a cause of limited walking speed [21]. I-Walk training system had slightly moveable footplate (upward and downward) that can assist ankle dorsiflexion and plantar flexion movement during walking training. The active assisted movement repeated over the time of I-Walk training maintained repetitive movement of plantar flexion and greater number of steps within a training session more than over-ground walking training. Forrester and colleagues in 2011 studied the effects of robotics assisted gait training for 60 min. per day, 3 days per week, 6 weeks on ankle motor control and gait function in chronic stroke. Their study showed improvement of paretic ankle motor control, along with faster and smoother movements. The gait performances also increased significantly [22]. These reflect performance of stepping on and off a footpath, and obstacle crossing.

Walking speed of the participants in the I-walk training group was improved after the training. Walking speed is an important parameter in gait performance that directly related to physical disorder. Gait performances are the indicators of mobility impairment and disability after stroke. This predicts mortality, morbidity, and risk of future stroke. A maximal walking speed is a measure of gait performance after stroke and strong predictor of community ambulatory competence[23]. Previous study found that improvement in walking speed related with increased stride length, step length, and cadence [23]. After 24 sessions of walking training, the experimental group had increased their walking speed by 0.33 m/s in preferred walking speed and

0.36 m/s in maximum walking speed. The minimal detectable change (MDC) of maximal walking speed for survivors of stroke has been reported to be 0.3 m/s [24]. Therefore, the improvement of walking speed in the experimental group was a true performance change that did not due to variability in performance or measurement error.

There are some limitations in this study. First, this study did not recruit patients in other stages of stroke such as acute or sub-acute stroke. Then, the study did not collect a retention period after the training with I-Walk has ceased. Finally, the current study did not evaluate the spatiotemporal parameters related with walking for example, symmetrical stance time of both legs. Therefore, *further studies* should evaluate the effect of I-Walk training in patients with various stages of post-stroke and with a range of lower extremity deficits. Follow-up period should be examined to assess effect of I-walk training. Moreover, it is interesting to assess other spatiotemporal parameters related with walking, for example symmetrical stance time of both legs.

Conclusion

The study investigated the effects of I-Walk training in patients with chronic stroke. After 8 week training, the participants demonstrated significant improvement in their motor impairments, lower extremity angles during walking and gait performances. The greater improvement have found in participants who were trained using the I-Walk. It is helpful for the capacity of walking in a community requirement.

Conflict of interest

None

Acknowledgments

The authors would like to thank all participants of this study. The authors gratefully acknowledge the financial support provided by the National Research Council of Thailand and Thammasat University Research Fund under the TU Research Scholar, Contract No. 36/2561.

References

1. Latham NK, Jette DU, Slavin M, Richards LG, Procino A, Smout RJ, et al. Physical therapy during stroke rehabilitation for people with different walking abilities. Arch Phys Med Rehabil 2005;86(12 Suppl 2):41-50.
2. Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: A systematic review. Lancet Neurol 2009;8(8):741-54.
3. Ilunga Tshiswaka D, Bennett C, Franklin C. Effects of walking trainings on walking function among stroke survivors: A systematic review. Int J Rehabil Res 2018;41(1):1-13.
4. Pound P, Gompertz P, Ebrahim S. A patient-centred study of the consequences of stroke. Clin Rehabil 1998;12(4):338-47.
5. Mehrholz J, Pohl M. Treadmill training and body weight support for walking after stroke. Cochrane Database Syst Rev 2014(1):CD002840.
6. Mehrholz J, Pohl M. Electromechanical-assisted gait training after stroke: A systematic review comparing end-effector and exoskeleton devices. J Rehabil Med 2012;44(3):193-9.
7. Schwartz I, Sajin A, Fisher I, Neeb M, Shochina M, Katz-Leurer M, et al. The effectiveness of locomotor therapy using robotic-assisted gait training in subacute stroke patients: a randomized controlled trial. PM R. 2009;1(6):516-23.
8. Hesse S, Schattat N, Mehrholz J, Werner C. Evidence of end-effector based gait machines in gait rehabilitation after CNS lesion. NeuroRehabilitation 2013;33(1):77-84.
9. Neto VP, Rombaldi A, Saes M, Siqueira F. Physical activity and gait kinematics in the elderly. Braz J Phys Ther 2015;20(3):243-50.
10. Pramodhyakul N, Amatachaya P, Sooknuan T, Arayawichanon P, Amatachaya S. Effects of a visuotemporal cue on walking ability of independent ambulatory subjects with spinal cord injury as compared with healthy subjects. Spinal Cord 2014;52(3):220-4.
11. Sayeed T, Samà A, Català A, Cabestany J, editors. Comparison and adaptation of step length and gait speed estimators from single belt worn

accelerometer positioned on lateral side of the body. Intelligent Signal Processing (WISP) IEEE 8th International Symposium; 2013 September 16-18; Funchal, Portugal: IEEE; 2013. 14-20.
12. Kirtley C. Clinical gait analysis: theory and practice. Edinburgh: Livingstone. 2006. 16-20.
13. Patterson KK, Gage WH, Brooks D, Black SE, McIlroy WE. Evaluation of gait symmetry after stroke: A comparison of current methods and recommendations for standardization. Gait Posture 2010;31(2):241-6.
14. Hesse S, Werner C, Uhlenbrock D, Frankenberg SV, Bardeleben A, Brandl-Hesse B. An electromechanical gait trainer for restoration of gait in hemiparetic stroke patients: Preliminary results. Neurorehabil Neural Repair 2001;15(1):39-50.
15. Ribeiro T, Britto H, Oliveira D, Silva E, Galvão E, Lindquist A. Effects of treadmill training with partial body weight support and the proprioceptive neuromuscular facilitation method on hemiparetic gait: a randomized controlled study. Eur J Phys Rehab Med. 2013;49(4):451-61.
16. Hesse S, Werner C. Post stroke motor dysfunction and spasticity: novel pharmacological and physical treatment strategies. CNS Drugs. 2003;17(15):1093-107.
17. Pollock A, Baer G, Pomeroy V, Langhorne P. Physiotherapy treatment approaches for the recovery of postural control and lower limb function following stroke. Cochrane Database Syst Rev 2007(1):249-62.
18. Hubbard IJ, Parsons MW, Neilson C, Carey LM. Task-specific training: Evidence and translation to clinical practice. Occup Ther Int 2009;16 (3-4):175-89.
19. Klimecki OM, Leiberg S, Lamm C, Singer T. Functional neural plasticity and associated changes in positive affect after compassion training. Cereb Cortex 2013;23(7):1552-61.
20. Damiano DL, Norman T, Stanley CJ, Park H-S. Comparison of elliptical training, stationary cycling, treadmill walking and overground walking. Gait Posture 2011;34(2):260-4.
21. Woolley SM. Characteristics of gait in hemiplegia. Top Stroke Rehabil 2001;7(4):1-18.
22. Forrester LW, Roy A, Krebs HI, Macko RF. Ankle training with a robotic device improves hemiparetic gait after a stroke. Neurorehabil Neural Repair. 2011;25(4):369-77.
23. Salbach NM, Mayo NE, Higgins J, Ahmed S, Finch LE, Richards CL. Responsiveness and predictability of gait speed and other disability measures in acute stroke. Arch Phys Med Rehabil 2001;82(9):1204-12.
24. Fulk G, L Echternach J. Test-retest reliability and minimal detectable change of gait speed in individuals undergoing rehabilitation after stroke. J Neurol Phys Ther 2008;32(1):8-13.

Effects of Intensive Dietary Counseling versus Standard Dietary Counseling in Chronic Kidney Disease Patients: The Pilot Study

Nut Boontawan, MD[1]
Wanjak Pongsittisak, MD, MSc[1*]
[1] Department of Internal Medicine, Faculty of Medicine, Navamindradhiraj University, Bangkok, Thailand
* Corresponding author, e-mail address : wanjak@nmu.ac.th
Vajira Med J. 2020; 64(4) : 255-62
http://dx.doi.org/10.14456/vmj.2020.25

Abstract

Background: Chronic kidney disease (CKD) is a major public health problem worldwide, particularly in Thailand. Several studies have recommended limiting protein and sodium intake with the benefit of delaying kidney deterioration. Hence, dietary counseling is recommended for CKD patients. We aimed to explore and compare the effects of intensive dietary counseling (In-counseling) and standard dietary counseling (Sd-counselling) for controlling protein and sodium intake.

Methods: The present study was an open-labeled randomized control trial. The participants were stage III – IV CKD patients who were stable on their current treatment. The Id-counseling group received 30-minute monthly lessons with advice on dietary intake. The Sd-counseling group received the usual standard of care. The outcomes were daily protein intake (DPI) and 24-hour urinary sodium (UNa) at two months.

Results: Twenty CKD patients were divided into two groups of 10 participants each. Baseline characteristics were similar in both groups, except there were more CKD stage 4 patients in Sd-counselling group (3 vs 1 participant). The three most common comorbidities were hypertension (80%), dyslipidemia (70%) and diabetes mellitus (50%). Baseline DPI and 24-hour UNa were similar in both groups. After 2 months, the DPI of the In-counseling group achieved greater target-control than Sd-counseling. There was a trend to decrease 24-hour UNa between before and after counseling in In-counseling group. However, the DPI and 24-hour UNa at the end of the study was not statistically significant.

Conclusion: Although our study did not show significant benefit from In-counselling, it might be due to a small sample size and short time period. There was, however, some trend showing a benefit of In-counselling. A larger scale randomized controlled trial should be conducted to explore this benefit.

Keywords: intensive dietary counseling, chronic kidney disease, dietary protein intake, sodium intake.

โครงการศึกษานำร่องทางคลินิกแบบสุ่มเปรียบเทียบประสิทธิภาพของการให้ความรู้และคำแนะนำด้านโภชนาการแบบเข้มข้นเทียบกับแบบปกติในผู้ป่วยโรคไตเรื้อรัง

ณัฏฐ์ บุญตะวัน พ.บ.[1]
วันจักร พงษ์สิทธิศักดิ์ พ.บ., วท.ม.[1*]

[1]ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช กรุงเทพมหานคร ประเทศไทย

* ผู้ติดต่อ, อีเมล: wanjak@nmu.ac.th

Vajira Med J. 2020; 64(4) : 255-62
http://dx.doi.org/10.14456/vmj.2020.25

บทคัดย่อ

บทนำ: โรคไตวายเรื้อรัง เป็นโรคที่พบบ่อยและเป็นปัญหาด้านสาธารณสุขที่สำคัญของโลกโดยเฉพาะในประเทศไทย เป็นโรคเรื้อรังที่รักษาไม่หายขาด จำเป็นต้องได้รับการรักษาต่อเนื่อง มีการศึกษาหลายการศึกษาโดยเฉพาะในคนไข้โรคไตเรื้อรังระยะก่อนบำบัดทดแทนไต ได้ศึกษาถึงความสำคัญของการจำกัดสารอาหารประเภทโปรตีนและโซเดียม ได้ประโยชน์ช่วยชะลอการเสื่อมของไตได้ ผู้วิจัยได้ศึกษาความสัมพันธ์เปรียบเทียบประสิทธิภาพของการให้ความรู้และแนะนำด้านโภชนาการ ในผู้ป่วยโรคไตเรื้อรังแบบเข้มข้นแบบตัวต่อตัวเทียบกับแบบปกติทั่วไป โดยวัดค่าโปรตีนที่ได้รับในแต่ละวัน

วิธีการดำเนินการศึกษา: การศึกษานี้ได้ศึกษาแบบ open – labeled, randomized control trial โดยใช้ระบบคอมพิวเตอร์ โดยกลุ่มที่ได้รับความรู้ทางด้านโภชนาการแบบเข้มข้นตัวต่อตัว (intensive nutritional counseling) จะได้รับคำแนะนำจากนักโภชนาการ 30 นาทีในทุกเดือน ส่วนในกลุ่มที่ได้รับความรู้ทางด้านโภชนาการแบบมาตรฐานในแผนกผู้ป่วยนอก (standard nutritional counseling) การวัดค่าโปรตีนที่ได้รับในแต่ละวัน (dietary protein intake) จะเก็บยูเรียในปัสสาวะ 24 ชั่วโมง และ ผู้วิจัยประเมินปริมาณโซเดียมที่ได้รับในแต่ละวันจากค่าโซเดียมในปัสสาวะ 24 ชั่วโมง โดยเปรียบเทียบผู้เข้าร่วมวิจัยในแต่ละวิธีการ ให้คำแนะนำและความรู้ด้านโภชนาการ วัดค่าผลลัพธ์หลัก คือ ค่าโปรตีนที่ได้ในแต่ละวัน ที่ 2 เดือน ปริมาณโซเดียมในปัสสาวะ การทำงานของไต ไขมันในเลือด ฟอสฟอรัสและค่าเกลือแร่ในร่างกาย

ผลการศึกษา: ผู้วิจัยได้รวบรวมผู้เข้าร่วมโครงการวิจัย 20 คน เป็นคนไข้ไตวายเรื้อรัง (แบ่งเป็นได้รับความรู้ทางโภชนาการแบบเข้มข้นตัวต่อตัว 10 คน และได้รับความรู้ทางโภชนาการแบบทั่วไป 10 คน) เก็บระหว่าง เดือนมกราคม 2561 ถึง ตุลาคม 2561 โดยลักษณะพื้นฐานทั้งสองกลุ่มไม่แตกต่างกันอย่างมีนัยสำคัญ โรคประจำตัวที่พบบ่อย 3 โรค ได้แก่ โรคความดันโลหิตสูงคิดเป็นร้อยละ 80 ไขมันในเลือดสูง ร้อยละ 70 และเบาหวานร้อยละ 50 ปริมาณค่าโปรตีนที่ได้ต่อวันก่อนเข้าโครงการทั้งสองกลุ่มไม่แตกต่างกัน คิดเป็นค่าเฉลี่ยที่ 0.77 กรัม/กิโลกรัม/วัน ในกลุ่มเข้มข้นตัวต่อตัว และ 0.80 กรัม/กิโลกรัม/วัน ในกลุ่มมาตรฐาน ค่าโซเดียมในปัสสาวะ 24 ชั่วโมงมีแนวโน้มลดลงในกลุ่มเข้มข้นตัวต่อตัว แต่ไม่มีนัยสำคัญทางสถิติ

สรุป: ถึงแม้ว่าการศึกษาของเราจะไม่แสดงความแตกต่างอย่างมีนัยสำคัญในการให้ความรู้และคำแนะนำด้านโภชนการในผู้ป่วยโรคไตเรื้อรังด้วยการประเมินค่าบริโภคโปรตีนในแต่ละวัน แต่ก็มีแนวโน้มว่าการคุมการรับประทานเกลือจะดีขึ้นในกลุ่มที่ได้รับความรู้ทางโภชนาการแบบเข้มข้นตัวต่อตัว ดังนั้นการศึกษาที่มีขนาดตัวอย่างเพิ่มขึ้นน่าจะแสดงประสิทธิภาพของการได้ความรู้ทางโภชนาการแบบเข้มข้นตัวต่อตัวได้

คำสำคัญ: ประสิทธิภาพของการให้ความรู้, โรคไตเรื้อรัง, การวัดค่าโปรตีนที่ได้รับในแต่ละวัน, ปริมาณโซเดียม

Introduction

Chronic Kidney Disease (CKD) is a significant problem in Thailand and the prevalence of CKD is on the rise[1]. If CKD is not properly treated, the disease will worsen until it becomes end-stage renal failure requiring dialysis, which is increasing in prevalence and incidence in Thailand[2]. Several studies have found dietary control contributes to delaying kidney deterioration, particularly dietary control aimed at limiting protein and sodium intake. The recommendation of the Nephrology Society of Thailand in 2015 on limiting protein for Stage 3 Chronic Kidney Disease (CKD) patients was not to limit protein, but not to exceed protein intake of 1.3 grams per kilogram of the patient's recommended weight and to consume high-quality protein or complete amino acids. For CKD at the stage where estimated glomerular filtration rate (eGFR) is less than 30 ml/min/1.73m^2 patients are advised to limit protein intake to less than 0.8 grams per kilogram of the patient's recommended weight. Many previous studies have recommended intensive or individual dietary counseling as being more useful and yielding better outcomes than practical or standard counseling in patients on dialysis, CKD patients[3]. diabetes mellitus patients[4]. and patients with malnutrition[5].

Hence, this study aimed to explore the effects of intensive dietary counseling versus standard counseling in CKD patients.

Material and methods

Study design and population

This was an open-labeled randomized control study. We enrolled participants between July 1st, 2018 and October 31st, 2018 at a university hospital. The patients who visit the nephrology clinic were invited to participate. The eligibility criteria were age between 18 – 70 years, diagnosed stage 3 – 4 CKD, and treatment with maximum, or tolerated dose, of renin-angiotensin-aldosterone system (RAAS) inhibitor for 2 months. The exclusion criteria were: (1) current treatment with dialysis, (2) active infection, (3) pregnancy, (4) active malignancy, (5) malnutrition with serum albumin below 3.5 mg/dL, and (6) declined to participate.

Randomization

When participants had been screened and met the inclusion criteria for enrollment in the study, they were randomized into the following two groups with a computer-based randomization system: the group offered intensive dietary counseling (Id-counseling) and the group offered standard dietary counseling (Sd-counseling).

Treatment

For the Id-counseling group, the participants received individual dietary counseling directly from a nutritionist for 30 to 45 minutes in a CKD clinic. They were advised to make proper adjustments tailored to each individual, including interactions aimed at helping the patients gain understanding and improve their knowledge. For example, key points were emphasized by providing information sheets, following up, and providing advice every month. The participants in Sd-counseling group received standard or routine counseling, which had been individual counseling at regular visits to the nephrology clinic. During the study period, RAAS inhibitors were maintained at the same doses as they were at enrollment.

Data collection

After enrollment in the study, the participants were interviewed on their respective backgrounds, diagnosis of diseases, weight, height and waist circumference. They were then given physical examinations and baseline laboratory tests for Blood Urea Nitrogen (BUN), creatinine (Cr), electrolyte, albumin, blood sugar, hemoglobin A1c (HbA1c), calcium, magnesium, phosphate, lipid profile and 24-hour urine for urea, sodium, and protein. The urinary samples were taken at 24 hours by having the patients urinate as usual immediately after awakening. Then, the patients provided urine samples all day until the next morning with the last sample being given after the patients awoke the next day.

We assessed daily protein intake (DPI) based on the normalized protein equivalent of nitrogen appearance (nPNA) by calculating based on urinary samples taken at 24 hours to test for urea and protein, and then calculated as follows:

nPNA = ([(UUN + (0.031 x BW)) x 6.25] + Up) / BW

nPNA, normalized protein equivalent of total nitrogen appearance (g/day); UUN, 24-hour urinary urea nitrogen (g/day); Up, 24-hour urinary protein (g/day); and BW, body weight.

For the DPI-targeted, we assigned subjects based on the stage of CKD: CKD stage III, 0.8 – 1 g/kg/day and CKD stage IV, 0.6 – 0.8 g/kg/day. We assessed the sodium intake by taking urine samples at 24 hours to test for sodium.

Outcomes

The primary outcome was to compare the efficiency of protein control by the methods of Id-counseling versus Sd-counseling in CKD patients. The secondary outcome was to compare the efficiency of controlling sodium intake between both groups, including follow-up by comparing the changes in cholesterol levels, blood glucose levels and phosphorous levels.

Statistical analysis

The sample size was not calculated as this was a pilot study. Continuous variables are presented as mean and Standard Deviation (SD) or median (Interquartile range (IQR)), depending on distribution. Categorical variables are presented as proportions. For comparisons, independent t-test was used when data were normally distributed and Mann–Whitney U test when data were not normally distributed. Additionally, chi-squared and Fisher's exact tests were used for comparing categorical variables. The statistical analysis was performed by using the R version 3.4.4 program (R Foundation for Statistical Computing, Vienna, Austria) for analyzing the results with statistical significance set at P-value <0.05.

Ethical Considerations

The present study was certified by the Institutional Review Board (COA 113/60) for considering ethics in research involving human subjects (Research Promotion Department, Faculty of Medicine, Navamindradhiraj University, Bangkok, Thailand).

Results

Baseline characteristics

Twenty-four patients met eligibility criteria and four patients declined participation in the study. Ten of the participants were randomized to Id counseling group and the other ten participants received Sd-counseling (Figure 1). The general baseline characteristics of the patients in both groups had no statistically significant differences (Table 1).

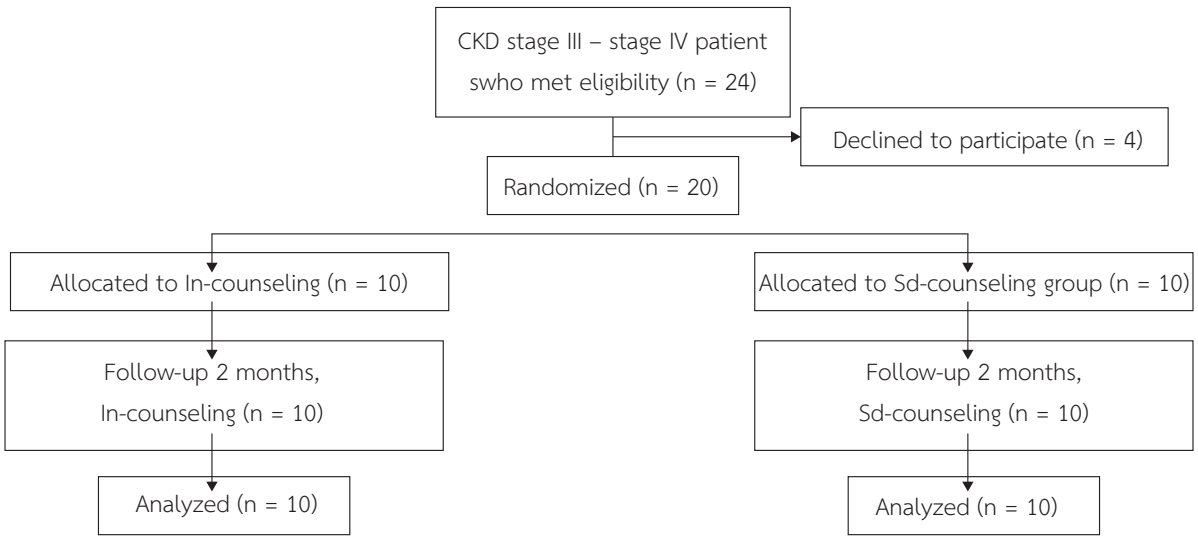

Figure 1: Flowchart of the participants in randomized control of nutritional intervention in the study. Abbreviation: CKD, Chronic Kidney Disease; In-counselling, intensive counselling; n, numbers; Sd-counselling, standard counselling.

