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EDITORIAL

This third issue of Thai Journal of Obstetrics and Gynaecology (TJOG) 2023 contains many interesting articles. One special article is "Marijuana in Obstetric Patients". The detail of article includes scientific knowledge about marijuana, Thai law on marijuana, and maternal and fetal effect of marijuana use during pregnancy and lactation.

Editor in Chief and managing staff of TJOG already attended "the 14th Thai Journal Development Network Seminar" on Wednesday, March 15, 2023 at the Royal Jubilee Ballroom, G Floor, IMPACT Building. Challenger, Muang Thong Thani, Nonthaburi, Thailand. TCI conducts activities and a project to continuously improve the quality of Thai journals since 2004. The aims of this meeting were to improve the national policy on research and quality development of Thai journals and notify editors of the revised evaluation criteria for TCI journals whose journals are currently indexed in the TCI. Editorial Board of TJOG looks forward to continuously raising the quality of the TJOG.

Editor in Chief and managing staff of TJOG were invited from TCI to attend "Policy, Achievement and Award Ceremony for Outstanding Performance Journals in the TCI-TSRI Collaboration Project" on Friday, 26th May 2023 at 08.30-13.30 hrs. at the Phaya Thai 3-4 Rooms, Level 6, Eastin Grand Hotel Phayathai, Ratchathewi, Bangkok, Thailand

Prof. Vorapong Phupong, M.D.
Editor in Chief

Thai Journal of Obstetrics and Gynaecology
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SPECIAL ARTICLE

Marijuana in Obstetric Patients

Tharangrut Hanprasertpong, M.D.*,
Jitti Hanprasertpong, M.D.**

** Department of Obstetrics and Gynaecology, Faculty of Medicine, Srinakharinwirot University, Ongkharak, Nakhorn Nayok, Thailand*
*** Department of Research and Medical Innovation, Faculty of Medicine, Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand*

ABSTRACT

Marijuana is a popular psychoactive substance in Thailand in this period after a recent Thai law announcement allowing the opportunity for its legal use in some medical situations. However, the increasing inclusion of marijuana in foods and beverages as well as its illegal recreational use may increase its use, including possibly by women during pregnancy and lactation. The aim of this article is to address the scientific knowledge, Thai law concerning marijuana, maternal and fetal effects of marijuana use during pregnancy and lactation, and to offer some suggestions about marijuana use in patients for obstetricians.

Keywords: marijuana, pregnancy, lactation, law.

Correspondence to: *Tharangrut Hanprasertpong, M.D., Department of Obstetrics and Gynaecology, Faculty of Medicine, Srinakharinwirot University, Ongkharak, Nakhorn Nayok, 26120 Thailand. E-mail: tharangrut@hotmail.com, tharangrut@gmail.com*

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Marijuana is the second-most commonly used psychoactive substance (after alcohol) among pregnant women[1]. In the United States, approximately 7% of pregnant women reported using marijuana[2]. The prevalence of marijuana use in Thai pregnant woman has never been reported. However, interest in marijuana use in Thailand has risen recently following the Thai government's relaxation of its marijuana laws in 2022. Hence, it is important that Thai obstetricians learn more about the effects of marijuana on the mother and fetus during pregnancy, and postpartum, and how to deal with it.

Scientific knowledge about marijuana

Marijuana comes from a plant called hemp, which contains several chemical substances. It is a member of the Cannabaceae family, with the scientific name Cannabis sativa. The chemical substances derived from Cannabis sativa that affect humans are called cannabinoids[3], which act on the cannabinoid receptors. The two known major

cannabinoids are tetrahydrocannabinol (THC) and cannabidiol (CBD)[3]. THC influences the human central nervous system and is responsible for the "high feeling" and for making users relaxed. Some side effects of THC are dry lips, thirstiness, tachycardia, slow response, and pink eye[4]. CBD is non-psychoactive and a THC antagonist. It can reduce seizures and vomiting and also has an anti-inflammatory property[4].