Table 1:

The baseline characteristics and laboratory results of participants

Characteristic	In-counseling (n = 10)	Sd-counseling (n = 10)	p–value
Age, years	67 (63.5, 69.0)	64 (62.2, 66.7)	0.268
Gender: male, n (%)	5 (50)	5 (50)	1.000
CKD stage, n (%)			0.582
- III	9 (90)	7 (70)	
- IV	1 (10)	3 (30)	
Type 2 DM, n (%)	6 (60)	4 (40)	0.654
Hypertension, no (%)	8 (80)	9 (90)	0.453
Dyslipidemia, no (%)	5 (50)	9 (90)	0.104
Drug, n (%)			
- RAAS inhibitor	9 (80)	10 (10)	
- Lipid lowering	8 (80)	8 (80)	
- Diuretics	0	0	
Cr, mg/dl	1.4 ± 0.3	1.5 ± 0.6	0.593
eGFR, ml/min/1.73 m^2	52 ± 6	48 ± 8	0.643
Blood sugar, mg/dl	139.0 ± 49.3	118.7 ± 25.4	0.267
HbA1C, %	6.1 (5.2, 6.9)	6.2 (5.9, 7.1)	0.910
Cholesterol, mg/dl	181.7 ± 43.5	220.2 ± 32.1	0.311
Phosphorus, mg/dl	4.4 ± 1.3	3.9 ± 0.9	0.427
Serum albumin, mg/dl	3.7 (3.3, 4.0)	3.8 (3.6, 4.0)	0.648
DPI, g/kg/day	0.7 (0.6, 0.8)	0.8 (0.7, 0.9)	0.599
Target DPI, n (%)	10 (100)	8 (80)	0.456
24- hour UNa, mmol/d	142.7 ± 44.5	151.5 ± 47.6	0.674

Abbreviations: CKD, chronic kidney disease; Cr, creatinine; DM, diabetes mellitus; DPI, daily protein intake; eGFR, estimated glomerular filtration rate; HbA1C, hemoglobin A1C; In-counseling, intensive counseling; LDL, low density lipoprotein; n, numbers; RAAS, renin-angiotensin-aldosterone system; Sd-counselling, standard counseling; Una, urinary sodium.

The median age was 65 years and 50 percent of the subjects were male. The chronic diseases reported by the subjects were diabetes mellitus, hypertension, and high blood cholesterol at 60, 80 and 50 percent, respectively. The laboratory test results were similar for the two groups in terms of Cr, HbA1c, blood sugar, cholesterol, LDL, phosphorus and albumin. The RAAS inhibitor was prescribed in similar proportions to both groups.

The DPI at the beginning of In-counseling and Sd-counseling was similar [0.77 (0.67 – 0.81) vs. 0.80 (0.72 – 0.90) mg/kg/day; p-value = 0.599]. The DPI for individual subjects was within a range of 10/10 (100%) for subjects in the In-counseling group versus 9/10 (90%) for subjects in the Sd-counseling group (p-value = 0.456). Furthermore, 24-hour urine sodium values were also similar at the beginning of the study at 142.7 mmol per day in the Id-counseling group and 151.5 mmol in the Sd-counseling group (p-value = 0.674). there was no dropout and all participants in Id-counseling group visited CKD clinic regularly.

Outcomes

At two months after the completion of the study, the DPI between both groups were similar (p-value = 0.241) (table 2). The In-counseling group had more individual DPI values within a target based on CKD staging of 9/10 (90%) than the Sd-counseling with 6/10 (60%) subjects, but with no statistical significance (p-value = 0.303). The individual and overall DPI changes of both groups at 2 months are shown in Figure 2. The 24-hour urine sodium at 2 months equaled 136.1 (42.3) mmol/day for the In-counseling group versus 153.2 (47.1) mmol/day for Sd-counselling group. The In-counseling group tended to have lower 24-hour urine sodium than the Sd-counseling group (Table 2 and Figure 2); however, they were not statistically significant.

There were no statistically significant differences between the two groups for cholesterol, HbA1c, phosphate and bicarbonate levels at two months. Nevertheless, the potassium level in the In-counseling group indicated better control than the Sd-counseling group with statistical significance (p-value = 0.034). However, no patient developed hyperkalemia.

Discussion

The present study showed that In-counseling could be set up in a chronic kidney disease clinic. The participants had good compliance with regularly visits to the In-counseling nutritionist. There was a tendency for Sd-counselling not to control DPI. The DPI after 2 months of Sd-counselling group was higher than at enrollment time (p-value = 0.064). However, the DPI was still at target level in both groups. There was no statistical difference for controlled sodium intake between both groups.

When patients ingest higher amounts of protein, it increases endogenous acid production. Recent studies have reported an association between endogenous acid production and CKD progression[6-8]. A high salt diet is associated with high blood pressure and fluid retention, which subsequently increase cardiovascular death[9-11]. Numerous studies have shown limiting protein intake and lowering dietary sodium could slow the progression of CKD[11-13]. The implementation of dietary knowledge for CKD patients was recommended. However, there are many and various obstacles such as lack of time for counseling by physician, the complexity of dietary advice, or suboptimal knowledge of basic nutrition for specific diseases.

Table 2:

Outcome of patients between intensive nutritional counseling group and standard nutritional counseling group

Outcomes	In-counseling	Sd-counseling	p–value
2-month DPI, g/kg/day	0.7 (0.6, 0.7)	0.8 (0.7, 0.9)	0.241
Difference of DPI†, g/kg/day	-0.017 (-0.092, 0.165)	-0.053 (-0.079, -0.026)	0.545
2-month target DPI, n (%)	9 (90)	6 (60)	0.303
24-hour UNa, mmol/day	136.1 ± 42.3	153.2 ± 47.1	0.404
Difference of 24-hour Una‡, mmol/day	6.5 (1.25, 11.75)	-2.5 (-4.00, 2.25)	0.240
Cholesterol, mg/dl	188.6 ± 42.8	224.4 ± 58.0	0.324
HbA1c, %	7.1 ± 2.4	6.4 ± 0.8	0.399
Phosphate, mg/dl	3.7 ± 0.96	3.8 ± 0.7	0.675
Potassium, mg/dl	3.8 ± 0.2	4.3 ± 0.6	0.034
HCO_3, mg/dl	27.1 ± 3.8	27.3 ± 3.8	0.908

†DPI at pre-study minus DPI at 2 months. ‡ 24-hour Una at pre-study minus 24-hour Una at 2 months. Abbreviations: CKD, Chronic Kidney Disease; DPI, Daily Protein Intake; HbA1C, hemoglobin A1C; HCO_3, serum bicarbonate; In-counseling, intensive counseling; n, numbers; Sd-counseling, standard counseling; UNa, urinary sodium.

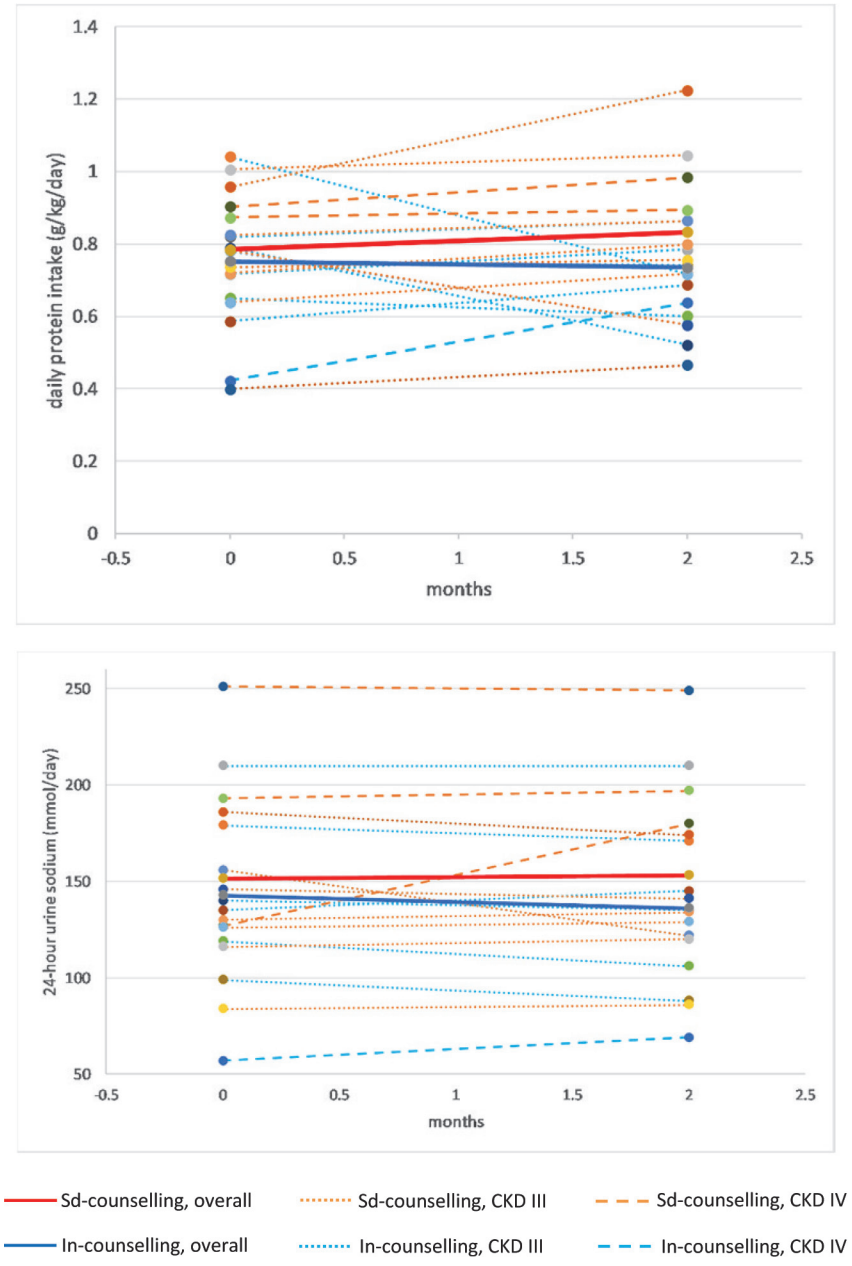

Figure 2: The scatter plot between outcomes and treatments.
The top figure shows DPI at pre-study and the end of the study. The bottom figure shows 24-hour Una at pre-study and the end of the study. These results were plotted by individual participants and median of overall participants classified by treatment group. The plots were also classified by CKD staging. Abbreviations: CKD, Chronic Kidney Disease; DPI; Daily Protein Intake; In-counseling, intensive counseling; Sd-counseling, standard counseling; UNa, urinary sodium.

A study from Brazil reported that implementation of a nutrition education program in the CKD clinic for 6 months could significantly lower dietary protein intake[14]. However, our study's baseline DPI in both groups were nearly achieved the target level; it could because of our results that show the DPI reduction in Sd-counselling group.

Our study had some limitations. The sample size was too small to show statistical significance. The follow-up period was short. If patients were in In-counseling and followed up over a longer period of time, it may increase patients' knowledge resulting in better controlled protein and salt intake, or it may cause patient fatigue leading to poor compliance clinic with visits. Our study showed the feasibility of an intensive nutritional counseling program provided by a nutritionist at CKD clinic over a short-term period. Hence, the challenge is how to develop a nutritional counseling program that our patients would be able to visit regularly.

Conclusion

Intensive dietary counseling with regular monitoring of CKD patients at stages 3-4 can effectively decrease daily dietary protein intake and reduce sodium in the urine. However, the decrease was not statistically significant when compared to standard dietary counseling. To confirm our finding, future studies with larger populations and longer follow-up periods are required.

Acknowledgement

The research was funded by Navamindradhiraj University Research Fund.

References

1. Ingsathit A, Thakkinstian A, Chaiprasert A, et al. Prevalence and risk factors of chronic kidney disease in the Thai adult population: Thai SEEK study. Nephrol Dial Transplant. 2010; 25: 1567-75.
2. Chuasuwan A and Praditpornsilpa K. Thailand Renal Replacement Therapy year 2013. Nephrology Society of Thailand, 2013, p. 27-37.
3. Mafra D and Leal VO. A practical approach to a low protein diet in Brazil. BMC Nephrol. 2016; 17: 105.
4. Johansen MY, MacDonald CS, Hansen KB, et al. Effect of an Intensive Lifestyle Intervention on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Clinical Trial. JAMA. 2017; 318: 637-46.
5. Akpele L and Bailey JL. Nutrition counseling impacts serum albumin levels. J Ren Nutr. 2004; 14: 143-8.
6. Scialla JJ and Anderson CA. Dietary acid load: a novel nutritional target in chronic kidney disease? Adv Chronic Kidney Dis. 2013; 20: 141-9.
7. Scialla JJ, Asplin J, Dobre M, et al. Higher net acid excretion is associated with a lower risk of kidney disease progression in patients with diabetes. Kidney Int. 2017; 91: 204-15.
8. Rebholz CM, Coresh J, Grams ME, et al. Dietary Acid Load and Incident Chronic Kidney Disease: Results from the ARIC Study. Am J Nephrol. 2015; 42: 427-35.
9. Stamler J, Stamler R and Neaton JD. Blood pressure, systolic and diastolic, and cardiovascular risks. US population data. Arch Intern Med. 1993; 153: 598-615.
10. Sasaki S, Zhang XH and Kesteloot H. Dietary sodium, potassium, saturated fat, alcohol, and stroke mortality. Stroke. 1995; 26: 783-9.
11. Bibbins-Domingo K, Chertow GM, Coxson PG, et al. Projected effect of dietary salt reductions on future cardiovascular disease. N Engl J Med. 2010; 362: 590-9.
12. Effects of dietary protein restriction on the progression of moderate renal disease in the Modification of Diet in Renal Disease Study. J Am Soc Nephrol. 1996; 7: 2616-26.
13. Menon V, Kopple JD, Wang X, et al. Effect of a very low-protein diet on outcomes: long-term follow-up of the Modification of Diet in Renal Disease (MDRD) Study. Am J Kidney Dis. 2009; 53: 208-17.
14. Paes-Barreto JG, Silva MI, Qureshi AR, et al. Can renal nutrition education improve adherence to a low-protein diet in patients with stages 3 to 5 chronic kidney disease? J Ren Nutr . 2013; 23: 164-71.

Knowledge and Attitudes of Metropolitan Women towards Cervical Cancer Prevention with Human Papillomavirus Vaccination: A Cross-sectional Study

Busaba Supawattanabodee, PhD (Statistics)[1]*
Woraphot Chaowawanit, MD[2]
Thanaporn Kittisiam , MD[2]
Budsaba Wiriyasirivaj, MD[2]
Siriwan Tangjitgamol, MD[2]

[1] Department of Basic Medical Science, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand
[2] Department of Obstetrics and Gynecology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand
* Corresponding author, e-mail address : busabasupa@yahoo.com
Vajira Med J. 2020; 64(4) : 263-74
http://dx.doi.org/10.14456/vmj.2020.26

Abstract

To evaluate the knowledge and attitudes of Bangkok Metropolitan women towards Human Papillomavirus (HPV) vaccinations. Thai women aged 25–65 years old who had lived in Bangkok for 5 years or over were invited to the study. Participants were asked to complete the questionnaire. 4,405 of 5,000 women completed the questionnaires. Approximately two-thirds of women had heard about HPV vaccination (61.4%). Approximately two-thirds of them had correct answers about the causes or risk factors of cervical cancer (65.7%), including HPV as an etiologic agent (67.4%). However, only few understood the relationship of HPV and cervical cancer (2.8%) or the types of HPV (6.2%). Regarding knowledge of cervical cancer and HPV, a quarter knew the method of HPV transmission (25.6%). Although most accepted the HPV vaccination (78.6%), only one-third knew about the particular groups of women who would benefit from this vaccination (34.6%). In conclusion, more than half of women knew about the cause of cervical cancer and HPV vaccine. However, only a few women knew about the relationship between HPV and cervical cancer or the types of HPV.

Keywords: cervical cancer, HPV vaccination, knowledge, attitude, urban area

ความรู้และทัศนคติของสตรีต่อการตรวจคัดกรองมะเร็งปากมดลูกและวัคซีนป้องกันมะเร็งปากมดลูก : การศึกษาภาคตัดขวาง

บุษบา ศุภวัฒน์ธนบดี, ปรด. (สถิติ)[1]*

วรพจน์ เชาวะวณิช, พ.บ. ว.ว. สูติศาสตร์ นรีเวชวิทยา[2]

ธรรณพร กิตติสยาม, พ.บ. ว.ว. สูติศาสตร์ นรีเวชวิทยา[2]

บุษบา วิริยะสิริเวช, พ.บ. ว.ว. สูติศาสตร์ นรีเวชวิทยา[2]

ศิริวรรณ ตั้งจิตกมล, พ.บ. ว.ว. พยาธิกายวิภาค ,ว.ว. สูติศาสตร์ นรีเวชวิทยา[2]

[1] ภาควิชาวิทยาศาสตร์การแพทย์พื้นฐาน คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช กรุงเทพมหานคร ประเทศไทย

[2] ภาควิชาสูติศาสตร์นรีเวชวิทยา คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช กรุงเทพมหานคร ประเทศไทย

* ผู้ติดต่อ, อีเมล: busabasupa@yahoo.com

Vajira Med J. 2020; 64(4) : 263-74

http://dx.doi.org/10.14456/vmj.2020.26

บทคัดย่อ

เพื่อประเมินความรู้และทัศนคติของสตรีกรุงเทพมหานครต่อวัคซีนป้องกันมะเร็งปากมดลูก เก็บข้อมูลสตรีไทยอายุ 25-65 ปี ที่อยู่ในกรุงเทพมหานคร 5 ปีขึ้นไปที่ยินยอมเข้าร่วมวิจัยด้วยแบบสอบถาม มีผู้ตอบกลับ 4,405 จาก 5,000 ราย (อัตราการตอบกลับร้อยละ 88.1) ผลการวิจัยพบว่า ประมาณสองในสาม (ร้อยละ 61.4) เคยได้ยินเกี่ยวกับวัคซีนป้องกันมะเร็งปากมดลูก ตอบสาเหตุหรือปัจจัยเสี่ยงของมะเร็งปากมดลูกได้ถูกต้อง (ร้อยละ 65.7) รวมทั้งรู้ว่า HPV เป็นสาเหตุ (ร้อยละ 67.4) อย่างไรก็ตามสตรีจำนวนน้อยรู้ว่า HPV สัมพันธ์กับมะเร็งปากมดลูก (ร้อยละ 2.8) รู้ชนิดของ HPV (ร้อยละ 6.2) ส่วนความรู้เรื่องมะเร็งปากมดลูกและHPV พบว่าหนึ่งในสี่ (ร้อยละ 25.6) รู้ว่า HPV มีการติดต่ออย่างไร แม้ว่าส่วนใหญ่ (ร้อยละ 78.6) ยอมรับวัคซีน HPV แต่มีเพียงหนึ่งในสาม (ร้อยละ 34.6) ที่รู้ว่าวัคซีนนี้ใช้ได้ผลเฉพาะสตรีเพียงบางกลุ่ม โดยสรุป สตรีเกินครึ่งหนึ่งรู้สาเหตุของการเกิดมะเร็งปากมดลูกและรู้ว่ามีวัคซีนHPV ส่วนน้อยที่รู้ว่า HPV สัมพันธ์กับมะเร็งปากมดลูกและชนิดของ HPV อย่างไรก็ตามส่วนใหญ่ยอมรับวัคซีน HPV

คำสำคัญ: มะเร็งปากมดลูก, วัคซีน HPV, ความรู้, ทัศนคติ, เขตเมือง

Introduction

Cervical cancer is the fourth most common cancer in women worldwide with an estimated 528,000 new cases and 266,000 deaths in 2012[1]. The majority of cervical cancer (84% or 445,000 cases) and deaths (87% or 230,000 cases) occur in less developed regions[1]. These high incidence and mortality rates in less developed regions are partly because the majority of the patients have locally advanced stages or advanced stage cancers at the time of diagnosis[2]. In Thailand, cervical cancer is the second most common cancer among women. In 2012, the numbers of new cases and deaths from cervical cancer were 8,184 and 4,513, respectively[3].

Human Papillomavirus (HPV) is the most important cause of anogenital warts and cervical cancer[4]. The virus is divided into two major groups. First is low-(LR-HPV)risk HPV group and second is high-risk HPV group(HR-HPV). The majority of HPV infections spontaneously subside. While some infections may be persistent, especially with HR-HPV,. This latter group of women have a higher risk of cervical cancer development. The most common types of HR-HPV causing cervical cancer are types 16 and 18[5].

An effective cervical cancer screening with cervical cytology and/or HPV testing can detect pre-invasive cervical lesions or early stage cancer. However, a suboptimal screening coverage, particularly in less developed countries, is still a major problem that has led to the unsuccessful reduction in cervical cancer[6].

The US Center for Disease Control and Prevention has initially suggested that an individual should receive the vaccine starting from the age of 9–15 years old[7]. With the use of HPV vaccinations against HPV type 16 and 18 infection, the incidence of cervical cancer should be more effectively controlled[8]. The subsequent recommendation has later been extended to an age that is older than 16–26 years[9]. To date, the HPV vaccination program has been included as an essential vaccination program in girls or even boys in many countries, such as Australia, England, etc.[10].

During the previous decades when the HPV vaccine was newly launched, there were many studies investigating the knowledge of HPV and HPV vaccine as well as knowledge, attitude and acceptability of HPV vaccination among students and their parents. Few studies in Asia reported moderate to poor knowledge about HPV infection and HPV vaccination[11] and low rate of HPV vaccination[12]. In Thailand, the HPV vaccine has been readily available commercially since 2007. In the early phase after the introduction of this vaccine, there were many studies investigating the knowledge, attitude, acceptability of school students and their parents toward HPV vaccination. This included our group cross-sectional survey of 1997 parents of female students in private and public schools in Bangkok in 2008[13]. Although approximately 55–76% knew the cause of cervical cancer, only a few respondents possessed knowledge of HPV (10–26%). Nevertheless, the parents' attitude toward vaccines was overall positive. To date, researches focusing on young adults and the general population have been limited.

Few researches have recently reported the cost-effectiveness of the vaccination in order to support an implementation of HPV vaccine in a national vaccination program without any medical charges for young female adolescents who will obtain the maximum benefit from the vaccine[14]. In the meantime, when the vaccine has not yet been included in the program, the data about their knowledge, acceptance and the cost that the girls' guardians and the women whose ages are beyond the target group (but still have modest benefit) are willing to pay are important. The aim of this study was to evaluate knowledge, attitudes and the

cost that women residing in Bangkok Metropolitan are willing to pay for the HPV vaccination.

Materials and Methods

The study obtained an approval from the Ethical Committees of the institution. This cross-sectional survey study was a parallel project of the studies evaluating the prevalence and associated factors of abnormal cytology and high risk HPV DNA among Bangkok metropolitan women conducted during September 2014 to the end of December 2014[15], which involved the assessment of knowledge, attitude and behavior of Bangkok Metropolitan women towards cervical cancer screening[16], HPV and self-sampled HPV testing[17]. This study focused on the knowledge and attitudes of women towards HPV vaccinations.

In brief, Thai women aged 25–65 years old who had lived in Bangkok for 5 years or over were invited to participate in the study. Convenience sampling was conducted to recruit women living in various districts in Bangkok. We excluded the women with a history of pre-invasive or invasive cervical lesions, other gynecologic cancer or who previously had HPV vaccination(s). All potential participants were informed about the purpose and contents of the study. The women who agreed to participate in the study signed consent forms prior to answering the questionnaires. The set of questionnaires used in this study was modified from our previous study, which investigated similar issues of HPV vaccination among Thai students[13]. Our previous questionnaire was constructed from both quantitative and qualitative studies[18-19], validated in thirty mothers of girls' children and validated again in thirty women before survey. The questionnaire was divided into three parts. The first part contained demographic data including sexual experienced (7 items), the second part involved knowledge about cervical cancer and HPV (9 items) and the third part was for this particular study as it involved the attitude and acceptability towards HPV vaccinations including the requirement of cervical cancer screening after vaccination (8 items). Each statement of the second and third parts had three options of answer (yes/no/don't know). The answer 'don't know' was considered to be incorrect. The multiple choice answers were intended to determine the cost that the women were willing to pay for the vaccine.

Data were analyzed using SPSS statistical software version 22.0 (IBM Corporation, Armonk, NY, USA). Descriptive statistics were used for demographic data, knowledge, attitudes and acceptance of HPV vaccine including the cost that the women were willing to pay for the vaccine.

Results

A total of 5,000 questionnaires were distributed and 4405 women completed the questionnaires (response rate of 88.1%). Table 1 shows the baseline characteristics of the women. The median age was 47 years [interquatile range (IQR) of 25–65 years]. Most of the participants had sexual experience (90.6%), but only 63.2% were married. Almost all were Buddhist (95.5%). Nearly half (47.8%) had a bachelor degree and two-thirds (60.2%) of participants had a family monthly income more than 600 USD.

Table 1:

Characteristics of women participating in this study.

Data	N	%
Marital status (*n* = 4,393)		
Single	1077	25.5
Married	2778	63.2
Separated/divorced	538	12.3
Age group (years) (*n* = 4,405)		
21 – 30	302	6.8
31 – 40	963	21.9
41 – 50	1453	33.0
51 – 60	1342	30.5
61 – 65	345	7.8
Median (range)	47 (25–65)	
Educational level (*n* = 4,389)		
No education	56	1.3
Primary education	509	11.6
High school/Diploma	1202	27.4
Bachelor	2100	47.8
Master or higher	522	11.9
Occupation (*n* = 4,375)		
Unemployed	1049	24.0
Government sector/retirement	722	16.5
Employee	290	6.6
Private sector	989	22.6
Freelance	1325	30.3
Income (USD) [1] (*n* = 4,405)		
<600	1753	39.8
≥600	2652	60.2
Religion (*n* = 4,376)		
Buddhism	4179	95.5
Muslim	103	2.4
Others	94	2.1
Had sexual experience (*n* = 4,375)	3963	90.6

Remark: [1] USD approximated to 33 Baht.

Regarding the knowledge of cervical cancer, nearly two-thirds of the women knew the cause of cervical cancer (65.7%). Among the 9 related questions, multiple sexual partners (66.1%), sexually transmitted diseases (63.3) and HPV (58.5%) were answered correctly by more than half, which were 3 items focusing on etiology. For the knowledge of HPV and HPV vaccination, approximately two-thirds of the participants had heard about HPV (67.4%) and the prevention of HPV infections (64.7%). Despite around half of them knowing that high risk HPV is the cause of cervical cancer (49.7%), only a few of them knew about the relationship between HPV and cervical cancer (2.8%) and knew different HPV types (6.2%). A quarter of the participants knew about the method of HPV transmission (25.6%), with the most frequently chosen answer being sexual intercourse (52.1%) (Table 2).

Table 2:

Knowledge of cervical cancer and HPV.

Questions on Knowledge towards Cervical Cancer and HPV	N	%
1. Knew cause of cervical cancer with correct response (*n* = 4339)	2,851	65.7
2. Cause of cervical cancer (*n* = 2851)		
- Multiple sexual partners	1,886	66.1
- Sexually transmitted disease	1,804	63.3
- Human Papilloma Virus (HPV)	1,668	58.5
- Poor genital hygiene/use of public toilets	1,236	43.4
- Viral infections	1,194	41.9
- Early sexual intercourse	1,103	38.7
- Non-barrier contraception	957	33.6
- Frequent sexual intercourse	890	31.2
- Stress	608	21.3
- Smoking	615	21.6
- Oral contraceptive pills	401	14.1
- Others	53	1.9
3. Heard about HPV (*n* = 4311)	2,907	67.4
4. Knew the relationship of HPV with cervical cancer (4190)	116	2.8
5. Knew about prevention of HPV (*n* = 2865) (sexual intercourse, HPV vaccination)	1,855	64.7
6. Knew types of HPV (*n* = 2894)	180	6.2
7. Low risk HPV causes Condyloma (*n* = 2875)	442	15.4
8. High risk HPV causes cervical cancer (*n* = 285)	1,425	49.7
9. Knew method of HPV transmission (*n* = 4085)	1,045	25.6
- Sexual intercourse	2,128	52.1
- Use of public toilets	490	12.0
- Blood transfusion	419	10.3
- Needle sharing	370	9.1
- Genetic	311	7.6
- Others	14	0.3

Among 4,300 women who responded to the question of attitude towards HPV vaccination, two-thirds of them had heard about the HPV vaccination (61.4%). Most of the 4,294 women accepted the HPV vaccine (78.6%). Nearly half (46.6%) learnt about the vaccination program from their health care provider. Slightly more than one-third of the participants knew which age group would benefit from the vaccine (34.6%). However, very few knew the type of HPV that the vaccine provides protection against (3.5%). Only a few of them knew the vaccine schedule, the cost of the vaccine and how long the vaccine protection lasts (18.2% and 9.9%, respectively). Most were aware that a regular cervical Pap smear was still required after vaccination (90.5%) (Table 3).

The women aged 25–30 years old preferred a price range of 3,001–5,000 Thai baths (83.4–138.9 USD), which was higher than women aged 31–40 years old, 41–50 years old, 51–60 years old and 61–65 years old, respectively (Figure 1). A greater proportion of the women aged 25–40 years old accepted the vaccine (Figure 2).

Table 3:

Attitude of women towards HPV vaccination.

Questions on Attitude towards HPV Vaccination	N	%
1. Knew about HPV vaccination (*n* = 4,300)	2,641	61.4
2. Source of information about HPV vaccination (*n* = 2,542)		
- Healthcare provider	1,185	46.6
- Television/radio	1,004	39.5
- Newspapers/magazine	850	33.4
- Friends	761	29.9
- Internet	706	27.8
- Community's leaders	305	12.0
3. Knew which type of HPV the vaccine protects against (*n* = 2,630)	156	3.5
4. Knew about schedule of HPV vaccination and cost (*n* = 2,615)	477	18.2
5. Knew that vaccine is beneficial to which target group (*n* = 2,625)	910	34.6
6. Knew how long the vaccine protection lasts (*n* = 2,631)	261	9.9
7. Women need to regularly get a Pap test after vaccination (*n* = 2,614)	2,365	90.5
8. HPV vaccination considered to be acceptable (*n* = 4,294)	3,376	78.6

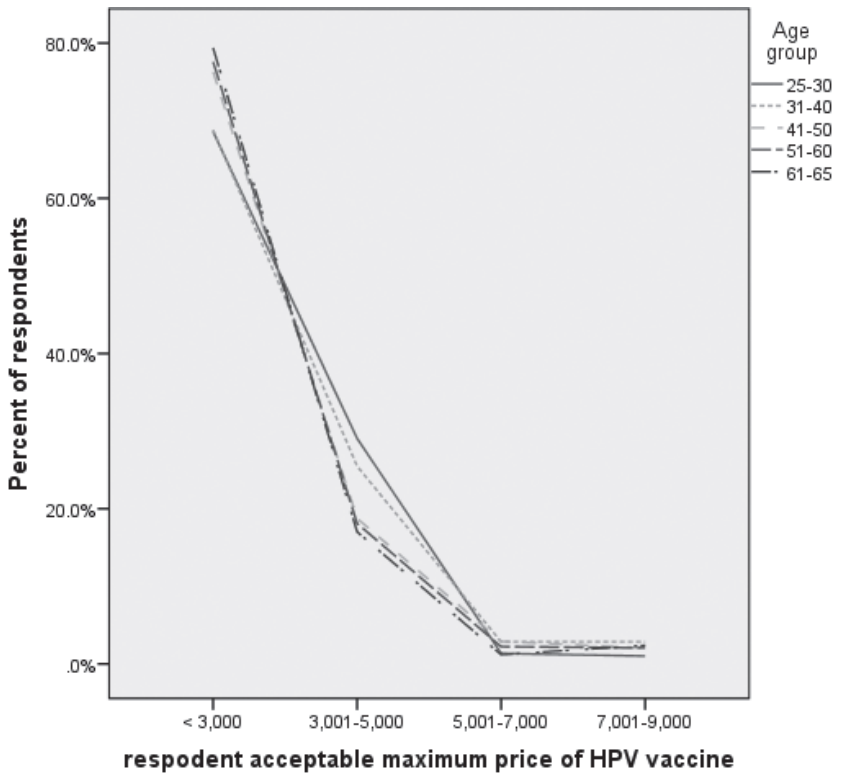

Figure 1: Expectation of the maximum price of HPV vaccine.

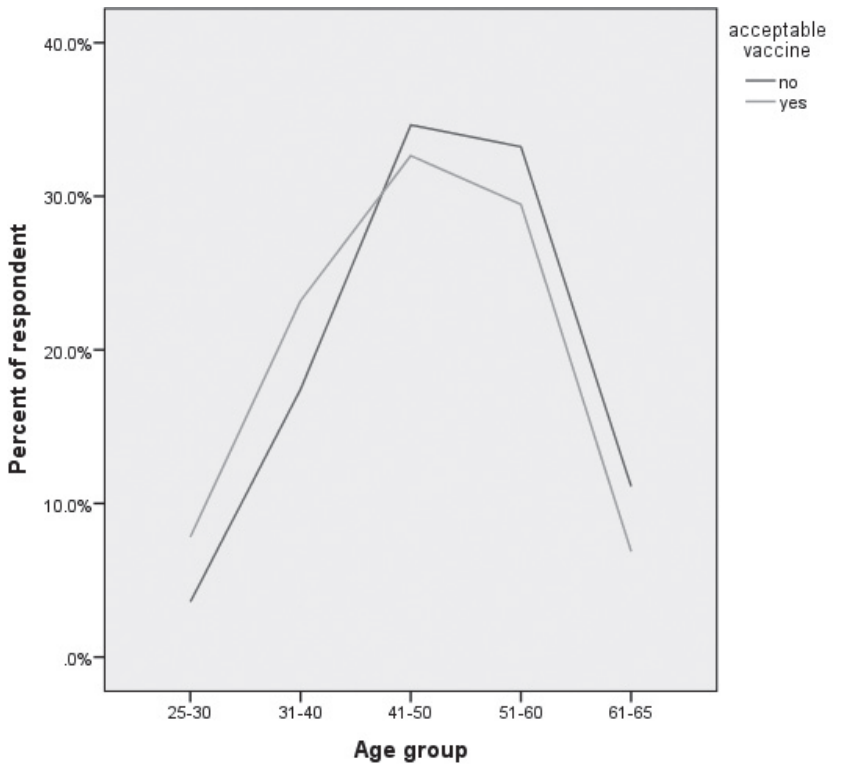

Figure 2: Characteristics of the groups that accepted and did not accept the HPV vaccine

Discussion

This study was a parallel project with the cervical cancer screening project in Bangkok women[15]. We excluded women who should have better basic knowledge than others, including those with a history of pre-invasive or invasive cervical lesions, other gynecologic cancer or those who had received HPV vaccination(s). This study found that Bangkok women had a modest level of knowledge about the cause of cervical cancer (66%). This was consistent with the findings from previous studies, which reported that only 55% of the parents of school girls in Bangkok[13] and Malaysia[10] had knowledge on this subject. The level of education certainly has an impact on the level of knowledge. Studies showed that a higher percentage of students themselves who were in the active learning phase generally had knowledge about cervical cancer. For example, 82% of the college students in India had knowledge about cervical cancer[20] compared to 50.3–66.3% of the secondary school students in Malaysia[21]. However, education level may not be the only important factor because one study in university students in Hong Kong were found to have knowledge that varied from poor to good[12].

Regarding the knowledge of HPV and HPV vaccination, our study found that only 2.8% knew of the relationship between HPV and cervical cancer, while there was poor knowledge of different HPV types (6.2%). Different findings were reported from India and Malaysia as almost half of the participants (42–52.8%) knew the relationship between HPV and cervical cancer, while a few of them knew about the different types of HPV (1–37.7%) [20-21]. The reason for this difference is that previous studies focused on young students, while our target population was older than 15 years. In terms of the knowledge of HPV vaccination, 61.4% of Bangkok women knew about the HPV vaccination in our current study. This was higher than the proportions of 8% and 20% demonstrated in our previous study, which focused on the parents of school girls (public and private schools, respectively)[13]. This may be due to the launch of HPV vaccine in Thailand and recommendations by clinicians for almost 10 years, while our previous study was conducted after the vaccine was marketed for only one year.

Regarding the attitude towards HPV vaccine and their acceptability, the percentage of vaccine acceptability in women was higher than in Thai parents of school girls from public and private schools in our previous study (76% and 59.1%, respectively)[13]. The high proportion of HPV vaccine acceptability, reflecting the positive attitudes to vaccine, was similar to previous studies[11,20]. An increased amount of information related to HPV and cancer through various media has led to more acceptance and positive attitudes[22].

About the price of HPV vaccine, two previous studies reported that the respondents required that the government should cover the cost of HPV vaccination in health care insurance[11,13]. Because the policy of inclusion of this vaccine into the program is underway and we were aware of the national health budget, we assessed the cost that women who may not be included as the target group in the national vaccination program because of a lesser benefit were willing to pay. We found the women who accepted the vaccination were willing to pay a higher cost (3001–5000 Thai baths; 90.9–151.5 USD) for the vaccine compared to the cost cited by the group that did not accept the vaccination (lower than 3000 Thai baths; <90.9 USD). The cost that women aged between 25–30 years old were willing to pay was higher than other groups. This may be due to their active work lives and their higher incomes, which makes this cost affordable. Nevertheless, the cost of HPV vaccine in Thailand was still higher than

the cost that all women in this study were willing to pay. Therefore, the HPV vaccination program should be fully or partially subsidized by the government in order to increase the coverage of HPV vaccination in the future.

Our study identified some problems that policy planning should focus on. Knowledge and attitudes towards cervical cancer especially caused by HPV, HPV vaccine could be improved by various strategies, e.g. health education, public relation or press conferences with mass media through celebrities/ambassadors or society volunteers to re-assure that those women understandable Health care providers should also routinely educate and promote screening and vaccination program when the patients come to hospital. In the meantime, public health providers should be proactive in educating people in the area. In Thailand where conservative culture is common, self-collected specimen for HPV testing may consider to be an alternative way.

In summary, the current situation of knowledge about cervical cancer and its vaccine has not greatly improved compared to the reports during the first few decades after the launch of HPV vaccination. With an inclusion of HPV vaccination into the national universal program for adolescent girls at certain age, this may raise the awareness of the parents and general population as well. Hence, more effort should be made e.g. commercial campaigns to generalize knowledge and acceptance of HPV vaccination to all Thai women especially the target group who are beyond the national vaccination coverage but still have benefit from HPV vaccine.

Limitation

Our study plan to recruit women from different districts of Bangkok in order to represent Metropolitan women. Unfortunately, the electronic database had incomplete number and information of registrants during the time frame, the questionnaires were distributed on hospital based instead. Hence, our results was not represented the distribution of women from each district.

Conclusions

More than half of women living in Bangkok knew the cause of cervical cancer and HPV vaccine. Only a few knew about the relationship of HPV with cervical cancer and the different types of HPV. Although most women in the study have a positive attitude towards the HPV vaccine, the cost that they were willing to pay for the vaccine was lower than the current market price. These financial and marketing issues should be a national focus in order to increase the number of women who can afford the vaccination, which will ultimately decrease the rates of cervical cancer.

Acknowledgement

The research was funded by Faculty of medicine Vajira hospital research fund, Navamindradhiraj University.

References

1. Ferlay, J.; Steliarova-Foucher, E.; Lortet-Tieulent, J.; Rosso, S.; Coebergh, J.W.W.; Comber, H.; Forman, D.; Bray, F. Cancer incidence and mortality patterns in Europe: Estimates for 40 country in 2012. *Eur. J. Cancer* 2013; *49* : 1374–1403.
2. Moore, M.A.; Attasara, P.; Khuhaprema, T.; Ngoan, L.T.; Nga, N.T.H.; Raingsey, P.P.; Sriamporn, S.S.; Sriplung, H.; Srivanatanakul, P.; Tung, B.D.; et al. Cancer epidemiology in mainland South-East Asia—Past, present and future. *Asian Pac. J. Cancer Prev.* 2010; *11*: 67–80.
3. International Agency for Research on Cancer. Population Fact Sheets. [Internet]. 2016.

[cited 20 May 2016]; Available from: http://globocan.iarc.fr/Pages/ fact_sheets population.aspx.

4. Winer, R.L.; Lee, S.-K.; Hughes, J.P.; Adam, D.E.; Kiviat, N.B.; Koutsky, L.A. Gentile human papillomavirus infection: incidence and risk factors in cohort for female university student. *Am. J. Epidemiol.* 2013; *157*: 218–26.
5. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). Human papillomavirus and related cancers in world Summary Report 2017. [Internet].2017. [cited 1 December 2017]; Available from: www.who.int/hpvcentre.
6. Lowndess, C.M. Vaccine for cervical cancer. *Epidemiol. Infect*. 2006; *134*: 1–12.
7. Basu, P.; Banerjee, D.; Singh, P.; Bhattacharya, C.; Biswas, J. Efficacy and safety of human papillomavirus vaccine for primary prevention of cervical cancer: A review of evidence from phase III trails and national programs. *South Asian J. Cancer* 2013; *2*: 187–92.
8. CDC Human Papillomavirus (HPV) vaccine information for young women. [Internet].2017. [cited 1 December 2017];Available from: http://www.cdc.gov/std/hpv/STDFact-HPV-vaccine-young-women.htm.
9. Harper, D.M.; Demars, L.R. HPV vaccine: A review of the first decade. *Gynecol. Oncol*. 2017; *146*: 196–204.
10. WHO Immunization , vaccine and biologicals. [Internet].2017. [cited 1 December 2017]; Available from:http://www.who.int/immunization/diseases/hpv/decision_implementation/en/.
11. Rajiah, K.; Maharajan, M.K.; Chin, N.S.; Num, K.S.F. Awareness and acceptance of human papillomavirus vaccination among health sciences student in Malaysia. *Virus Dis*. 2015; *26*: 297–303.
12. Chiang, V.C.L.; Wong, H.T.; Yeung, P.C.A.; Choi, Y.K.; Fok, M.S.Y.; Mak, O.I.; Wong, H.Y.; Wong, K.W.; Wong, S.Y.; Yan, S.; et al. Attitude , acceptability and knowledge of HPV vaccination among local university students in Hong Kong. *Int. J. Environ. Res. Public Health* 2016; *13*: 486.
13. Supawattanabodee, B.; Wiriyasirivaj, B. Knowledge and attitude of school girl's parents towards a prevention of cervical cancer through human papilomavirus vaccination. *Vajira Med. J.* 2009; *53*: 187–96.
14. Kosen, S.; Andrijono, A.; Ocviyanti, D.; Indriatmi, W. The Cost-Effectiveness of Quadrivalent Human Papillomavirus Vaccination in Indonesia. *Asian Pac. J. Cancer Prev.* 2017; *18*: 2011–17.
15. Tangjitkamol, S.; Kantathavorn, N.; Kittisiam, T.; Chaowawanit, W.; Phoolcharoen, N.; Manusirivithaya, S.; Khunnarong, J.; Srijaipracharoen, S.; Saeloo, S.; Krongthong, W.; et al. Prevalence and associated factors of abnormal cervical cytology and high risk HPV DNA among Bangkok Metropolitan women. *Asian Pac. J. Cancer Prev*. 2016; *17*: 3147–53.
16. Chaowawanit, W.; Tangjitgamol, S.; Kantathavorn, N.; Phoolcharoen, N.; Kittisiam, T.; Kittisiam, T.; Khunnarong, J.; Supawattanabodee, B.; Srijaipracharoen, S.; Thavaramara, T.; et al. Knowledge, attitude and behavior of Bangkok Metropolitan women towards cervical cancer screening. *Asian Pac. J. Cancer Prev*. 2016; *17*: 945–52.
17. Kittisiam, T.; Tangjitgamol, S.; Chaowawanit, W.; Khunnarong, J.; Srijaipracharoen, S.; Thavaramara, T.; Pataradool, K. Knowledge and attitudes of Bangkok Metropolitan women towards HPV and self-sampled HPV testing. *Asian Pac. J. Cancer Prev*. 2016; *17*: 2445–51.
18. Khan JA, Rosenthal SL, Hamann T, Bernstein DI. Attitudes about human papillomavirus vaccine in young women. *Int J STD AIDS*. 2003; 14: 300-6.

19. Waller J, Marlow LAV, Walder J. Mother's attitude towards preventing cervical cancer through human papillomavirus vaccination: A qualitative study. *Cancer Epidemiol Biomarkers Prev* 2006; 15: 1257-61.
20. Rashid, S.; Labani, S.; Das, B.C. Knowledge, awareness and attitude on HPV, HPV vaccine and cervical cancer among the college students in India. *PLoS ONE*, 2016; *11*: e0166713, doi:10.1371/journal.pone.0166713.
21. Jalani, F.F.M.; Rani, M.D.M.; Isahak, I.; Aris, M.S.M.; Roslan, N. Knowledge, attitude and practice of human papillomavirus (HPV) vaccination among secondary school students in rural areas of Negeri Sembilan, Malaysia. *Int. J. Collab. Res. Intern. Med. Public Health* 2016; *8*: 56–70.
22. Kim, J. The Relationship of Health Beliefs with Information Sources and HPV Vaccine Acceptance among Young Adults in Korea. *Int. J. Environ. Res. Public Health* 2018; *15*: 673, doi:10.3390/ijerph15040673.