During pregnancy, cannabinoids can pass through the placenta from the mother to the fetus[5]. Mothers can store these in body fat, especially in breast milk, and so they can be slowly passed down to the baby over time, even after the mother has stopped using marijuana[5]. THC increases in strength and concentration when it is mixed with other substance, such as alcohol or heating[6]. Pregnant woman can intake marijuana through several routes, such as eating, dabs, and smoking or vaporization. After absorption, THC works in the endocannabinoid (ECB) system, which is found throughout the human body, including the central nervous system[7]. THC is metabolized in the liver. Its half-life varies depending on the frequency of usage, from 20 - 36 hours to 4 - 5 days for occasional to heavy users, and its complete excretion period may be longer than 30 days for heavy users[8].

Thai law on marijuana

In 2022, the Thai government announced several policies concerning marijuana as follows:[9]

(i) On February 8, 2022, the Ministry of Public Health with the approval of the Narcotics Control Board announced that the chemical extracted from all parts of marijuana (guncha) or hemp (gunchong), which is a plant in the Cannabis genus, is a Category 5 narcotic under Thailand's narcotic code, except for extracts that contain THC of no more than 0.2% by weight. This exception applies only to marijuana or hemp that is domestically grown. In addition, under Thailand's narcotic code, if such narcotics are substances that are used for the analysis of substance quality control and/or for the quality control of drug testing in humans - and therefore considered as medical devices under the laws related to medical devices and used under the purposes of such medical devices - they shall be exempted from being deemed as a Category 5 narcotic. The rules allow people to grow the plant at home. However, the recreational use of marijuana is still discouraged.

(ii) On June 2, 2022, the Ministry of Public Health forbids the importation of marijuana or hemp, except by government agencies whose mission involves research or education.

(iii) On June 13, 2022, the Ministry of Public Health defined certain actions, including recreational use that causes a smell or smoke of marijuana or hemp or other nuisance plants that could affect the well-being or be harmful to health or cause small particles to be possible to enter the lungs by inhaling the smoke and causing a risk of illness, such as asthma or bronchitis, to be nuisance actions, according to the public health law, and stated that anyone who creates such a smell or nuisance in public would be charged.

Maternal and fetal effect of marijuana use during pregnancy and lactation

At present, the absolute effect of marijuana on pregnancy and lactation is still uncertain because there are several potential confounding factors, such as poverty, malnutrition, inadequate antenatal care seeking, and the potential use of other illicit drugs (e.g., alcohol and tobacco), which have been reported to be more prevalent in marijuana users than non-users[10]. To date, Thailand and the United States, through the US Food and Drug Administration, have never approved any marijuana-derived medication for treating any illness or disease during pregnancy and lactation including for morning sickness or hyperemesis relieve; albeit the available evidence does not definitely support marijuana being associated with fetal structural defects, a risk of stillbirth, perinatal death, birth weight less than 2,500 g, or preterm birth[8]. However, there is some data showing an increase in fetal anencephaly risk when

marijuana was used in the first month of pregnancy[11]. In terms of the long-term neurological development of children who are heavily exposed to marijuana in utero, several studies have demonstrated an increased chance of attention deficiency, more hyperactivity, and lower scores in reading, math, and spelling[12].

What are the main suggestions about marijuana for obstetricians to consider?[8, 12]

1. Reproductive age woman should be assessed regarding illicit drug use, including marijuana, during pre-conception, antenatal care, and postpartum. Obstetricians should inform them to discontinue such drug use because it can potentially harm themselves and their babies. They should also be reassessed at each visit regarding potential illicit drug use.

2. Marijuana is not recommended to treat morning sickness or other medical indications during pregnancy[13].

3. Smoking marijuana may increase the level of maternal serum carbon monoxide and decrease the amount of oxygen delivered to the baby[14].

4. Pregnant marijuana users tend to have adverse socioeconomic conditions more often, such as poverty, malnutrition, experience of partner violence, and are less likely to take folic supplements[15]. Proper support and supplements may be warranted.

Conclusion

Thai obstetricians should be alert about the use of marijuana in clinical practice by patients, who may be increasingly exposed to marijuana after the recent announcements about changes in the marijuana law in Thailand. Patients should be informed about the potential harm to the mother and fetus during pregnancy and should be advised to avoid using it.

Potential conflicts of interest

The authors declare no conflicts of interest.