Knowledge and Behavior of Contact Lens Wear in Medical Students and Medical Residents in Vajira Hospital

Chantaka Supiyaphun, MD[1*]
Puncharut Preechaharn, MD[1]

[1] Department of ophthalmology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University. Bangkok, Thailand
* Corresponding author, e-mail address : chantaka@nmu.ac.th
Vajira Med J. 2020; 64(4) : 275-86
http://dx.doi.org/10.14456/vmj.2020.27

Abstract

Objective: To determine knowledge and behavior of contact lens wear in medical students and medical residents in Vajira hospital.

Methods: A cross-sectional study using questionnaire was conducted among medical students and medical residents who wore contact lenses within the recent one year in Vajira hospital.

Results: A total of 660 (480 of medical students and 180 of residents) were recruited in this study. Twenty-four percent in medical student group and 17% in resident group wore contact lens in recent one year. The majority was female in both groups (79.3% and 80.6%, respectively). The average age was 21.4 years in medical student group and 27.8 years in resident group. The main reason for wearing contact lens is visual correction (67.3%). Approximately sixty percent in both groups wore monthly soft contact lens following by daily disposable lens (43.5%). Six improper contact lens compliance and care practices were reported as sleeping with their lens (22.6%), swimming with lens (26.5%), topping off lens storage solution (20.0%), not cleaning lens case daily (57.7%), prolonged wear over replacing schedule (18.4%) and no rubbing and rinsing (33.7%). Seventy-three percent in medical student group and 48.4% in residency group were classified as good behavior. The prevalence of good contact lens behavior in medical students were significantly higher than that of medical resident (p=0.013). However, the majority of participants in both groups were categorized in good knowledge (p=0.297). In all participants, we found statistical significant different between behavior and knowledge (p=0.001)

Conclusion: The majority of participants in both groups have good knowledge. However, medical student group has better behavior in contact lens wear and care compare with medical resident group.

Keywords : contact lens, medical student, resident, behavior, knowledge

สำรวจเปรียบเทียบความรู้และพฤติกรรมการใส่เลนส์สัมผัสในนักศึกษาแพทย์และแพทย์ประจำบ้าน คณะแพทยศาสตร์วชิรพยาบาล

ฉันทกา สุปิยพันธุ์ พ.บ., ว.ว. จักษุวิทยา สาขากระจกตาและการแก้ไขสายตาผิดปกติ[1*]

ปัญชรัช ปรีชาหาญ พ.บ.[1]

[1]ภาควิชาจักษุวิทยา คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช กรุงเทพมหานคร ประเทศไทย

* ผู้ติดต่อ, อีเมล: chantaka@nmu.ac.th

Vajira Med J. 2020; 64(4) : 275-86

http://dx.doi.org/10.14456/vmj.2020.27

บทคัดย่อ

วัตถุประสงค์: สำรวจความรู้และพฤติกรรมการใส่เลนส์สัมผัสของนักศึกษาแพทย์และแพทย์ประจำบ้าน คณะแพทยศาสตร์วชิรพยาบาล

วิธีดำเนินการวิจัย: วิธีศึกษาแบบตัดขวางด้วยแบบสอบถามกับกลุ่มอาสาสมัครนักศึกษาแพทย์และแพทย์ประจำบ้านในคณะแพทยศาสตร์วชิรพยาบาลที่สวมใส่เลนส์สัมผัส ภายในช่วงเวลา 1 ปีผลลัพธ์ จากกลุ่มอาสาสมัครทั้งหมด 660 ราย (นักศึกษาแพทย์ 480 รายและแพทย์ประจำบ้าน 180 ราย) พบว่ามีจำนวนนักศึกษาแพทย์ร้อยละ 24 และ แพทย์ประจำบ้านร้อยละ 17 ที่ใส่เลนส์สัมผัสภายในระยะเวลา 1 ปีจากวันที่ตอบแบบสอบถาม เพศหญิงใส่เลนส์สัมผัสร้อยละ 79.3 ในกลุ่มนักศึกษาแพทย์และร้อยละ 80.6 ในกลุ่มแพทย์ประจำบ้าน อายุเฉลี่ยของผู้สวมใส่เลนส์สัมผัสคือ 21.4 ปีในกลุ่มนักศึกษาแพทย์และ 27.8 ปีในกลุ่มแพทย์ประจำบ้าน วัตถุประสงค์หลักในการสวมใส่เลนส์สัมผัสคือแก้ไขภาวะสายตาผิดปกติร้อยละ 67.3 โดยประมาณร้อยละ 60 ของอาสาสมัครจากทั้งสองกลุ่มใส่เลนส์สัมผัสแบบรายเดือน และรองมาใส่เลนส์สัมผัสแบบรายวันร้อยละ 43.5 พฤติกรรมที่ไม่เหมาะสม 6 ประการในการสวมใส่และดูแลเลนส์สัมผัสคือ นอนหลับระหว่างใส่เลนส์สัมผัสพบร้อยละ 22.6 ว่ายน้ำในขณะสวมใส่เลนส์สัมผัสพบร้อยละ 26.5 เติมน้ำยาแช่เลนส์สัมผัสใหม่ลงบนน้ำยาเก่าร้อยละ 20.0 ไม่ทำความสะอาดตลับเลนส์สัมผัสทุกวันร้อยละ 57.7 เปลี่ยนเลนส์สัมผัสช้ากว่าระยะเวลาที่กำหนดร้อยละ 18.4 และไม่ถูล้างเลนส์สัมผัสร้อยละ 33.7 โดยร้อยละ 70 ในกลุ่มนักศึกษาแพทย์และร้อยละ 48.4 ในกลุ่มแพทย์ประจำบ้านถูกจำแนกประเภทเป็นผู้ที่มีพฤติกรรมการดูแลเลนส์สัมผัสดี จำนวนของผู้ที่ถูกจำแนกว่ามีพฤติกรรมการดูแลเลนส์สัมผัสดีพบในกลุ่มนักศึกษาแพทย์มากกว่ากลุ่มแพทย์ประจำบ้าน (p=0.013) อย่างไรก็ตามอาสาสมัครทั้ง 2 กลุ่มส่วนใหญ่ถูกจำแนกประเภทเป็นผู้ที่มีความรู้ดี (p=0.297) และในกลุ่มอาสาสมัครทั้งหมดทางคณะผู้วิจัยพบความแตกต่างอย่างมีนัยยะสำคัญทางสถิติระหว่างพฤติกรรมการดูแลเลนส์สัมผัสและความรู้ (p=0.001)

สรุปการวิจัย: อาสาสมัครส่วนใหญ่จากทั้ง 2 กลุ่มเป็นผู้ที่มีความรู้ดี อย่างไรก็ตามกลุ่มนักศึกษาแพทย์มีพฤติกรรมการดูแลเลนส์สัมผัสได้ดีกว่ากลุ่มแพทย์ประจำบ้าน

คำสำคัญ: เลนส์, นักศึกษาแพทย์, แพทย์ประจำบ้าน, พฤติกรรม, ความรู้

Introduction

Contact lens is an ocular medical device used by over 150 million people worldwide[1] The prevalence of contact lens user was increasing from 125 million people in 2014[2], and 40.9 million in 2015 to 45 million in 2019 in the United states[3-4] which considered as the largest contact lens prescribing country in the world[5]. Contact lens can be worn for refractive error correction which offers many advantages over glasses such as better peripheral vision and convenience, particularly who participate in sports. For cosmetic reason, persons who wish to improve self-perception without glasses frame or even change the eye color can use cosmetic colored or big eye contact lens for these purposes. Special corneal conditions such as irregular cornea[6], keratoconus and high anisometropia[7] also need contact lens for therapeutic reason. Despite many researches show contact lens is safe even in young population[8-10], the complications from CL wearer consisting of dryness, conjunctivitis and microbial keratitis, were reported[11-13]. These unwanted events mostly caused by poor behavior of contact lens wear and care[14]. Healthcare professional especial medical students and medical residents are the chief of health care personnel in hospital to educate and to be the role model of their patients. However, many publications reported unsatisfied knowledge and non-compliance of contact lens wear and care in Medical student and healthcare worker[15-17]. The purpose of this study was to determine behavior and knowledge in contact lens wear and care in medical students and residents in Vajira hospital.

Methods

The study was a cross-sectional study that conducted during November 2018 to January 2019. The participants consisted of first to sixth year medical students and residencies (Department of Medicine, Surgery, Pediatric, Obstetrics and Gynecology, Emergency Medicine, Otolaryngology, Ophthalmology, Orthopedic and Family medicine) Faculty of Medicine, Vajira hospital, Navamindradhiraj University, Bangkok, who had used contact lens once for any period of time in recent 1 year. Based on the questionnaire from Leeamornsiri S et al.[17], and additional questions were modified on the basis of the contact lens care guidelines of the American Academy of Ophthalmology[18]. The paper-based questionnaire composed of 3 parts. The first part of questionnaire included sex, gender, age, purpose for using contact lens, type of contact lens, replacing schedule of lens, duration of wearing lens, daily hours using lens, and purchasing place. The second part of questionnaire included participant's behavior during wearing, hygiene of caring contact lens and complication management from their lens. The last part of questionnaire queried the general knowledge of lens wear and care including complication from lens worn. This study protocol was approved by the research committee of Navamindradhiraj University, and was carried out in accordance with the Declaration of Helsinki. Group comparisons were performed with Fisher's exact test using two-sided analysis.

Results

Demographic data of participants and characteristic of contact lens (table 1)

The interviewer-administered questionnaire was conducted among 480 medical students and 180 medical residents, only 116 (24.2%) and 31 (17.2%) wore contact lens within recent 1 year, and the average age is 21.4 (±1.9) and 27.8 (±1.1) years, respectively. Women were the majority accounting for 92 (79.3%) of contact lens used medical students and 25 (80.6%) of contact lens used medical residents. The main reason of wearing contact lens was visual correction (68.1%) in medical students group and 64.5% in medical resident group, following by both cosmetic and visual correction reason. Nearly 90% in both groups wore soft contact lens which mostly monthly renewable

lens 66 (56.9%) in medical student group and 18 (58%) in resident group following by daily disposable lens 49 (42.2%) and 15 (48.8%) in medical student group and medical resident group, respectively. The optical shop was the place that most of participants in both groups purchasing contact lens (96.5% and 87%) following by eye clinic (2.6% and 9.7%) and online internet (1.7% and 6.5%). Approximately one-third of resident groups and one-fifth of medical student group have ever worn big eye or cosmetic contact lens. Participant demographic data and type of contact lens used were not statistic difference between both groups.

Participant's behavior of contact lens wear and care (table 2)

In medical student group, 31 of 116 participants (26.7%) wore lens longer than recommended replacing schedule compared with 11 of 31 (35.5%) in resident group. Sixty-eight of 116 (59.1%) medical students and 21 of 31 (67.7%) in medical residents wore contact lens more than 1 year. Approximately 70% in both groups wore lens more than 8 hours per day. Only 1 of 116 participants (0.9%) in medical student group shared their lens with others which was no statistically significant compared to 2 of 32 (6.5%) in medical resident group. Approximately 23.2% of medical student group and 38.7% of medical resident group swam while wearing lens.

One-fifth of medical student groups and one-third of residency group had experience slept while wearing lens overnight, which was no statistical significance between groups.

Most of participants, 101 of 116 (87.1%) in medical student group and 24 of 31 (77.4%) in medical resident group, always washed their hands before handling lens. Interestingly, 26 of 67 participants (38.8%) in medical student group and 2 of 16 participants (12.5%) in residency group did not rub and rinse lens before wearing the lens, which was statistic significantly different between both groups. Minority of both groups, 7.5% and 6.2% in medical student group and medical resident group had ever rinsed their lens with tap water. The majority of participants in medical student group (84.6%) and medical resident group (66.7%) always changed lens storage solution daily only 3.1% and 6.7% replaced the solution by topping off respectively. Almost half of participants in medical student group and approximately a quarter of participants in medical resident group always cleaned lens case daily. In medical student group, 7 of 65 participants (10.8%) replaced lens case more than every 3 months. On the other hand, all of participants in medical resident group replaced lens case within
3 months.

Participant's knowledge of contact lens wear, care and complications (table 3)

We developed questionnaire in close end question, which did not relate with their behavior, queried knowledge of good compliance for contact lens wear and care, and complications. In the knowledge part of contact lens care, more than 80% in both groups answered correctly as shown in Table 3. Approximately 60% in both groups knew that the lens care solution was not allowed to transfer into smaller travel-size containers. All of participants in both groups knew that the lens should not be rinsed with tap water. The majority in both groups knew that the complications from contact lens included dry eye, contact lens related allergic conjunctivitis, corneal abrasion and microbial keratitis.

Table 1:

Characteristic of participant between medical student group and resident group

	Medical students (N=116) (%)	Residencies (N=31) (%)	p-value
Number of lens wearer/ total number	116/480 (24.2)	31/180 (17.2)	0.059
Mean Age (SD)(year)	21.4 ± 1.9 (18-30)	27.8 ± 1.1 (25-30)	<0.001
Gender			>0.999
Male	24/116 (20.7)	6/31 (19.4)	
Female	92/116 (79.3)	25/31 (80.6)	
Reason of wearing contact lens			0.345
Vision correction	79/116 (68.1)	20/31 (64.5)	
Cosmetic	2/116 (1.7)	2/31 (6.5)	
Both	35/116 (30.2)	9/31 (29)	
How long had been a contact lens wearer			0.047
<1 month	16/115 (13.9)	4/30 (13.3)	
1-6 months	14/115 (59.4)	3/30 (10.0)	
6-12 months	17/115 (14.8)	2/30 (6.7)	
1-5 years	43/115 (37.4)	6/30 (20.0)	
≥ 5 years	25/115 (21.7)	15/30 (50.0)	
Type of contact lens			>0.999
Soft CL	104/116 (89.6)	28/31 (90.3)	
RGP	1/116 (0.9)	0	
Unknown	11/116 (9.5)	3/31 (9.7)	
Replacing schedule			
Daily disposable	49/116 (42.2)	15/31 (48.8)	0.548
Two-weekly renewable	9/116 (7.8)	1/31 (3.2)	0.461
Monthly renewable	66/116 (56.9)	18/31 (58)	>0.999
Place to buy CL (participants can choose more than one choice)			
Eye clinic/ Hospital	3/116 (2.6)	3/31 (9.7)	0.108
Optical shop	112/116 (96.5)	27/31 (87)	0.061
Market	1/116 (0.08)	0	>0.999
Internet	2/116 (1.7)	2/31 (6.5)	0.196
Have the participants ever worn color or big eye CL			
5-7 day/week	5/115 (4.3)	2/31 (6.5)	0.220
3-4 day/week	3/115 (2.6)	2/31 (6.5)	
1-2 day/week	15/115 (13.0)	7/31 (22.6)	
Never worn cosmetic CL	92/115 (80.0)	20/31 (64.5)	

Table 2:

Participant's behavior related to hygiene of contact lens wear and handling of contact lens care solution and the lens cases among medical students and residencies

* exclude daily wear contact lens	Medical students group (%)	Residencies group (%)	p-value
Have you ever slept while wearing CL?			0.235
5-7 day/week	2/115 (1.7)	-	
3-4 day/week	1/115 (0.9)	1/31 (3.2)	
1-2 day/week	20/115 (17.4)	9/31 (29.0)	
Never slept while wearing CL	92/115 (80.0)	21/31 (67.7)	
Sharing contact lens			0.113
5-7 day/week	-	-	
3-4 day/week	1/116 (0.9)	1/31 (3.2)	
1-2 day/week	-	1/31 (3.2)	
Never share CL with other people	115/116 (99.1)	29/31 (93.5)	
Swimming while wearing CL			0.089
5-7 day/week	-	-	
3-4 day/week	4/116 (3.4)	-	
1-2 day/week	23/116 (19.8)	12/31 (38.7)	
Never share CL with other people	89/116 (76.7)	19/31 (61.3)	
Have you ever used tap water for rising lens? *			0.536
5-7 day/week	1/66 (1.5)	-	
3-4 day/week	1/66 (1.5)	1/16 (6.2)	
1-2 day/week	3/66 (4.5)	-	
Never use tap water for rinsing lens	61/66 (92.5)	15/16 (93.8)	
Do you always change lens storage solution daily? *			0.243
Everyday	55/65 (84.6)	10/15 (66.7)	
Every 2-3 days	6/65 (9.2)	3/15 (20.0)	
Every 4-7 days	1/65 (1.5)	-	
Once a week	3/65 (4.6)	2/15 (13.3)	
Topping off lens solution *			0.241
Everyday	2/65 (3.1)	1/15 (6.7)	
Always (>80%)	-	-	
Sometime (<80%)	9/65 (13.8)	4/15 (26.7)	
Never topping off lens solution	54/65 (83.1)	10/15 (66.7)	

Table 2:

Participant's behavior related to hygiene of contact lens wear and handling of contact lens care solution and the lens cases among medical students and residencies (continued)

* exclude daily wear contact lens	Medical students group (%)	Residencies group (%)	p-value
Replacing lens cases *			0.313
Monthly	23/65 (35.4)	8/15 (53.3)	
≤ 3 months	35/65 (53.8)	7/15 (46.7)	
> 3 months	7/65 (10.8)	-	
Do you always cleaned lens case?*			0.094
Everyday	29/63 (46.0)	4/15 (26.7)	
Every 2-3 days	13/63 (20.6)	3/15 (20.0)	
Every 4-7 days	2/63 (3.2)	3/15 (20.0)	
Weekly	16/63 (25.4)	3/15 (20.0)	
> 1 week	3/63 (4.8)	2/15 (13.3)	
Have you always washed hand before handling lens?			0.407
Every time	101/116 (87.1)	24/31 (77.4)	
Always (>80%)	11/116 (9.5)	6/31 (10.4)	
Sometime (<80%)	3/116 (2.6)	1/31 (3.2)	
Do not washed hand before handling lens	1/116 (0.9)	-	
Rub and rinse lens before wearing lens *			0.035
Every time	24/67 (35.8)	9/16 (56.2)	
Always (>80%)	9/67 (13.4)	5/16 (31.2)	
Sometime (<80%)	8/67 (11.9)	-	
Do not rub and rinse lens before wearing lens	26/67 (38.8)	2/16 (12.5)	
Delayed replace lens schedule			0.800
Yes	22/115 (19.1)	5/31 (16.1)	
No	93/115 (80.9)	26/31 (83.9)	

Table 3:

General knowledge of contact lens wear and care among medical students and residencies evaluated by using 10 closed- questions. Do you agree or disagree in following situations

	Medical student group		Residency group		p-value
	Agree	Disagree	Agree	Disagree	
Wearing contact lens while sleeping don't lead to get eye infection	12/116	104/116	2/31	29/31	0.735
Contact lens can be shared to others	1/116	115/116	2/31	29/31	0.113
Prolong using lens longer than replacing schedule was allowed	12/116	104/116	2/31	29/31	0.735
Using tap water rinsed contact lens was allowed due to chloride can kill the microbe on lens surface	0	116/116	0	31/31	-
Contact lens can wear while swimming	18/116	98/116	9/31	22/31	0.115
Should change storage solution daily to remove the microbe	106/116	10/116	25/31	6/31	0.106
We don't have to change lens storage every 3 months because the case does not relate with the growth of microbe	18/116	98/116	6/31	25/31	0.592
We can Topping off lens solution without replacing lens solution	3/116	112/116	2/31	29/31	0.607
Normal saline and/or artificial tears can be used instead of multipurpose solution for cleaning contact lens	25/116	89/116	12/31	19/31	0.109
Do not transfer contact lens solution into smaller travel-size containers	70/116	46/116	20/31	11/31	0.836

Comparison between behavior and knowledge (Figure 1, 2)

Following the information in table 2, the number of correct answers were counted and the participants were divided into 3 groups according to the following criteria. Good behavior participants were defined if the score was equal or greater than 8. The fair behavior was defined if the score was 6-7. The participants who had score less than 6 were defined as poor behavior group. Seventy-three percent of medical students and 48.4% of residents were good behavior, while 5.2 % of medical student group and 3.2% of residency group were poor behavior. There was statistically significant difference in behavior among both groups. (p=0.013)

The knowledge of lens care and wear including contact lens complication were divided in 3 groups by using criteria as follows, the good knowledge was defined if the participants had score equal or greater than 8, the poor knowledge was defined if the score is less than 6. The participants with the score of 6-7 were identified as fair knowledge. More than three-quarter of both medical student and residency group were defined in good knowledge.

The minority of both groups (1.7 % of medical students and 3.2% of residents) were poor knowledge. There was no statistically significant difference in terms of the knowledge among both groups (p=0.297). In all participants, our study found statistic significant difference between knowledge and behavior
(p=0.001).

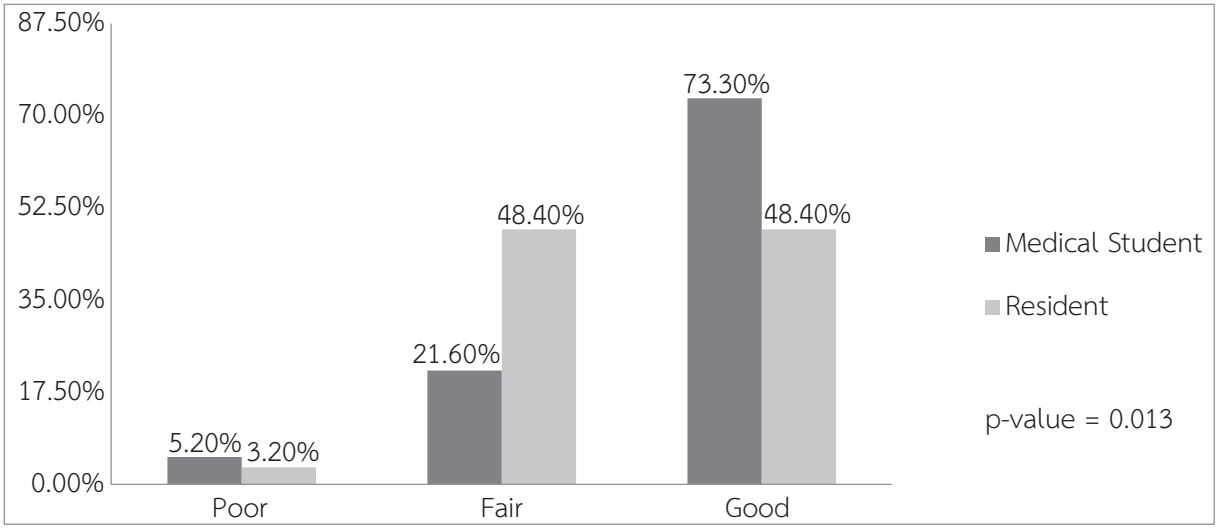

Figure 1: Comparison of behavior in contact lens wear and care between medical student and resident

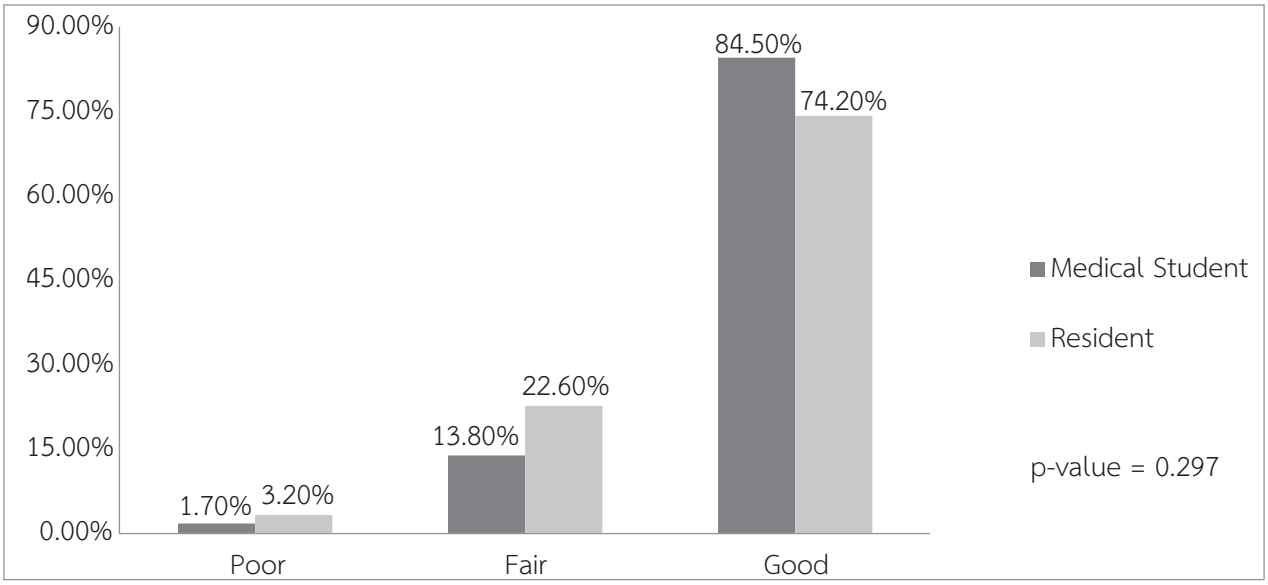

Figure 2: Comparison of knowledge in contact lens wear and care between medical student and resident

Discussion

Vajira hospital locates in Bangkok, the capital city of Thailand, where the majority of contact lens users live in and the We found lots of complications from using contact lens such as conjunctivitis, contact lens related allergic conjunctivitis and microbial keratitis which continuously increased especially in contact lens user who had poor compliance and lens care hygiene. The knowledge and understanding of contact lens care, including awareness of complications especially in medical students and medical residents are very important for primary educating patients as a role of health care providers. In this study, the prevalence of contact lens wearer was 24.2% in medical student group and 17.2% in medical resident group which lesser than the previous study was varied from Ibrahim NK and Leeamornsiri S that reported 32.2-40.5%[16-17]. Our study defined who wore lens in recent 1 year as same as from Leeamornsiri S. study[17] in Thailand. The difference of prevalence may be from time frame difference. Whereas the study from Ibrahim NK[16] enrolled medical students who had ever worn contact lens once that cause higher prevalence than our study. Female contact lens user is the majority in this study (80%) which was similar to many previous studies[16-17]. Approximately 65% in both groups used contact lenses for visual correction following by both cosmetic and vision correction reason (30%). The reason of increasing of cosmetic and visual correction from the study in 2015[17] due to the difference in study time frame and variety of available contact lens design in the market which can provide power in lens for visual correction and aesthetic color in the same time. Almost 90% of participants wore soft contact lens which are not difference from others[16-17]. Furthermore 42.2% in medical student group and 48.8% in residency group used daily disposable type lens increasing from 27.6%[17] but difference from King Abdulaziz University, Saudi Arabia[16] which reported yearly type as the commonest type of contact lens used. We found the majority of participants purchased contact lens at optical shop, similarly to the study from Thammasart hospital in Thailand. On the other hand, previous study in Sydney reported that most of participants bought lenses from optometrist's prescription[19]. The difference of buying place depend on the law regulation in each country.

According to the behavioral factor, we found 6 improper contact lens compliance and care practices including sleeping with their lens, swimming with lens, topping off lens storage solution, not cleaning case daily, prolong using lens over replacement schedule and not rubbing and rinsing before handling lens. Twenty percent of medical student group and 32.3% in medical resident group slept while wearing contact lens compared to 9.6% in Thammasart University and 29.5%[17] in King Abdulaziz University[16]. The difference from others study especially in medical resident group due to we included both nap and overnight slept in our study. Additionally, harder works and having night shifts in medical resident group might be the factor that made medical residents trended to easily slept before taking off their lens. However, the study from USA reported 50.2% of adult wearer slept overnight with their lens[3]. The difference type of lens, country and population may affect the behaviors of contact lens users. Our study found 23.3% in medical student group swam with their lens which coincide with the results from other studies[16-17,20]. Wearing lens longer than recommended were found approximately one-third of participants in both groups which was the same prevalence as found in Thammasart study[17]. Only one-third in medical student group and a half in residency group rubbed and rinsed their lens everytime before putting on which had not been reported from previous studies. We also found that the lens care hygiene and compliance in CLs wearer in medical student group were significantly better than medical resident group. The possible reason was a lack of

time to follow lens wear and care instructions in medical resident group.

Regarding the knowledge questions, more than 80% in both groups had good knowledge (correct answers at least 8 of 10 questions). Approximately 40% in both groups answered incorrectly in 2 questions consisting of using normal saline or artificial tears instead of multipurpose solution for cleaning lens and transfer lens solution in smaller travel-size containers. However, the previous study reported the knowledge of contact lens wear and care among medical students in Saudi Arabia which was less than our study[16]. We suspected that they possibly do not know the difference action of normal saline and multi-purpose cleaning solution for cleaning contact lens. Some people think that normal saline can be used to clean contact lens and they do not emphasize using multipurpose solution to remove bacteria before using normal saline solution. We found most of participants in both groups had good knowledge but less proportion in good behavior of lens wear and care hygiene especially in medical resident group.

Limitations

This study included only medical students and residents from a single university hospital, which might not represent contact lens knowledge and behavior in general medical students and residents. We also did not include other healthcare professionals such as pharmacist, nurse and medical staffs in the survey. therefore, our results cannot infer to contact lens situation in that population.

Conclusion

The majority of participants in medical student and residency group have good knowledge contrast to their behaviors of contact lens care. This indicates that the contact lens educational strategy in Thailand nowadays is still ineffective enough to change the behavior of contact lens users. Even in the medical personnel, the poor behavior was high especially in medical students. The awareness of contact lens complications causing form poor contact lens care in Thai society should be raised. Further study is needed to identify factors that affect in good contact lens behavior in order to reduce severe ocular complications from using contact lens. The limitation in this study is small number of participants that can not represent the knowledge and behavior of contact lens wear and care in whole medical profession in Bangkok, Thailand.

References

1. Moreddu R, Vigolo D and Yetisen AK. Contact lens technology: From fundamentals to applications. Adv Healthc Mater. 2019;8(15): e1900368
2. Barr JT. Contact Lens Spectrum's annual report of major corporate and product developments and events in the contact lens industry in 2004, as well as predictions for 2005 [internet]. Contact Lens Spectrum.2005[cited 2019 Oct 16]. Available from: https://www.clspectrum.com/issues/2005/january-2005/2004-annual-report
3. Cope JR, Collier SA, Rao MM, Chalmers R, Mitchell GL, Richdale K, et al. Contact lens wearer demographics and risk behaviors for contact lens-related eye infections-United States, 2014. MWWR Morb Mortal Wkly Rep 2015;64(32): 865-84.
4. Konne NM, Collier SA, Spangler J and Cope JR. Healthy contact lens behaviors communicated by eye care providers and recalled by patients-United States, 2018. MWWR Morb Mortal Wkly Rep 2019;68(32):693-7.
5. Efron N, Nichlos JJ, Woods CA and Morgan PB. Trends in US contact lens prescribing 2002-2014. Optom Vis Sci 2015;92(7):758-67.
6. Arumugam AO, Rajan R, Subramanian, Mahadevan R. PROSE for irregular corneas at a tertiary eye care center. Eye Contact Lens 2014;40:71-3.

7. Tan DTH, Pullum KW, Buckley RJ. Medical applications of scleral contact lenses: 1. A retrospective analysis of 343 cases. Cornea 1995;14:130-7.
8. Walline JJ, Long S, Zadnik K. daily disposable contact lens wear in myopic children. Optom Vis Sci 2004;81:255-9.
9. Chharm J, Cheung SW, Cho P. Practitioners' analysis of contact lens practice in Hong Kong. Cont Lens Anterior Eye 2010;33:104-11.
10. Morgan PB, Efron N, Helland M, Itoi M, Jones D, Nichols JJ, et al. Demographics of international contact lens prescribing. Cont Lens Anterior Eye 2010;33:27-9.
11. Lim CHL, Stapleton F and Mehta JS. Review of contact lens-related complications. Eye & Contact Lens 2018;0:1-10.
12. Alipour F, Khaheshi S, Soleimanzadeh M, Heidarzadeh S and Heydarzadeh S. Contact lens-related complications: A review. J Ophthalmic Vis Res 2017;12(2):193-204.
13. Arshad M, Carnt N, Tan J, Ekkeshis I and Stapleton F. Water exposure and the risk of contact lens-related disease. Cornea 2019;38(6):791-7.
14. Sauer A, Meyer N, Bourcier T. Risk facots for contact lens-related microbial keratitis: A case-control multicenter study. Eye & Contact Lens 2016;42(3):158-62.
15. Khan MH, Mubeen SM, Chaudhry TA, Khan SA. Contact lens use and its compliance for care among healthcare workers in Pakistan. Indian J Ophthalmol 2013;61(7):334-7.
16. Ibrahim NK, Seraj H, Khan R, Baabdullah M, Reda L. Prevalence, habits and outcomes of using contact lenses among medical students. Pak J Med Sci 2018;34(6):1429-34.
17. Leeamornsiri S, Titawattanakul Y. Comparative knowledge and behavior of contact lens care between medical and non-medical students. J Med Assoc Thai. 2015;98 (suppl. 3):S16-23.
18. Boyd K. How to Take Care of Contact Lenses [Internet]. American Academy of Ophthalmology; 2019[cited 2019 Nov 5]. Available from: https://www.aao.org/eye-health/glasses-contacts/contact-lens-care.
19. Wu Y, Carnt N, Stapleton F. Contact lens user profile, attitudes and level of compliance to lens care. Cont Lens Anterior Eye. 2010;33(4): 183-8.
20. Gyawali R, Nestha Mohamed F, Bist J, Kandel H, Marasini S, Khadka J. Compliance and hygiene behavior among soft contact lens and wearers in Maldives. Cli Exp Optom. 201497(1):43-7.

Relationship between Serum Ferritin Levels and Biochemical Markers of Bone Turnover in Postmenopausal Women

Somnimit Luengratsameerung MD[1*]

[1] Department of Obstetrics and Gynecology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand

* Corresponding author, e-mail address : somnimit@nmu.ac.th

Vajira Med J. 2020; 64(4) : 287-96

http://dx.doi.org/10.14456/vmj.2020.28

Abstract

Objective: To study the relationship between serum ferritin levels and biochemical markers of bone turnover in postmenopausal women.

Methods: This cross-sectional study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine Vajira Hospital, Bangkok, Thailand. One hundred and twenty four postmenopausal Thai women were recruited from menopause clinic between December 2015 and March 2016. The inclusion criteria were age 40 years or more, body mass index (BMI) of 19-30 kg/m^2, not use menopausal hormone therapy (MHT) within the last 3 months, adequate cessation period of any bone antiresorptive agent, no underlying disease which possibly associated with chronic anemia, and no history of steroid hormone, anabolic agent, or anticoagulant use. The subjects were excluded if their blood specimens were unsuccessfully collected or incompletely analyzed. Two kinds of biochemical markers of bone turnover were selected to study. The first one was a bone-formation marker, called procollagen type I N- terminal propeptide (P1NP) and the second was a bone-resorption marker, namely C-terminal cross-linked telopeptide of type I collagen (CTx). Each marker was evaluated its relationship to serum ferritin.

Results: After recruitment, one subject was excluded because her blood specimen was loss during transfer, therefore 123 cases were left for analysis. Mean (SD) age, BMI, duration of menopause, and number of parity of the overall subjects were 56.8 (4.2) years, 24.3 (3.1) kg/m^2, 7.1 (5.3) years, and 1.3 (1.1), respectively. Mean (SD) serum ferritin, P1NP, and CTx levels were 147.75 (95.11), 63.90 (16.70), and 0.463 (0.154) ng/ml, respectively. Serum ferritin levels were negatively correlated with P1NP and with CTx levels (r = -0.149, p = 0.099 and r = -0.038, p = 0.677, respectively).

Conclusion: Serum ferritin levels had non-significant inverse relationship with P1NP and CTx levels in postmenopausal women. The long-term effects of low iron storage on biochemical markers of bone turnover are needed to be further evaluated.

Keywords: Iron deficiency anemia, ferritin, osteoporosis, biochemical markers of bone turnover

ความสัมพันธ์ระหว่างระดับเฟอร์ริตินในน้ำเหลืองของเลือดและดัชนีชีวเคมีของกระบวนการสร้างและสลายกระดูกในสตรีวัยหมดระดู

สมนิมิตร เหลืองรัศมีรุ่ง พ.บ., ว.ว. สูติศาสตร์-นรีเวชวิทยา[1*]

[1] ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช กรุงเทพมหานคร ประเทศไทย

* ผู้ติดต่อ, อีเมล: somnimit@nmu.ac.th

Vajira Med J. 2020; 64(4) : 287-96

http://dx.doi.org/10.14456/vmj.2020.28

บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ระหว่างระดับเฟอร์ริตินในน้ำเหลืองของเลือดและดัชนีชีวเคมีของกระบวนการสร้างและสลายกระดูกในสตรีวัยหมดระดู

วิธีดำเนินการวิจัย: ดำเนินการศึกษาแบบภาคตัดขวาง ณ ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช กรุงเทพมหานคร ประเทศไทย โดยคัดเลือกสตรีไทยวัยหมดระดู จำนวน 124 คน ที่มารับการตรวจในคลินิกวัยทอง ตั้งแต่เดือนธันวาคม พ.ศ. 2558 ถึง เดือนมีนาคม พ.ศ. 2559 โดยมีเกณฑ์คัดเข้า ได้แก่ อายุ 40 ปีขึ้นไป มีค่าดัชนีมวลกาย 19-30 กิโลกรัม/เมตร^2 ไม่มีการใช้ฮอร์โมนเพื่อรักษาภาวะหมดระดูใน 3 เดือนที่ผ่านมา หยุดยาต้านการสลายกระดูกมาในระยะเวลาที่เพียงพอ ไม่มีโรคประจำตัวที่สัมพันธ์กับภาวะโลหิตจางเรื้อรัง และไม่มีประวัติการใช้สารสเตียรอยด์ สารอะนาบอลิก หรือยาละลายลิ่มเลือด อาสาสมัครจะถูกคัดออกในกรณีที่เก็บตัวอย่างเลือดไม่ได้หรือมีผลการวิเคราะห์ที่ไม่สมบูรณ์ ดัชนีชีวเคมีที่ทำการศึกษามี 2 ชนิด ได้แก่ ดัชนีการสร้างกระดูกชนิด procollagen type I N- terminal propeptide (P1NP) และดัชนีการสลายกระดูกชนิด C-terminal cross-linked telopeptide of type I collagen (CTx) ค่าของดัชนีแต่ละชนิดจะนำไปวิเคราะห์หาความสัมพันธ์กับระดับเฟอร์ริตินในน้ำเหลืองของเลือด

ผลการวิจัย: หลังการคัดเข้า มีอาสาสมัคร 1 รายถูกคัดออกเนื่องจากตัวอย่างเลือดที่เก็บมามีการสูญหายระหว่างนำส่งตรวจ จึงเหลืออาสาสมัครที่จะนำมาวิเคราะห์จำนวน 123 ราย ค่าเฉลี่ย (ส่วนเบี่ยงเบนมาตรฐาน) อายุ ดัชนีมวลกาย ระยะเวลาการหมดระดู และจำนวนการคลอดของอาสาสมัครทั้งหมด เท่ากับ 56.8 (4.2) ปี 24.3 (3.1) กิโลกรัม/เมตร^2 7.1 (5.3) ปี และ 1.3 (1.1) ตามลำดับ ค่าเฉลี่ย (ส่วนเบี่ยงเบนมาตรฐาน) ของระดับเฟอร์ริตินในน้ำเหลืองของเลือด P1NP และ CTx เท่ากับ 147.75 (95.11), 63.90 (16.70), และ 0.463 (0.154) นาโนกรัม/มิลลิลิตร ตามลำดับ ระดับเฟอร์ริตินในน้ำเหลืองของเลือดมีความสัมพันธ์ในทิศทางตรงกันข้ามกับระดับของ P1NP และ CTx ($r = -0.149$, $p = 0.099$ and $r = -0.038$, $p = 0.677$ ตามลำดับ)

สรุป: ระดับเฟอร์ริตินในน้ำเหลืองของเลือดในสตรีวัยหมดระดู มีความสัมพันธ์ในทิศทางตรงกันข้ามกับระดับของ P1NP และ CTx อย่างไม่มีนัยสำคัญ จำเป็นต้องทำการศึกษาเพิ่มเติมต่อไปเกี่ยวกับผลระยะยาวของการมีธาตุเหล็กสะสมในปริมาณต่ำ ที่มีต่อดัชนีชีวเคมีของกระบวนการสร้างและสลายกระดูก

คำสำคัญ: ภาวะโลหิตจางจากการขาดธาตุเหล็ก, เฟอร์ริติน, โรคกระดูกพรุน, ดัชนีชีวเคมีของกระบวนการสร้างและสลายกระดูก

Introduction

Osteoporosis is a common health problem among postmenopausal women[1]. It has long been believed that pathophysiology of the disease in women of this age-group is related to estrogen deficiency after menopause[2]. However, much previous epidemiological data showed that osteoporosis was not present in every postmenopausal women[3]. Such information suggested that mechanisms of this disease are possibly complex[4]. Even estrogen deficiency might be a main contributor it is not the sole risk factor of the development of postmenopausal osteoporosis. Several known risk factors which participate in the mechanisms are age, genetics, inadequate calcium and vitamin D intake, smoking and thinness[5]. At present, there is still no conclusion about which factor is the most important, therefore the diagnosis of osteoporosis is based primarily on screening tools developed by combining multiple risk factors[5].

Because prior researches reported that osteoporosis was 2 to 6 times more prevalent in female than male population[1,6], thereafter later studies usually focused on risk factors of the disease that specific to female sex, for example, serum estrogen levels. However, the results did not show any statistically significant association between serum estrogen levels and bone turnover rates[5].

Other health factors that probably relate to osteoporosis in female population are iron deficiency anemia (IDA)[7-10] and hemoglobin levels[11-12]. Previous study on hematologic status revealed that IDA was more common and average hemoglobin levels were less in women than men[13]. In other words, women usually have lower iron storage for hemoglobin synthesis because of repeated losses during menstruations and pregnancies[14].

Continuing iron losses during pubertal and reproductive ages may induce bone marrow to be more active in women than men. Bone marrow hyperactivity in women, on one hand, is a physiologic compensation resulting in a more red blood cell progenitor synthesis for the prevention of IDA[4]. On the other hand, this hyperactivity is supposed to be a pathophysiologic process which cause an excessive proliferation of other progenitor cells including osteoclasts[4]. Excessive osteoclast proliferation may induce a faster bone resorption and a more prevalent osteoporosis in women than men[4].

Owing to the evidence that depleted iron storage may affect bone turnover rate especially in women[4], there were several studies those evaluating the associations between IDA and osteoporosis[7-9,12]. All of those studies used hemoglobin and/or hematocrit levels as markers of IDA and Bone Mineral Density (BMD) or the incidence of osteoporotic fracture as a marker of osteoporosis. There was only one study which analyzed relationship between markers of iron storage e.g. serum ferritin and biochemical markers of bone turnover[10]. That study showed a significant reverse relationship between serum ferritin and bone resorption marker. However, the study was conducted in premenopausal women. Because of the shortness of study which designed to investigate the relationship between markers of iron storage and biochemical markers of bone turnover in postmenopausal period, the present study was designed to evaluate the relationship between serum ferritin levels and biochemical markers of bone turnover in postmenopausal women.

Methods

This cross-sectional study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine Vajira Hospital, Bangkok, Thailand. One hundred and twenty four postmenopausal Thai women, aged 40 years or more, were recruited from the menopause clinic between December 2015 and March 2016. Subjects were included to study if they had body mass index (BMI) of 19-30 kg/m^2, no prior use of menopausal hormone therapy (MHT) within the last 3 months,

and adequate cessation period after osteoporosis treatment with antiresorptive agents, i.e. at least 2 years after intravenous regimen, 1 year after subcutaneous regimen, and 2 years, 1 year, 6 months, and 2 months after oral regimens for 48 weeks or longer, 8-48 weeks, 2-8 weeks, and less than 2 weeks, respectively. All studied subjects had no history of gastrointestinal bleeding, malabsorption, gastric ulcers, gastrointestinal tract surgeries, inflammatory bowel diseases, coronary artery diseases or congestive heart failure, chronic renal failure, thyroid diseases, parathyroid diseases, malignancies, hematologic diseases, or vitamin D deficiency, and no history of steroid hormone, anabolic agent, or anticoagulant use. Informed consent process were performed by investigator or the nurse at menopause clinic who was assigned as a research assistant in this study. Subjects were excluded if they withdrew from the study, refused to undergo venous puncture or their blood samples were unsuccessfully or inadequately collected. Subjects were also excluded if their blood specimens were not completely analyzed due to any error on the handling or transferring process. Additional BMD tests were performed in subjects who had the levels of biochemical markers of bone turnover higher than the cut-off points (48.35 ng/ml for P1NP or 0.328 ng/ml for CTx). Then standard treatments of osteoporosis were given if they had T-score of BMD less than -2.5. Subjects who had ferritin levels below the cut-off point of iron deficiency (100.00 ng/ml) were referred to hematologist for further investigations and treatments.

The sample size was estimated by using Pearson's correlation coefficient between ferritin level and biochemical marker of bone turnover, named as procollagen N-terminal propeptide from the previous study which revealed the value of 0.73[15]. Initially, with a level of bilateral significance of 95% (α error=0.05) and a power of 80% (β error=0.2), the sample size was 13 subjects. Then the number was increased to be 113 because the relationships between 10 other studied factors and biochemical markers of bone turnover were also planned to be analyzed. Finally, the recruitment was increased up to 124 for preventing a probable 10% loss of the data.

The study was approved by the Institutional Review Board of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand, and all subjects provided their written informed consent before recruitment.

Two kinds of biochemical markers of bone turnover were selected to study. The first one was a bone-formation marker, called procollagen type I N- terminal propeptide (P1NP) and the second was a bone-resorption marker, namely C-terminal cross-linked telopeptide of type I collagen (CTx). Each marker was evaluated its relationship to serum ferritin. After recruitment, subjects were undergone history taking and physical examinations to collect and record for baseline data and controlled factors including age, body built (weight, height and BMI), duration of menopause, parity, history of MHT use, underlying diseases, history of osteoporosis/ fractures, history of cigarette smoking/ alcohol consumption, levels of education and physical activity levels (PAL). Then, each subject's blood sample was drawn from cubital vein in a volume of 6-10 milliliters on the next official day between 8:00 and 9:00 a.m. after an overnight fast for at least 8 hours. Blood samples were collected in EDTA blood tubes and then sent to be analyzed for the serum levels of ferritin, P1NP and CTx.

Laboratory assays

Blood samples were centrifuged at 3,000 rpm for 10 min and the separated serum samples were stored at -20°C until assay. Ferritin, P1NP and CTx levels were analyzed by a commercially available electrochemiluminescence immunoassay or ECLIA (Roche Elecsys 2010, Mannheim, Germany). The lower-upper detection limits of the assay are 0.5-2,000, 5-1,200 and 0.01-6 ng/ml for ferritin,

P1NP, and CTx, respectively. And the coefficients of variation are ranged from 1.5-2.5, 1.2-2.1, and 2.2-3.5% for ferritin, P1NP, and CTx, respectively. Normal ranges of ferritin, P1NP, and CTx levels are 13.00-150.00, 40.78-48.35, and 0.293-0.328, respectively. Laboratory assays in this study were performed in-house, and calibrated in every new lot of reagents. Internal and external quality controls were tested in daily and monthly basis, respectively.

Statistical analysis

Data presentation and statistical analysis were performed as following. Descriptive statistics (mean (standard deviation, SD) or median (range) and percentage were used to express demographic, baseline, and measurement outcome data. Relationships between each biochemical marker of bone turnover (P1NP and CTx) and ferritin were tested by an analysis of Pearson's correlation. All other controlled factors which affecting bone turnover were analyzed by chi-square or Fisher-exact test. A p level of < 0.05 was considered statistically significant.

Results

One hundred and twenty four subjects who met the inclusion criteria were recruited to the study. One subject was excluded because her blood specimen was loss during transfer, therefore 123 cases were left for analysis. The mean (SD) age, BMI, duration of menopause, and number of parity of the overall subjects were 56.8 (4.2) years, 24.3 (3.1) kg/m^2, 7.1 (5.3) years, and 1.3 (1.1), respectively. The overall mean (SD) ferritin, P1NP, and CTx levels were 147.75 (95.11), 63.90 (16.70), and 0.463 (0.154) ng/ml, respectively. Serum ferritin levels were negatively correlated with P1NP and with CTx levels but the degree of correlations were not statistically significant (r = -0.149, p = 0.099 and r = -0.038, p = 0.677, respectively). Both correlations are shown in figure 1 and 2.

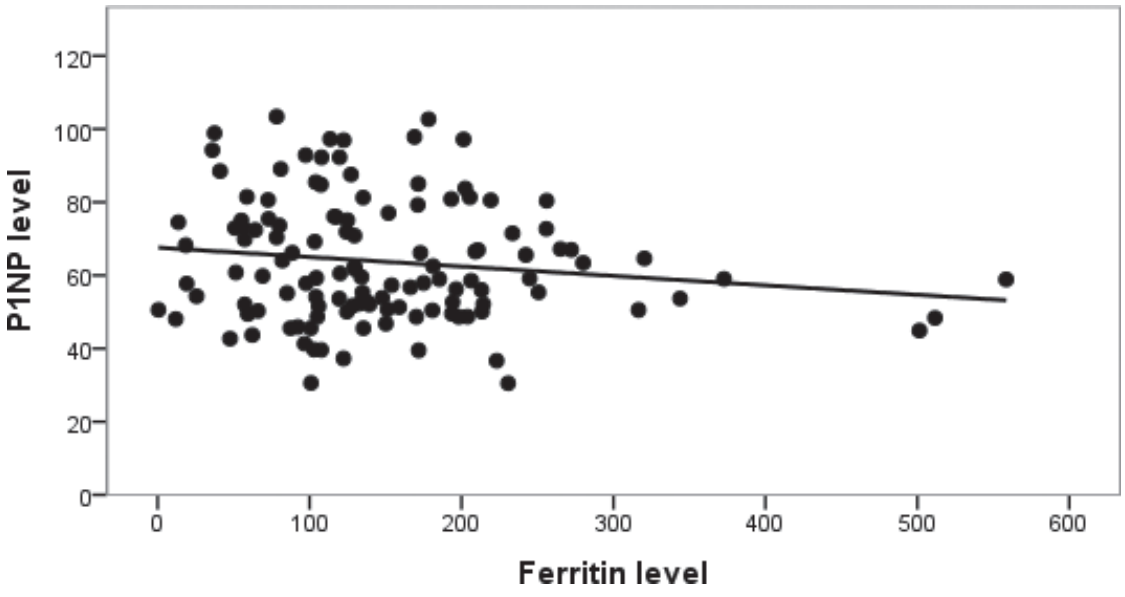

Figure 1: Pearson's correlation between ferritin and procollagen type I N- terminal propeptide (P1NP) levels

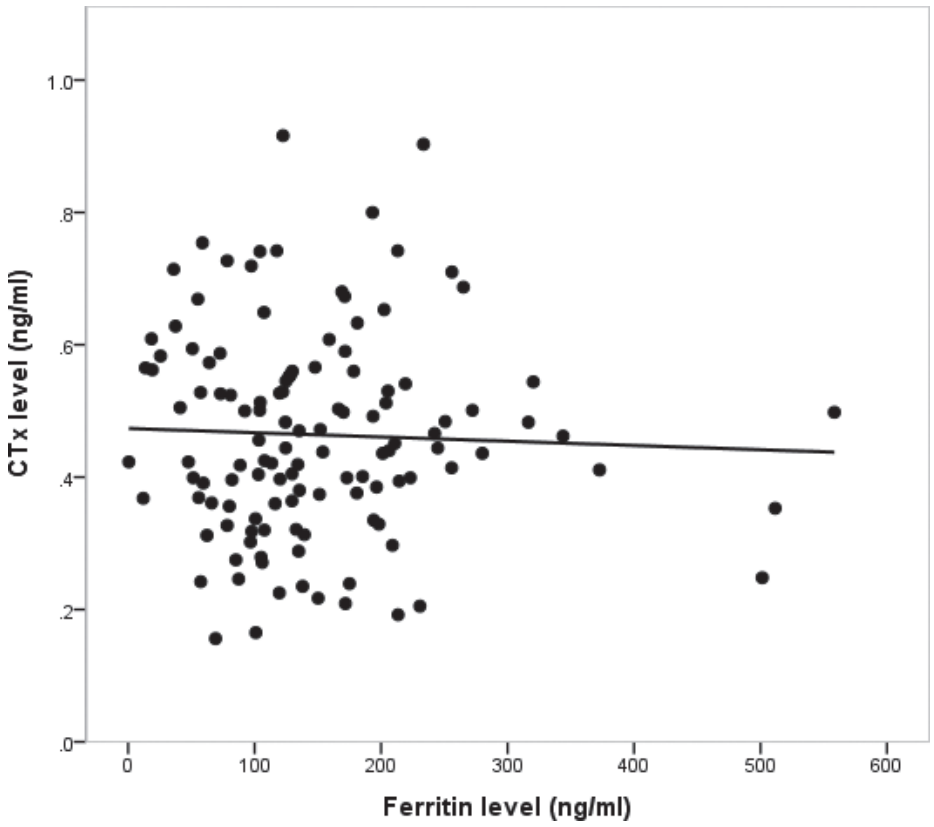

Figure 2: Pearson's correlation between ferritin and C-terminal cross-linked telopeptide of type I collagen (CTx) levels

When categorized subjects by the levels of biochemical markers of bone turnover, there was no statistically significant difference in subjects' characteristics between groups of normal and high P1NP and CTx levels (Table 1).

A proportion of subjects who had history of prior use of MHT is statically higher in normal CTx group than high CTx group (20.83% vs. 3.03%, p = 0.007). Subjects in high P1NP group had statistically significant higher PAL than normal P1NP group (63.21% vs 29.41% who had moderate to high activity, p = 0.024). All other studied factors categorized by levels of biochemical markers of bone turnover are shown in Table 2.

Discussion

Relationship between IDA and osteoporosis has been hypothesized and frequently studied since the last 10 years[7-10,12]. However, results of those studies are still conflicting and most of the studies used hemoglobin and/or hematocrit levels as markers of IDA and BMD or the incidence of osteoporotic fracture as a marker of osteoporosis[7-9,12]. Serum ferritin is the best international standard and the least invasive single test for the evaluation of iron storage[17]. Additionally, biochemical markers of bone turnover were claimed in many previous reports that they were beneficial for clinical uses in terms of predicting the risk of occurrence and monitoring the therapeutic response of osteoporosis[18-23]. However, there was only one

study which analyzed relationship between serum ferritin and biochemical markers of bone turnover[10]. Therefore, such a relationship is valuable to be additionally studied and, in my knowledge, this study might be one of the few which design to investigate this relationship.

Both results of correlation analysis between ferritin and P1NP, and, ferritin and CTx in this study were in negative direction. These seem to answer the hypothesis that the lower iron storage might cause the higher bone marrow activity resulting in more proliferation of progenitor cells including osteoclasts which activate bone remodeling. Nevertheless, the degree of both correlations was low and did not reach statistical significance. Thus, whether IDA is the risk factor of osteoporosis could not be concluded. Design of this study that was cross-sectional may involve in the non-significant results. Because it is possible that the status of low iron storage might need to sustain for a longer period before inducing an increase in bone remodeling activity. Therefore, studies which are prospectively designed might be more appropriate to prove this assumption.

When compared with the previous one study which also analyzed relationship between markers of iron storage and biochemical markers of bone turnover[10], this study had both the different and the same results. The previous study showed that IDA subjects had statistically significant higher bone-resorption marker than non-IDA subjects, but this study did not. On contrary, both studies also showed that IDA did not have statistically significant effect on the levels of bone-formation marker. However, the previous study conducted in premenopausal women with continuing menstrual cycles. IDA in the studied group might have a more severity and/or longer duration than in this study, therefore effects on the change of bone-resorption marker were more obvious.

Table 1:

Characteristic factors of subjects categorized by levels of biochemical markers of bone turnover. Data are given as mean (SD).

Factors	Markers levels					
	P1NP* (ng/ml)		*P*	CTx* (ng/ml)		*p*
	Normal (n=17)	High (n=106)		Normal (n=24)	High (n=99)	
Age (years)	57.71 (4.65)	56.68 (4.10)	0.348[a]	55.79 (3.80)	57.07 (4.24)	0.179[a]
BMI (kg/m^2)	23.77 (3.16)	24.35 (3.15)	0.482[a]	24.95 (2.98)	24.11 (3.17)	0.238[a]
Duration of menopause (years)	7.12 (5.61)	7.05 (5.29)	0.959[a]	7.46 (5.18)	6.96 (5.36)	0.681[a]
Ferritin levels (ng/ml)	103.40 (109.12)	149.32 (93.15)	0.650[a]	140.394 (90.39)	149.53 (96.57)	0.675[a]

BMI; body mass index, P1NP; procollagen type I N- terminal propeptide, CTx; C-terminal cross-linked telopeptide of type I collagen,
* Cut-off points between normal and high levels for P1NP and CTx are 48.35 and 0.328 ng/ml, respectively. a; t-test

Table 2:

Proportion of subjects categorized by studied factors and levels of biochemical markers of bone turnover. Data are given as number (percent).

Factors	Markers levels					
	P1NP* (ng/ml)		*p*	CTx* (ng/ml)		*p*
	Normal (n=17)	High (n=106)		Normal (n=24)	High (n=99)	
Ferritin level** (ng/ml)						
Normal	11 (64.71)	75 (70.75)	0.255[a]	16 (66.67)	70 (70.71)	0.150[a]
Low	6 (35.29)	31 (29.25)		8 (33.33)	29 (29.29)	
MHT use						
Never	16 (94.12)	99 (93.40)	1.000[b]	19 (79.17)	96 (96.97)	0.007[b]
Prior use	1 (5.88)	7 (6.60)		5 (20.83)	3 (3.03)	
Underlying diseases***						
Absent	15 (88.24)	100 (94.34)	0.305[b]	21 (87.50)	94 (94.95)	0.187[b]
Present	2 (11.76)	6 (5.66)		3 (12.50)	5 (5.05)	
Previous osteoporosis/ fractures	16 (94.12)	103 (97.17)	0.453[b]	23 (95.83)	96 (96.97)	1.000[b]
No	1 (5.88)	3 (2.83)		1 (4.17)	3 (3.03)	
Yes						
Physical activity levels						
Sedentary	4 (23.53)	6 (5.66)	0.024[b]	2 (8.33)	8 (8.08)	0.655[b]
Low	8 (47.06)	33 (31.13)		9 (37.50)	32 (32.32)	
Moderate	5 (29.41)	59 (55.66)		13 (54.17)	51 (51.52)	
High	0 (0.00)	8 (7.55)		0 (0.00)	8 (8.08)	

MHT; menopausal hormone therapy, P1NP; procollagen type I N- terminal propeptide, CTx; C-terminal cross-linked telopeptide of type I collagen, * Cut-off points between normal and high levels for P1NP and CTx are 48.35 and 0.328 ng/ml, respectively. ** Cut-off point between normal and low levels ferritin is 100.00 ng/ml[16]. ***diabetes mellitus/ hypertension/ dyslipidemia, a; chi-square test, b; Fisher exact test

Two of all other studied factors which were statistically significant associated with the changes in biochemical markers of bone turnover were history of prior use of MHT and PAL. The prior use of MHT was present in a higher proportion in normal CTx subjects. Long-term positive effect of MHT on bone health i.e. decreased bone resorption was confirmed in the study which start the therapy in early postmenopausal period[18]. Moderate to high PAL was found to be associated with high P1NP level in this study. Such an association may reflect that higher physical activity can stimulate more bone formation and could support the theory of life style risk factors of osteoporosis. However, the sample size of this study was not calculated based on the association of these two factors with biochemical markers of bone turnover, so the results should be interpreted with caution. In addition, these results are not new knowledge and also expected to be found.

This study was limited by non-prospective design, no randomization between the studied and controlled groups, and small number of subjects.

In conclusion, serum ferritin levels had non-significant inverse relationship with P1NP and CTx levels in postmenopausal women. Laboratory investigations to determine iron storage are still not recommended to use as screening tests of osteoporosis in postmenopausal women. The long-term effects of low iron storage, categorized by different duration and/or severity, on biochemical markers of bone turnover are needed to be further evaluated.

Acknowledgement

The research was funded by Research Fund.

References

1. Limpaphayom KK, Taechakraichana N, Jaisamrarn U, Bunyavejchevin S, Chaikittisilpa S, Poshyachinda M, et al. Prevalence of osteopenia and osteoporosis in Thai women. Menopause 2001; 8: 65-9.
2. Tella SH, Gallagher JC. Prevention and treatment of postmenopausal osteoporosis. J Steroid Biochem Mol Biol 2014; 142: 155-70.
3. Gómez-de-Tejada Romero MJ, Navarro Rodríguez MD, Saavedra Santana P, Quesada Gómez JM, Jódar Gimeno E, Sosa Henríquez M. Prevalence of osteoporosis, vertebral fractures and hypovitaminosis D in postmenopausal women living in a rural environment. Maturitas 2014; 77: 282-6.
4. Gurevitch O, Slavin S. The hematological etiology of osteoporosis. Med Hypotheses 2006; 67: 729-35.
5. North American Menopause Society. Management of osteoporosis in postmenopausal women: 2010 position statement of The North American Menopause Society. Menopause 2010; 17: 25-54.
6. Pongchaiyakul C, Apinyanurag C, Soontrapa S, Soontrapa S, Pongchaiyakul C, Nguyen TV, et al. Prevalence of osteoporosis in Thai men. J Med Assoc Thai 2006; 89: 160-9.
7. D'Amelio P, Cristofaro MA, Tamone C, Morra E, Di Bella S, Isaia G, et al. Role of iron metabolism and oxidative damage in postmenopausal bone loss. Bone 2008; 43: 1010-5.
8. Chen Z, Thomson CA, Aickin M, Nicholas S, Van Wyck D, Lewis CE, et al. The relationship between incidence of fractures and anemia in older multiethnic women. J Am Geriatr Soc 2010; 58: 2337-44.
9. Korkmaz U, Korkmaz N, Yazici S, Erkan M, Baki AE, Yazici M, et al. Anemia as a risk factor for low bone mineral density in postmenopausal Turkish women. Eur J Intern Med 2012; 23: 154-8.
10. Wright I, Blanco-Rojo R, Fernández MC, Toxqui L, Moreno G, Pérez-Granados AM, et al. Bone remodelling is reduced by recovery from iron-deficiency anaemia in premenopausal women. J Physiol Biochem 2013; 69: 889-96.
11. Cesari M, Pahor M, Lauretani F, Penninx BW, Bartali B, Russo R, et al. Bone density and hemoglobin levels in older persons: results from the InCHIANTI study. Osteoporos Int 2005; 16: 691-9.
12. Laudisio A, Marzetti E, Pagano F, Bernabei R, Zuccalà G. Haemoglobin levels are associated with bone mineral density in the elderly: a population-based study. Clin Rheumatol 2009; 28: 145-51.
13. Salvin HE, Pasricha SR, Marks DC, Speedy J. Iron deficiency in blood donors: a national cross-sectional study. Transfusion 2014; 54: 2434-44.
14. Clark SF. Iron deficiency anemia. Nutr Clin Pract 2008; 23: 128-41.
15. Jensen PD, Heickendorff L, Helweg-Larsen HM, Jensen FT, Christensen T, Ellegaard J. Serum procollagen III peptide concentration in iron overload. Eur J Haematol 1996; 57: 157-64.

16. Anker SD, Colet JC, Filippatos G, Willenheimer R, Dickstein K, Drexler H, et al. Ferric carboxymaltose in patients with heart failure and iron deficiency. N Engl J Med 2009; 361: 2436-48.
17. Polina V, Coriata R, Perkinsa G, Dhoogea M, Abitbola V, Leblanc S, et al. Iron deficiency: from diagnosis to treatment. Dig Liver Dis 2013; 45: 803-9.
18. Bjarnason NH, Christiansen C. Early response in biochemical markers predict long-term response in bone mass during hormone replacement therapy in early postmenopausal women. Bone 2000; 26: 561-9.
19. Dogan E, Posaci C. Monitoring hormone replacement therapy by biochemical markers of bone metabolism in menopausal women. Postgrad Med J 2002; 78: 727-31.
20. Seibel MJ. Clinical application of biochemical markers of bone turnover. Arq Bras Endocrinol Metabol 2006; 50: 603-20.
21. Lewiecki EM. Prevention and treatment of postmenopausal osteoporosis. Obstet Gynecol Clin N Am 2008; 35: 301-15.
22. Vasikaran SD. Utility of biochemical markers of bone turnover and bone mineral density in management of osteoporosis. Crit Rev Clin Lab Sci 2008; 45: 221-58.
23. Garnero P. Bone markers in osteoporosis. Curr Osteoporos Rep 2009; 7: 84-90.

Identification of Yeasts from Clinical Samples Using MALDI-TOF MS

Chanika Maenchantrarath BSc Medical Technology[1*]
Daranee Nutalai MSc Medical Technology[1]
Worada Samosornsuk PhD Veterinary Science[2]
Prirayapak Sakoonwatanyoo MD, PhD Molecular Genetics and Genetic Engineering[3]

[1] Microbiology Laboratory Unit, Department of Central Laboratory and Blood Bank, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand
[2] Department of Medical Technology, Faculty of Allied Health Sciences, Thammasat University, Rangsit Campus, Pathumthani, Thailand
[3] Department of Clinical pathology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand
* Corresponding author, e-mail address : chanika@nmu.ac.th
Vajira Med J. 2020; 64(4) : 297-310
http://dx.doi.org/10.14456/vmj.2020.29

Abstract

Objective: This research aimed to identify the yeasts from the clinical specimens by comparing MALDI-TOF MS using extended direct transfer technique (EDT-MALDI) and the conventional method.

Methods: This study was a retrospective cohort. The samples were the 557 yeasts isolated from the clinical specimens in the Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Thailand by comparing between the EDT-MALDI and the conventional method. The data were analyzed by using McNemar Test. Moreover, the unit cost and the turnaround time of the both methods were calculated. The other data such as age, sex, wards, types of the specimens and the prevalence of the species of yeasts, were collected and analyzed.

Results: The result showed that the EDT-MALDI can identify the yeast isolates into the species level more accurately than the conventional method at 100% and 93.2%, respectively. The conventional method was limited for correctly identification of *Trichosporon asahii*, *Cryptococcus neoformans*, some non-*albicans Candida*, *Magnusiomyces capitatus*, and *Candida rugosa*. However, both methods were not significantly different from each other. Even though the threshold score of the EDT-MALDI was reduced from ≥ 2 to ≥ 1.7, this will increase the acceptable results without effect to specificity, accuracy, and reliability in the species level. The EDT-MALDI was faster than the conventional method for at least 24 hours. Moreover, the unit cost of EDT-MALDI is lower than the conventional method (68 baht/test and 116 baht/test, respectively). In this data, the elderly female admitted to the hospital were the most patients who found yeast in specimens. *Candida albicans* (54.04%) were the most isolated species, followed by *Candida tropicalis* (26.21%).

Conclusion: The EDT-MALDI was a suitable method for the yeast identification in the routine laboratory because it was provided a shorter time of analysis, obtained reliable results and less expensive unit cost.

Keywords: Conventional method, MALDI-TOF MS, Extended direct transfer technique

การพิสูจน์แยกชนิดของยีสต์จากสิ่งส่งตรวจทางห้องปฏิบัติการด้วยเครื่องมัลดิทอฟเอ็มเอส

ชนิกา แม้นจันทรารัตน์ วท.บ. เทคนิคการแพทย์[1*]

ดารณี นุตาลัย วท.ม. เทคนิคการแพทย์[1]

วรดา สโมสรสุข PhD Veterinary Science[2]

ไปรยาภัค สกุลวทัญญู พ.บ., ว.ว. พยาธิวิทยาคลินิก, ปร.ด. อนูพันธุศาสตร์และพันธุวิศวกรรมศาสตร์[3]

[1] งานจุลชีววิทยา ฝ่ายชันสูตรโรคกลางและธนาคารเลือด คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช กรุงเทพมหานคร ประเทศไทย

[2] ภาควิชาเทคนิคการแพทย์ คณะสหเวชศาสตร์ มหาวิทยาลัยธรรมศาสตร์ ศูนย์รังสิต ปทุมธานี ประเทศไทย

[3] ภาควิชาพยาธิวิทยาคลินิก คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช กรุงเทพมหานคร ประเทศไทย

* ผู้ติดต่อ, อีเมล: chanika@nmu.ac.th

Vajira Med J. 2020; 64(4) : 297-310

http://dx.doi.org/10.14456/vmj.2020.29

บทคัดย่อ

วัตถุประสงค์: เพื่อพิสูจน์แยกชนิดของยีสต์จากสิ่งส่งตรวจทางห้องปฏิบัติการ ด้วยเครื่อง MALDI-TOF MS โดยใช้เทคนิค extended direct transfer (EDT-MALDI) เปรียบเทียบกับวิธี conventional

วิธีดำเนินการวิจัย: การวิจัยนี้เป็นการวิจัยเชิงวิเคราะห์แบบย้อนหลัง โดยใช้ตัวอย่างเป็นยีสต์จำนวน 557 ตัวอย่าง ที่แยกได้จากสิ่งส่งตรวจของผู้ป่วย ในคณะแพทยศาสตร์วชิรพยาบาล ตั้งแต่ เดือน พฤษภาคม 2558 ถึง กรกฎาคม 2558 ศึกษาการพิสูจน์แยกชนิดของยีสต์ด้วยวิธี EDT-MALDI เปรียบเทียบกับวิธี conventional ที่ใช้อยู่เดิม นำมาวิเคราะห์ข้อมูลโดยใช้สถิติ McNemar Test รวมถึงคำนวณราคาต้นทุนต่อหน่วย และระยะเวลารอคอยผล และวิเคราะห์ข้อมูลในปัจจัยด้านอายุ เพศ หอผู้ป่วย ชนิดของสิ่งส่งตรวจ และความชุกของยีสต์ชนิดต่างๆ

ผลการวิจัย: วิธี EDT-MALDI สามารถแยกชนิดของยีสต์ถึงระดับสปีชีส์ได้ 100% ส่วนวิธี conventional ได้ 93.2% เพราะวิธี conventional ไม่สามารถแยก *Trichosporon asahii*, *Cryptococcus neoformans*, non-*albicans Candida* บางชนิด, *Magnusiomyces capitatus* และ *Candida rugosa* ได้อย่างถูกต้อง แต่ทั้งสองวิธีไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ถึงแม้ว่าวิธี EDT-MALDI จะต้องลด threshold จาก ≥ 2 เป็น ≥ 1.7 แต่ไม่กระทบต่อความจำเพาะ ความถูกต้อง และยังเชื่อถือได้ถึงระดับสปีชีส์ วิธี EDT-MALDI ยังช่วยลดเวลาการวิเคราะห์ได้อย่างน้อย 24 ชั่วโมง และมีราคาต่อหน่วยถูกกว่าวิธี conventional คือ 68 และ 116 บาทต่อรายการตรวจ ตามลำดับ จากข้อมูลพบว่า ผู้ป่วยที่มักจะพบยีสต์ในสิ่งส่งตรวจส่วนมากเป็นผู้สูงอายุ เพศหญิงและนอนรักษาตัวในโรงพยาบาล *Candida albicans* (ร้อยละ 54.04) เป็นสปีชีส์ที่พบมากที่สุด รองลงมาคือ *Candida tropicalis* (26.21%)

สรุป: วิธี EDT-MALDI เหมาะสมที่จะนำมาใช้พิสูจน์ยีสต์ทางห้องปฏิบัติการ เพราะช่วยลดขั้นตอนการสกัดที่ยุ่งยาก ทำให้พิสูจน์ชนิดของเชื้อได้เร็วขึ้น ผลที่ได้น่าเชื่อถือและต้นทุนที่ถูกกว่า

คำสำคัญ: วิธี conventional, วิธี EDT-MALDI, เทคนิค extended direct transfer

Introduction

The infectious diseases are caused by many organisms such as bacteria, virus, fungi, and parasites. The infections are important causes of morbidity and mortality. Moreover, the cost of treatments is significantly increased every year. The most infections commonly caused by bacterial and fungal pathogens. Currently, fungi are one of the important roles in infectious diseases. The most common fungal diseases are caused by opportunistic fungi yeast such as candidiasis and cryptococcosis which have high mortality rate[1-3]. The yeast identification is a crucial method in clinical treatment for appropriate selection antifungal to treat the fungal infections, so the accurate and fast results need to be maintained[2, 4-7].

Generally, the conventional method used for identification of yeast into the species level by using the combination result from biochemical tests such as morphology observation, germ tube production, chlamydoconidia production, carbon assimilation tests, nitrogen assimilation tests, and sugar fermentation tests. Although this method is less expensive, the test step is tedious, time-consuming, and incorrectly identified in some non-*albicans Candida*[8-14]. Moreover, the false positive or false negative results can occur[8, 15]. Thus, the other test procedure which is faster than the conventional method should be used instead. The chromogenic media is used to separate yeasts from direct specimens or mixed-yeast cultures by generate the specific pigment of each species. However, it is limited used in some species such as *Candida albicans, Candida glabrata, Candida krusei,* and *Candida tropicalis*. Other than these species, they will produce the same color of colonies and cannot be correctly separated into species level[11, 12, 14, 16].

At present, the matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) is used to identify both bacteria and yeasts[17]. The use of MALDI-TOF MS to identify species of yeast provides simpler test procedure, more convenience, higher accuracy and more reliable result than the conventional method. Also, the use of MALDI-TOF MS does not require both biochemical test preparation and quality control, resulting in the increment of efficiency of the laboratory. These advantages of species classification of yeast are leading to potential enhancement of treatment: it is effective for physician to select appropriate drug for treatment[8, 10-13, 18-22]. However, the yeast identification with MALDI-TOF MS was recommended to perform the yeast extraction process with formic acid tube extraction before analysis[7, 23, 24] because of the thick and strong cell wall of yeasts[8, 25]. The result of yeast identification by MALDI-TOF MS depends on the quality of spectrum compared to the reference spectrum in a library. Its performance can distinguish species of yeast which has closely related species or subspecies such as *Candida parapsilosis/orthopsilosis/metapsilosis* or *Candida albicans/dubliniensis*, while biochemical tests cannot[8, 11, 13, 18, 25]. However, the standard yeast extraction of MALDI-TOF MS was contained many steps which are not appropriate for yeast identification in routine laboratory. To make it suitable for routine laboratory, the extended direct transfer technique (EDT-MALDI) had been developed[8, 12, 19, 25]. This technique is partial yeast extraction.

Normally, the determined threshold of identification with MALDI-TOF MS was accepted at score cut off more than 2.0 for accepting the result of both genus and species level. Although the most result from the EDT-MALDI shows a significantly lower score of identification than standard extraction and acceptable threshold (≤ 2.0), the identification results are also correct. The unreliable result was the identification in the cutoff below 1.7[22, 26]. The study of Vlek and staff found that the cutoff at 1.7 is the most suitable threshold for identifying yeast by MALDI-TOF MS regardless of the method used among the direct transfer, the EDT-MALDI, and formic acid tube extraction[10, 12, 20]. While Stevenson *et al.* and Dhiman *et al.*[10, 21] support that the reducing cutoff threshold to 1.8, the identification rate was increased equivalent to standard extraction without affect to accuracy and also trust 100% in species level[8, 19, 22, 24]. Constanza GT *et al.* use

EDT-MALDI and formic acid tube extraction with a cutoff value of 1.7 to correctly identify at species level with a 94% sensitivity and 96% specificity[27]. While Wang *et al.* use EDT-MALDI and cutoff 1.7, the results were 94.3% identical results with acceptable confidence values, 98.8% accuracy rate for overall identification of yeast isolates, and poorly 41.8% in the identification of *Cryptococcus* species because of the organism's carbohydrate-rich cell walls, making protein extraction more difficult with the direct on-plate testing method[28]. However the cutoff value of 1.7 have insufficient evidence (low number of isolates of each species) to support the use of this cutoff to correctly identify other yeast species. From the previous studies, Erin *et al.* and Mather *et al.* using EDT-MALDI and cutoff 1.7 with the other organisms; aerobic Gram-positive organisms and Mycobacterium, the results were 92.2% and 94.9% correctly identification in species level, respectively[29, 30].

MALDI-TOF MS (MALDI BioTyper) has been used in Microbiology Laboratory Unit, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand for use in bacterial identification. To empower using this instrument, the application for yeast identification would be done. Due to the complicated processes of yeast extraction, which is not suitable in routine laboratory; both the factors of high workload and limited turnaround time, the EDT-MALDI shall be applied. The EDT-MALDI, which reduces tedious steps and turnaround time, was selected to identify yeast with MALDI-TOF MS because this method can be used along with bacterial identification. This research aims to identify yeast isolated from patients using the EDT-MALDI compared to the conventional method and to observe the prevalence of yeasts in the hospital, thereby the comparison of unit cost and turnaround time of both methods were calculated.

Methods

Samples

This study was retrospective cohort. A total of 557 clinical yeast isolates were collected from 522 clinical patients specimens at Microbiological Laboratory Unit, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand (since May to July 2015). The types of clinical specimens infected with yeasts came from urine (n = 236, 45.2%), sputum (n = 204, 39.1%), stool (n = 28, 5.4%), hemoculture (n = 18, 3.4%), wound/pus (n = 11, 2.1%), tissue (n = 6, 1.1%), cervix (n = 5, 1.0%), vagina (n = 4, 0.8%), bile (n = 2, 0.4%), peritoneal dialysis (n = 2, 0.4%), CSF (n = 2, 0.4%), joint (n = 1, 0.2%), tip (n = 1, 0.2%), abdomen fluid (n = 1, 0.2%) and bronchial washing (n = 1, 0.2%). The following clinical information of patients was recorded from the hospital information system: ward, sex and age. The reference strains of yeasts came from National Institute of Health of Thailand consisting of *Candida albicans* DMST 5315**,** *Candida tropicalis* DMST 15495*, Candida glabrata* DMST 46683*, Candida parapsilosis* DMST 15315*, Candida krusei* DMST 15317 and *Cryptococcus neoformans* DMST 15319.

Yeast identification

All clinical yeast isolates from stock were recovered and subcultured on the blood agar plate containing 5% sheep blood. The plates were incubated in ambient air at 37°C for 24-48 hours. Then, the pure isolation of yeast colonies were identified the phenotype into species level using the EDT-MALDI in comparison to the conventional method.

Identification of the phenotype of yeasts with conventional method

The colony morphology was observed, dyed with gram stain and determined characteristics under a microscope. If suspected *Cryptococcus* spp., the india ink preparation was performed. The combination of biochemical tests such as germ tube production, chlamydoconidia production,

carbon assimilation tests, nitrogen assimilation tests, and sugar fermentation tests, were differently done. Moreover, the species of *Candida* were separated according to the color of the colony on CHROMagar *Candida*.

Identification of the phenotype of yeasts using MALDI-TOF MS with extended direct transfer technique (EDT-MALDI)

The isolation of the yeast colony was smeared and dried on the MALDI target plate. Yeasts reference strains were used as a control and bacterial test standard (BTS) was used as a calibrator. The partial extraction was performed by using 1 µL of 70% formic acid that was covered onto all smeared channels, except the BTS channel, and then, dried at room temperature. After that, 1 µL of Matrix HCCA was dropped onto all smeared channels, then dried at room temperature and analyzed by MALDI BioTyper 3.1.

The spectrum was measured by flexControl 3.3 software. The data was processed using MALDI BioTyper 3.1 program by comparing the spectrum result to the library. The results were interpreted as color and score following; green color means that the results can report and accept at species level which a score range is 2.00 – 3.00, yellow color means that the results can report and accept only genus level which a score range is 1.700 – 1.999, and red color means unidentified by MALDI or did not have database in library which a score range is 0.00 – 1.699 that had to be repeated.

Confirmation test

The uncorrelated results from both methods were confirmed by DNA sequencing (Sanger sequencing) at the Faculty of Allied Health Sciences, Thammasat University Rangsit campus. The sequences were compared to the reference data available at the Genbank database using the BLAST program to determine the species of yeast identification.

Data analysis

The results of yeast identification tested by the EDT-MALDI and the conventional method were compared, analyzed and presented into 2 parts of the following; the first is quantitative data including the ability of yeast identification, between the EDT-MALDI and the conventional method. The result was calculated by using McNemar Test, which was considered statistically significant when p-value <0.05. Also, the patient's age was presented by volume (%). The second is qualitative data including sex, ward, types of specimen, and the prevalence of yeast in each species was presented by percentage (%).

Calculation of unit cost and turnaround time

The unit cost and turnaround time of both methods were calculated and compared.

Results

The ability of yeast identification between the MALDI-TOF MS with extended direct transfer technique (EDT-MALDI) and conventional method

A total of 557 clinical yeast isolates were separated from 522 various clinical specimens of patients from May to July 2015. The results show that the conventional method can identify yeast isolates into species-level at 520 isolates (93.4%), which consists of *C. albicans* (301), *C. tropicalis* (147), *C. glabrata* (57), *C. dubliniensis* (7) and *C. krusei* (8). Meanwhile, the identification of yeast isolate into genus level was reported at 28 isolates (5.0%), which consists of *Trichosporon* spp. (20) and Encapsulated Budding Yeast suspected *Cryptococcus* spp. (8). However, this method report as "yeasts not *C. albicans* and *Cryptococcus* spp." at 8 isolates (1.4%), and unidentified was 1 isolate (0.2%) (see Table 1).

Meanwhile, the results of the EDT-MALDI report the identification of yeast isolate into species-level at 557 isolates (100.0%), which consist of *C. albicans* (301), *C. tropicalis* (146), *C. glabrata* (58), *C. dubliniensis* (7), *C. krusei* (8), *Trichosporon asahii* (20), *C. neoformans* (8), *Candid intermedia* (1), *C. metapsilosis* (2), *C. parapsilosis* (3), *C. orthopsilosis* (1), *Candida rugosa* (1), and *Magnusiomyces capitatus* (1) (see Table 1).

Table 1:

Comparison of yeast identification results from the conventional method and MALDI-TOF MS with Extended direct transfer technique in clinical yeast isolates

Clinical yeast isolates	Number of isolates	
	Conventional method	MALDI-TOF MS with Extended direct transfer technique
Species-level		
Candida albicans	301	301
Candida tropicalis	147[a]	146
Candida glabrata	57[b]	58
Candida dubliniensis	7	7
Candida krusei	8	8
Trichosporon asahii	0	20
Cryptococcus neoformans	0	8
Candida intermedia	0	1[c]
Candida metapsilosis	0	2[c]
Candida parapsilosis	0	3[c]
Candida orthopsilosis	0	1[c]
Candida rugosa	0	1[a]
Magnusiomyces capitatus	0	1[d]
Genus level		
Trichosporon spp.	20	0
Encapsulated Budding Yeast suspected *Cryptococcus* spp.	8	0
"Yeasts not *Candida albicans* and *Cryptococcus* spp."		
Yeasts not *Candida albicans* and *Cryptococcus* spp.	8[b]	0
Unidentified		
Unidentified	1[d]	0
Total (557)	**520/557 (93.4%)**	**557/557 (100%)**
Misidentified	1[a]	0
Total of species level	**519/557 (93.2%)**	557/557 (100%)

a; One isolate was reported as *C. tropicalis* by the conventional method while using MALDI-TOF MS with extended direct transfer technique was reported as *C. rugosa*.
b; One isolate was reported as yeasts not *C. albicans* and *Cryptococcus* spp. by the conventional method while using MALDI-TOF MS with extended direct transfer technique was reported as *C. glabrata*.
c; The conventional method was reported as yeasts not *C. albicans* and *Cryptococcus* spp.
d; The conventional method was unidentified while using MALDI-TOF MS with extended direct transfer technique was reported as *M. capitatus*.

The 38 discrepancy results between both methods shown in Table 1 were confirmed with DNA sequencing (Sanger sequencing). The retrieved sequence files were edited and subjected to pairwise alignment using BioEdit software (http://www.mbio.ncsu.edu/bioedit/bioedit.html). Edited sequences were compared with existing sequences in GenBank using BLASTn (http://blast.ncbi.nlm.nih.gov/Blast.cgi). The generated nucleotide sequences were compared to the deposited sequence in GenBank. All of the sequences were accepted when the percent identity or homology with other entires in the databases was over than 97%. The DNA sequencing confirmed that all of the 20 isolates of *Trichosporon* spp., and all of the 8 isolates of Encapsulated Budding Yeast suspected *Cryptococcus* spp., which reported by the conventional method, were *T. asahii,* and *C. neoformans*, respectively (see Table 2). Moreover, the 8 isolates of yeasts not *C. albicans* and *Cryptococcus* spp. reported by the conventional method were identified into *C. intermedia* (1), *C. metapsilosis* (2), *C. parapsilosis* (3), *C. orthopsilosis* (1), and *C. glabrata* (1). An unidentified isolate reported by the conventional method was identified as *M. capitatus*. Meanwhile, one of *C. tropicalis* reported by the conventional method, the DNA sequencing reported as *C. rugosa*. Besides, the results from the EDT-MALDI were confirmed and received the same result as the DNA sequencing report (see Table 2).

Although the results from the EDT-MALDI were correct, the acceptable results to species level are only 65.9% (threshold score ≥ 2.0). The acceptable results can increase by reducing the threshold score range. Therefore, the reduction in threshold score range to ≥ 1.90, ≥ 1.80 and ≥ 1.70, will increase the identification rate into species level to 87.1%, 97.9%, and 100%, respectively (Table 3).

Assessment and comparison yeast identification results between both methods using statistical analysis SPSS 15.0 Program

After confirming test results by the DNA sequencing, the conventional method and the EDT-MALDI have the potential to identify yeast isolation into species-level at 519 isolates (93.2%) and 557 isolates (100%), respectively. However, there was no statistical difference between both methods (*p*-value > 0.05).

Table 2:

Thirty-eight isolates of the discrepancy results between the conventional method and the MALDI-TOF MS using extended direct transfer technique confirm with DNA sequencing (Sanger sequencing)

Conventional method	No.	DNA sequencing (Sanger sequencing)	No.	Extended direct transfer technique	No.
Trichosporon spp.	20	*Trichosporon asahii*	20	*Trichosporon asahii*	20
Encapsulated Budding Yeast suspected *Cryptococcus* spp.	8	*Cryptococcus neoformans*	8	*Cryptococcus neoformans*	8
Yeasts not *Candida albicans* and *Cryptococcus* spp.	8	*Candida glabrata*	1	*Candida glabrata*	1
		Candida intermedia	1	*Candida intermedia*	1
		Candida metapsilosis	2	*Candida metapsilosis*	2
		Candida parapsilosis	3	*Candida parapsilosis*	3
		Candida orthopsilosis	1	*Candida orthopsilosis*	1
Unidentified	1	*Magnusiomyces capitatus*	1	*Magnusiomyces capitatus*	1
Misidentified	1	Candida rugosa	1	Candida rugosa	1
Total	**38**		**38**		**38**

Table 3:

Interpretation results analyzed by using MALDI-TOF MS with extended direct transfer technique into range score

Color	Range Score	The acceptance level	No.	%	Total	Total%
Red	0.00 – 1.699	Unidentified/No database in the library have to analyzed again	0	0	0	0
Yellow	1.700 – 1.799	Acceptable to genus level	12	2.2	190	34.1
	1.800 – 1.899		60	10.8		
	1.900 – 1.999		118	21.2		
Green	2.00 – 3.00	Acceptable to species level	367	65.9	367	65.9

Distribution of patients found yeasts in specimen by age and sex

As shown in Table 4, the specimens collected from female were found yeast rather than male. There were 177 (33.9%) male and 345 (66.1%) female clinical patients, ranging in age from 0 day to >90 years, among 522 patients who found yeasts in specimen. The number of patients suspected to be infected yeasts was the highest among those 81 to 90 years old (151 patients, 28.9%) following by 71 to 80 years old (145 patients, 27.8%) and 61 to 70 years old (76 patients, 14.6%), respectively.

Distribution of patients found yeasts in specimen by wards

Female Medicine, are the ward that mostly found yeast in the specimens (131 patients, 25.09%), following by OPD (47 patients, 9.00%).

Table 4:

The distribution of yeast isolates by age and sex during May - July 2015

Sex	Hospitalized patients (n=522)			Total (%)
	Age range	Male (n=177)	Female (n=345)	
Age group	<1	5	2	7 (1.3)
	1-10	4	5	9 (1.7)
	11-20	2	4	6 (1.2)
	21-30	1	5	6 (1.2)
	31-40	2	13	15 (2.9)
	41-50	5	18	23 (4.4)
	51-60	27	43	70 (13.4)
	61-70	27	49	76 (14.6)
	71-80	**62**	83	145 (27.8)
	81-90	36	**115**	**151 (28.9)**
	>90	6	6	12 (2.3)
	No data	0	2	2 (0.4)
	Total (%)	**177 (33.9)**	**345 (66.1)**	**522 (100.0)**

Distribution of yeast and yeast-like fungal isolates

A total of 557 clinical yeast isolates were separated from 522 various clinical specimens of patients from May to July 2015. *Candida* spp. and non-*Candida* spp. were identified in 528 and 29 isolates, respectively. The isolation frequency of *C. albicans* (n=301, 54.0%) is the highest in *Candida* spp. *T. asahii* (n=20, 3.6%) is the highest in non-*Candida* spp. as shown in (see Table 5). The distribution of species as follows: *C. albicans*, 301 (54.0%) isolates; *C. tropicalis,* 146 (26.2%) isolates; *C. glabrata,* 58 (10.4%) isolates; *T. asahii*, 20 (3.6%) isolates; *C. krusei*, and *C. neoformans,* 8 (1.4%) isolates each; *C. dubliniensis*, 7 (1.3%) isolates; *C. parapsilosis*, 3 (0.5%) isolates; *C. metapsilosis*, 2 (0.4%) isolates; *C. orthopsilosis, C. rugosa, C. intermedia,* and *M. capitatus*, 1 (0.2%) isolate each.

Characterization of patients, clinical samples, types of specimens and isolation frequency

Five-hundred and twenty-two clinical samples from May to July 2015 were yeast positive. The features of patients and the isolation frequency of clinical isolates according to age, sex, and type of specimen has been identified as the elderly female patients who were admitted in the hospital, whereas the prevalence of types of specimens was higher in urine (n = 236, 45.2%) and sputum (n = 204, 39.1%). Among 557 of yeast isolates, *C. albicans* was most frequently isolated in almost all clinical specimens; especially urine and sputum, except hemoculture and some specimens from sterile site which was often found non-*albicans* species. Non-*Candida* species was slightly found from clinical specimens. Urine was the most common clinical specimens for the isolation of Non-*Candida* spp. (20 isolates); all of them were *T. asahii*, followed by hemoculture (6 isolates); all of them were *C. neoformans*, CSF (2 isolates); all of them were *C. neoformans* and sputum (1 isolate); it was *M. capitatus.* Furthermore, the distribution of co-infection, found yeast isolates more than one species in the same specimens, were often isolated from sputum, urine, wound/pus, and bile, respectively.

Table 5: the distribution of yeast isolates by clinical sample type during May - July 2015

Isolates	(n=557)	*Candida* species n (%)									Non-*Candida* species n (%)			Total (%)
Sample type	(n=522)	*albicans*	*tropicalis*	*glabrata*	*metapsilosis*	*parapsilosis*	*krusei*	*dubliniensis*	*orthopsilosis*	*rugosa*	*intermedia*	*C. neoformans*	*M. capitatus*	*T. asahii*	
Hemoculture	18 (3.4)	1 (5.6)	10 (55.6)	1 (5.6)	-	-	-	-	-	-	-	6 (33.3)	-	-	18 (3.2)
Wound/Pus	11 (2.1)	7 (58.3)	3 (25.0)	1 (8.3)	-	1 (8.3)	-	-	-	-	-	-	-	-	12 (2.2)
Tissue	6 (1.1)	6 (100.0)	-	-	-	-	-	-	-	-	-	-	-	-	6 (1.1)
Joint	1 (0.2)	1 (100.0)	-	-	-	-	-	-	-	-	-	-	-	-	1 (0.2)
Bile	2 (0.4)	1 (33.3)	1 (33.3)	1 (33.3)	-	-	-	-	-	-	-	-	-	-	3 (0.5)
Peritoneal Dialysis	2 (0.4)	-	-	-	2 (100.0)	-	-	-	-	-	-	-	-	-	2 (0.4)
CSF	2 (0.4)	-	-	-	-	-	-	-	-	-	-	2 (100.0)	-	-	2 (0.4)
Tip	1 (0.2)	-	-	1 (100.0)	-	-	-	-	-	-	-	-	-	-	1 (0.2)
Abdomen	1 (0.2)	1 (100.0)	-	-	-	-	-	-	-	-	-	-	-	-	1 (0.2)
Sputum	204 (39.1)	152 (67.6)	57 (25.3)	2 (0.9)	-	1 (0.4)	4 (1.8)	6 (2.7)	1 (0.4)	1 (0.4)	-	-	1 (0.4)	-	**225 (40.4)**
Bronchial	1 (0.2)	1 (100.0)	-	-	-	-	-	-	-	-	-	-	-	-	1 (0.2)
Urine	236 (45.2)	111 (44.8)	62 (25.0)	49 (19.8)	-	1 (0.4)	4 (1.6)	-	-	-	1 (0.4)	-	-	20 (8.1)	**248 (44.5)**
Stool	28 (5.4)	15 (53.6)	12 (42.9)	-	-	-	-	1 (3.6)	-	-	-	-	-	-	28 (5.0)
Cervix	5 (1.0)	3 (60.0)	1 (20.0)	1 (20.0)	-	-	-	-	-	-	-	-	-	-	5 (0.9)
Vagina	4 (0.8)	2 (50.0)	-	2 (50.0)	-	-	-	-	-	-	-	-	-	-	4 (0.7)
Total (%)	**522 (100.0)**	**301 (54.0)**	**146 (26.2)**	58 (10.4)	2 (0.4)	3 (0.5)	8 (1.4)	7 (1.3)	1 (0.2)	1 (0.2)	1 (0.2)	8 (1.4)	1 (0.2)	20 (3.6)	557 (100.0)

Unit cost and turnaround time

The unit cost of the EDT-MALDI is approximately 68 baht/test while the conventional method is approximately 116 baht/test. Three cost calculations were analyzed in this study: Labor Cost (LC), Material Cost (MC), and Capital Cost (CC) that included technologist time, all material and reagent cost, and maintenance costs. After receiving a specimen, the turnaround time of the EDT-MALDI is 24-48 hours while the turnaround time of the conventional method is 48-72 hours.

Discussion

In this study, the assessment of the yeast identification between using the EDT-MALDI and the conventional method is not statistically significant difference. However, the EDT-MALDI has higher efficiency for identifying yeasts to species level more than the conventional method; the identification rate was 100% and 93.2%, respectively. So, the yeast identification using the EDT-MALDI is suitable to use in the laboratory because the routinely conventional method may be misidentified for many reasons. The first reason is the unclearness of colony color observation on CHROMagar *Candida* such as; *C. dubliniensis*, *C. glabrata*, *C. rugosa* and *M. capitatus*. Although some studies such as Kirkpatrick *et al.* and Pfaller *et al.*, support the reliability of the use of CHROMagar *Candida* for identifying *C. dubliniensis* and *C. glabrata*, some researcher disagree because the color of *C. dubliniensis* is difficult to distinguish from *C. albicans*[31]. Moreover, this method must using *C. albicans* as a control simultaneously, or incubating more than 72 hours[32], or using yeasts from primary specimens, otherwise, it can be affected by collected condition and subculture steps. As shown in the study of Eraso E *et al.*, they were used *C. albicans* from stock, found that colony color was changed from green to pink, then it misidentified to non-*C. albicans*. Also, *C. glabrata* is difficult to identify because of the color of the colony similar to the non-*C. albicans*[33]. They clarify one isolate of *C. glabrata* that cannot identify due to showing a white colony.

The second reason is the non-specific reporting isolates or report as yeasts not *C. albicans* and *Cryptococcus* spp. group, such as; *C. intermedia, C. metapsilosis, C. parapsilosis* and *C. orthopsilosis*. From Esposto MC *et al.*, the others non-*albicans Candida* such as *C. parapsilosis, Candida nivariensis* and *Candida bracarensis* could not identify on CHROMagar *Candida* because they could produce many colors and many morphology of colonies, but most of them are white[34]. The third reason is the misidentified from the limitation of test such as *C. rugosa*. This issue as a result of the colony characteristics of *C. rugosa* on CHROMagar *Candida* is similar to *C. krusei*, except the colony color that produced the blue color similar to *C. tropicalis* and *Trichosporon* spp. The colony morphology observation on CHROMagar *Candida* should be aware to prevent the mistake of interpretation[32]. The last reason is the inability to identify into the genus level such as *M. capitatus* and species-level such as; *Trichosporon* spp. and Encapsulated Budding Yeast suspected *Cryptococcus* spp. These reasons are caused by the limitation of the biochemical tests, which differently use in each laboratory, cover all of the yeast isolation that would like to identify or not. Also, the false positive or false negative results should be suspected.

Whereas using the EDT-MALDI is better. Other than simpler test procedure, more convenience, time-consuming, higher accuracy and more reliable result, it can correctly separate *C. dubliniensis* from *C. albicans*, and the others that closely related species. While currently the conventional method was provided the wrong results because the phylogenetic of them are very closer[21]. Meanwhile, the turnaround time is quicker than the conventional method at least 24 hours that useful for physicians to decide suitable antifungal drugs leading to improve potential treatment for patients. Although the price of MALDI-TOF MS instrument is expensive, the solution is not. In the long term use, it will give more high effectiveness of identification. The unit cost of EDT-MALDI was 68 baht whereas 116 baht from the conventional method.

However, the suitable cutoff of the threshold score range is one consideration to using EDT-MALDI. In this study, the reduction of threshold will increase the identification rate and the reliability rate in the same way as the study of Stevenson *et al.* and Dhiman *et al*[10, 21]. At cutoff score ≥ 1.7, the results of yeast identification are still 100% corrected in the species level. So, our study is following Vlek *et al.* which determine cutoff at 1.7 is the most suitable for identify yeasts by MALDI-TOF MS[20] because misidentified cutoff is score below 1.7[12]. This cutoff is the suitable threshold for decision acceptance for the results of yeast identification when using the EDT-MALDI[8, 19, 22, 24]. We should adjust the threshold according to the identification method for increasing the identification rate without effect to specificity, accuracy, and reliability in species-level.

In the experiment, 24 isolates (4.31%) using EDT-MALDI were repeated for identification twice or more which consists of *C. tropicalis* 9 isolates, *C. albicans* 5 isolates, *C. glabrata*, *C. neoformans* and *T. asahii* 3 isolates each, *C. orthopsilosis* 1 isolate. Due to the limitations of the EDT-MALDI depend on many factors such as the quality of spectrum, the thickness of organisms and smear, the quality of HCCA Matrix concentration, including the quality and the number of databases in the library. The EDT-MALDI can identify difficult organisms and closely related organisms, which prevent the mistake of identification. However, Gorton *et al*. suggested that the EDT-MALDI should do duplicate[10, 12, 20].

The part of an epidemiological study which is one of the benefits of using MALDI-TOF MS, when analyzing data in the aspect of age, sex, and wards, Female Medicine are the ward that mostly found yeast in the specimens because the patients who mostly found yeast in specimens were elderly female and admitted in the hospital. The most common specimens infected with yeasts in this study are urine. One reason is female anatomy which has short urethra and near the vagina and anus, causing risk factors for urinary tract infection[35]. Besides that, female who in the reproductive period commonly have yeast colonized or have yeast group *Candida* infection in the reproductive system[36].

Limitations

Limitations of our study include the sampling period only three months and all of isolates analyzed from only one hospital.

Conclusion

This study shows the prevalence of yeasts in each species that isolate from all types of specimens for monitoring the outbreak of yeasts in the Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand. Urine is the most common specimens found yeast, followed by sputum. The frequency of yeast species found in various specimens is *C. albicans* 54.04% (301/557), and *C. tropicalis* 26.21% (146/557 respectively, which were consistent with several studies such as Sumitra *et al*. that found *C. albicans* 52%, followed by *C. tropicalis* that is the most common of non *albicans* species[14]. Our study, urine is also found *C. glabrata* and *T. asahii* in third and fourth rank, respectively. From Mattede *et al*., urine was found the high prevalence of *Trichosporon* spp. in male (65%), age > 70 years (55%), ICU patients who associated with urinary catheter or use broad-spectrum antibiotics[35]. Likewise, our study found a high prevalence of *Trichosporon* spp. in males (10/177 patients, 5.65%), and females (10/345 patients, 2.90%). Hemoculture, first rank is *C. tropicalis* followed by *C. neoformans* same as some specimens from sterile site that found different species spreading such as peritoneal dialysis, CSF and catheter tip; especially in CSF which the outbreak is *C. neoformans*. Also, the types of specimens such as wound/pus, bile, sputum, urine, especially sputum and urine are often found co-infection. However, the situation of yeast infection prevalence in this study limited in specimens that sent to investigate in the microbiology laboratory only does not cover every patient in the hospital. The results could not be extended to the general population because the

study only in the Faculty of Medicine Vajira Hospital, Navamindradhiraj University.

Conflict of interest

The authors have not declared any conflict of interests.

Acknowledgements

We thank all microbiology staff of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University, for their cooperation to facilitate sample collection, sample storage and providing information. This work was supported by grants from the Navamindradhiraj University Research Fund (CEU/C 001/2559).

References

1. Gavalda J, Meije Y, Fortun J, Roilides E, Saliba F, Lortholary O, et al. Invasive fungal infections in solid organ transplant recipients. Clin Microbiol Infect. 2014; 7: 27-48.
2. Eggimann P, Que YA, Revelly JP, Pagani JL. Preventing invasive *candida* infections. Where could we do better? J Hosp Infect. 2015; 89: 302-8.
3. Arendrup MC, Boekhout T, Akova M, Meis JF, Cornely OA, Lortholary O. ESCMID and ECMM joint clinical guidelines for the diagnosis and management of rare invasive yeast infections. Clin Microbiol Infect. 2014; 20: 76-98.
4. Bille E, Dauphin B, Leto J, Bougnoux ME, Beretti JL, Lotz A, et al. MALDI-TOF MS Andromas strategy for the routine identification of bacteria, mycobacteria, yeasts, *Aspergillus* spp. and positive blood cultures. Clin Microbiol Infect. 2012; 18: 1117-25.
5. Emonet S, Shah HN, Cherkaoui A, Schrenzel J. Application and use of various mass spectrometry methods in clinical microbiology. Clin Microbiol Infect. 2010; 16: 1604-13.
6. Bader O, Weig M, Taverne-Ghadwal L, Lugert R, Gross U, Kuhns M. Improved clinical laboratory identification of human pathogenic yeasts by matrix-assisted laser desorption ionization time-of-flight mass spectrometry. Clin Microbiol Infect. 2011; 17: 1359-65.
7. Lacroix C, Gicquel A, Sendid B, Meyer J, Accoceberry I, François N, et al. Evaluation of two matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) systems for the identification of *Candida* species. Clin Microbiol Infect. 2014; 20: 153-8.
8. Buchan BW, Ledeboer NA. Advances in identification of clinical yeast isolates by use of matrix-assisted laser desorption ionization-time of flight mass spectrometry. J Clin Microbiol. 2013; 51: 1359-66.
9. Goyer M, Lucchi G, Ducoroy P, Vagner O, Bonnin A, Dalle F. Optimization of the preanalytical steps of matrix-assisted laser desorption ionization-time of flight mass spectrometry identification provides a flexible and efficient tool for identification of clinical yeast isolates in medical laboratories. J Clin Microbiol. 2012; 50: 3066-8.
10. Stevenson LG, Drake SK, Shea YR, Zelazny AM, Murray PR. Evaluation of matrix-assisted laser desorption ionization-time of flight mass spectrometry for identification of clinically important yeast species. J Clin Microbiol. 2010; 48: 3482-6.
11. Sendid B, Ducoroy P, François N, Lucchi G, Spinali S, Vagner O, et al. Evaluation of MALDI-TOF mass spectrometry for the identification of medically-important yeasts in the clinical laboratories of Dijon and Lille hospitals. Med Mycol. 2013; 51: 25-32.
12. Cassagne C, Cella AL, Suchon P, Normand AC, Ranque S, Piarroux R. Evaluation of four pretreatment procedures for MALDI-TOF MS yeast identification in the routine clinical laboratory. Med Mycol. 2013; 51: 371-7.
13. Fraser M, Brown Z, Houldsworth M, Borman AM, Johnson EM. Rapid identification of 6328 isolates of pathogenic yeasts using MALDI-ToF MS and a simplified, rapid extraction procedure that is compatible with the Bruker Biotyper platform and database. Med Mycol. 2016; 54: 80-8.

14. Sumitra DL, Megha M. Speciation of *Candida* species isolated from clinical specimens by using chrom agar and conventional methods. Int J Sci Res Pub. 2014; 4: 1-5.
15. Marinho SA, Teixeira AB, Santos OS, Cazanova RF, Ferreira CA, Cherubini K, et al. Identification of *Candida* spp. by phenotypic tests and PCR. Braz J Microbiol. 2010; 41: 286-94.
16. Bishop JA, Chase N, Lee R, Kurtzman CP, Merz WG. Production of white colonies on CHROMagar *Candida* medium by members of the *Candida glabrata* clade and other species with overlapping phenotypic traits. J Clin Microbiol. 2008; 46: 3498-500.
17. Murray PR. What is new in clinical microbiology-microbial identification by MALDI-TOF mass spectrometry: a paper from the 2011 William Beaumont Hospital Symposium on molecular pathology. J Mol Diagn. 2012; 14: 419-23.
18. Cassagne C, Normand AC, L'Ollivier C, Ranque S, Piarroux R. Performance of MALDI-TOF MS platforms for fungal identification. Mycoses. 2016; 59: 678-90.
19. Gorton RL, Seaton S, Ramnarain P, McHugh TD, Kibbler CC. Evaluation of a short, on-plate formic acid extraction method for matrix-assisted laser desorption ionization-time of flight mass spectrometry-based identification of clinically relevant yeast isolates. J Clin Microbiol. 2014; 52: 1253-5.
20. Vlek A, Kolecka A, Khayhan K, Theelen B, Groenewald M, Boel E, et al. Interlaboratory comparison of sample preparation methods, database expansions, and cutoff values for identification of yeasts by matrix-assisted laser desorption ionization-time of flight mass spectrometry using a yeast test panel. J Clin Microbiol. 2014; 52: 3023-9.
21. Dhiman N, Hall L, Wohlfiel SL, Buckwalter SP, Wengenack NL. Performance and cost analysis of matrix-assisted laser desorption ionization-time of flight mass spectrometry for routine identification of yeast. J Clin Microbiol. 2011; 49: 1614-6.
22. Jamal WY, Ahmad S, Khan ZU, Rotimi VO. Comparative evaluation of two matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) systems for the identification of clinically significant yeasts. Int J Infect Dis. 2014; 26: 167-70.
23. Steensels D, Verhaegen J, Lagrou K. Matrix-assisted laser desorption ionization-time of flight mass spectrometry for the identification of bacteria and yeasts in a clinical microbiological laboratory: a review. Acta Clin Belg. 2011; 66: 267-73.
24. Deak E, Charlton CL, Bobenchik AM, Miller SA, Pollett S, McHardy IH, et al. Comparison of the Vitek MS and Bruker Microflex LT MALDI-TOF MS platforms for routine identification of commonly isolated bacteria and yeast in the clinical microbiology laboratory. Diag Microbiol Infect Dis. 2015; 81: 27-33.
25. Bernhard M, Weig M, Zautner AE, Gross U, Bader O. Yeast on-target lysis (YOTL), a procedure for making auxiliary mass spectrum data sets for clinical routine identification of yeasts. J Clin Microbiol. 2014; 52: 4163-7.
26. Sahand IH, Maza JL, Eraso E, Montejo M, Moragues MD, Aguirre JM, et al. Evaluation of CHROM-Pal medium for the isolation and direct identification of *Candida dubliniensis* in primary cultures from the oral cavity. J Med Microbiol. 2009; 58: 1437-42.
27. Hospenthal DR, Beckius ML, Floyd KL, Horvath LL, Murray CK. Presumptive identification of *Candida* species other than *C. albicans*, *C. krusei*, and *C. tropicalis* with the chromogenic medium CHROMagar *Candida*. Ann Clin Microbiol Antimicrob. 2006; 5: 1.
28. Eraso Elena, D. Moragues Maria, Villar-Vidal Maria, H. Sahand Ismail, Gonzalez-Gomez Nagore, Ponton Jose´, et al. Evaluation of the new chromogenic medium *Candida* ID 2 for isolation and identification of *Candida albicans* and other medically important *Candida* Species. J Clin Microbiol. 2006; 44: 3340-5.

29. Esposto MC, Prigitano A, Romeo O, Criseo G, Trovato L, Tullio V, et al. Looking for *Candida nivariensis* and *C. bracarensis* among a large Italian collection of *C. glabrata* isolates: results of the FIMUA working group. Mycoses. 2013; 56: 394-6.
30. Mattede M, Piras C, Mattede KD, Ferrari AT, Baldotto LS, Assbu MS. Urinary tract infections due to *Trichosporon* spp. in severely ill patients in an intensive care unit. Rev Bras Ter Intensiva. 2015; 27: 247-51.
31. Brandolt TM, Klafke GB, Goncalves CV, Bitencourt LR, Martinez AM, Mendes JF, et al. Prevalence of *Candida* spp. in cervical-vaginal samples and the *in vitro* susceptibility of isolates. Braz J Microbiol. 2017; 48: 145-50.

ใบแทรก

ปีที่ 64 ฉบับที่ 3 พฤษภาคม-มิถุนายน พ.ศ. 2563

บทความเรื่อง **Prosperity of celecoxib for pain relief after elective cesarean delivery, a double-blind randomized controlled trial** หน้าที่ 165-166 มีแก้ไขดังนี้

หน้า 165 ที่อยู่/สถาบัน ตามการอ้างอิงเชิงอรรถที่ 2 แก้ไขเป็น **[2]Department of Basic Medical Science, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand**

หน้า 166 คุณวุฒิตัวย่อของผู้นิพนธ์ลำดับที่ 3 แก้ไขเป็น **บุษบา ศุภวัฒน์ธนบดี ปรด.สถิติ**

นิพนธ์ต้นฉบับ (Original Articles)

- การใช้สื่อวีดีทัศน์เพื่อเพิ่มการทำหนังสือแสดงเจตนาไม่ประสงค์ จะรับบริการสาธารณสุขที่เป็นไปเพียงเพื่อยืดการตายในวาระสุดท้ายของชีวิต หรือเพื่อยุติการทรมานจากการเจ็บปวด ณ คลินิกผู้สูงวัยสุขภาพดีโรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย : การศึกษาเชิงทดลองเปรียบเทียบระหว่างกลุ่มที่ใช้สื่อวีดีทัศน์และกลุ่มที่ได้รับคำแนะนำตามปกติ
  (An Educational Video Intervention to Increase Advance Care Planning in A Geriatric Clinic: A Randomized Controlled Trial)
- ผลของการฝึกด้วยเครื่องไอ-วอล์คต่อสมรรถนะของการเดินในผู้ป่วยโรคหลอดเลือดสมองระยะเรื้อรัง
  (Effects of I-Walk Training on Gait Performances in Patients with Chronic Stroke)
- โครงการศึกษานำร่องทางคลินิกแบบสุ่มเปรียบเทียบประสิทธิภาพของการให้ความรู้และคำแนะนำด้านโภชนาการแบบเข้มข้นเทียบกับแบบปกติในผู้ป่วยโรคไตเรื้อรัง
  (Effects of Intensive Dietary Counseling versus Standard Dietary Counseling in Chronic Kidney Disease Patients: The Pilot Study)
- ความรู้และทัศนคติของสตรีต่อการตรวจคัดกรองมะเร็งปากมดลูกและวัคซีนป้องกันมะเร็งปากมดลูก : การศึกษาภาคตัดขวาง
  (Knowledge and Attitudes of Metropolitan Women towards Cervical Cancer Prevention with Human Papillomavirus Vaccination: A Cross-sectional Study)
- สำรวจเปรียบเทียบความรู้และพฤติกรรมการใส่เลนส์สัมผัสในนักศึกษาแพทย์และแพทย์ประจำบ้าน คณะแพทยศาสตร์วชิรพยาบาล
  (Knowledge and Behavior of Contact Lens Wear in Medical Students and Medical Residents in Vajira Hospital)
- ความสัมพันธ์ระหว่างระดับเฟอร์ริตินในน้ำเหลืองของเลือดและดัชนีชีวเคมีของกระบวนการสร้างและสลายกระดูกในสตรีวัยหมดระดู
  (Relationship between Serum Ferritin Levels and Biochemical Markers of Bone Turnover in Postmenopausal Women)
- การพิสูจน์แยกชนิดของยีสต์จากสิ่งส่งตรวจทางห้องปฏิบัติการด้วยเครื่องมัลดิทอฟเอ็มเอส
  (Identification of Yeasts from Clinical Samples Using MALDI-TOF MS)

คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช
ฝ่ายวิชาการ คณะแพทยศาสตร์วชิรพยาบาล
681 ถนนสามเสน เขตดุสิต กรุงเทพมหานคร 10300
โทร. 0-2244-3522, 0-2668-7088 แฟกซ์ 0-2668-7088