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GYNAECOLOGY

Clinical Characteristics, Prognostic Factors and Overall Survival of Patients with Uterine Sarcoma at King Chulalongkorn Memorial Hospital during 2002-2019

Rujira Manorompattarasarn, M.D.*,
Shina Oranratanaphan, M.D.*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand*

ABSTRACT

Objectives: The primary objective aimed to evaluate overall survival (OS) of patients with leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS) and carcinosarcoma (CS) at King Chulalongkorn Memorial Hospital (KCMH) from 1st January 2002 to 31st December 2019. The secondary objectives were to identify disease-free survival (DFS), clinical characteristics, prognostic factors, and treatment modalities of LMS, ESS and CS treatments.

Materials and Methods: A retrospective study was conducted. Patients who were diagnosed with LMS, ESS or CS, received primary treatment at KCMH and had pathology specimens for review were recruited. Patients who had insufficient data were excluded. General characteristics, surgical treatment, prognostic factors, DFS and OS of patients were collected. Statistical analysis was performed by STATA version 14.1.

Results: One hundred and fourteen cases were reviewed. Thirteen cases were excluded due to incomplete data. OS at 2, 5, and 10 years of LMS group were 74.0%, 59.8%, and 41.9%; of ESS group were 80.8%, 80.8%, and 64.7%; and of CS group were 59.6%, 49.8%, and 49.8% respectively. Uterine weight of 400 grams or more had a significant effect on OS in CS group (hazard ratio (HR) 5.65, 95% confidence interval (CI) 1.34-23.82, p = 0.018). Pelvic lymph node status had a significant effect on DFS in LMS group (HR 8.92, 95% CI 1.09-72.97, p = 0.041).

Conclusion: Only half of the LMS and CS patients survived up to 5 years but 80% of ESS survived more than 5 years. Uterine weight of 400 grams or more was the significant prognostic factor for OS in CS, while pelvic lymph node status was the significant prognostic factor for DFS in LMS.

Keywords: uterine sarcoma, prognostic factors, overall survival, disease-free survival.

Correspondence to: *Shina Oranratanaphan, M.D., Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, 10330, Thailand. E-mail: dr_shina@hotmail.com*

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การศึกษาลักษณะทางคลินิก ปัจจัยพยากรณ์โรค และอัตราการรอดชีวิตของผู้ป่วยมะเร็งมดลูกชนิดซาร์โคมา ในโรงพยาบาลจุฬาลงกรณ์ ในช่วงเวลาปี 2545-2562

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บทคัดย่อ

วัตถุประสงค์: *วัตถุประสงค์หลักของการศึกษานี้เพื่อประเมิน อัตราการรอดชีวิตของผู้ป่วยมะเร็งมดลูกชนิด Leiomyosarcoma (LMS) มะเร็งมดลูกชนิด Endometrial stromal sarcoma (ESS) และ มะเร็งมดลูกชนิด Carcinosarcoma (CS) ที่รับการรักษาในโรงพยาบาลจุฬาลงกรณ์ ในช่วงเวลาปี พ.ศ. 2545-2562 วัตถุประสงค์รอง เพื่อประเมิน ระยะเวลาปลอดโรค ลักษณะทางคลินิก ปัจจัยพยากรณ์โรค และการรักษาที่ได้รับ ในผู้ป่วยกลุ่มดังกล่าว*

วัสดุและวิธีการ: *เป็นการศึกษาแบบย้อนหลัง ในกลุ่มผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็น LMS, ESS และ CS ที่เข้ารับการรักษาในโรงพยาบาลจุฬาลงกรณ์ และมีชิ้นเนื้อทางพยาธิวิทยาที่สามารถตรวจสอบย้อนหลังได้ ผู้ป่วยที่มีข้อมูลไม่เพียงพอในการวิเคราะห์จะถูกตัดอออกจากการศึกษา ลักษณะทางคลินิกของผู้ป่วย การผ่าตัดรักษา ปัจจัยพยากรณ์โรค การรักษา ระยะเวลาปลอดโรค และ อัตราการรอดชีวิตของผู้ป่วยจะถูกเก็บรวบรวม และ นำมาวิเคราะห์ด้วยโปรแกรม STATA version 14.1*

ผลการศึกษา: *ประวัติของผู้ป่วย 114 ราย ได้ถูกนำมาประเมิน มีผู้ป่วย 13 ราย ถูกตัดออกจากการศึกษา เนื่องจากมีข้อมูลไม่เพียงพอในการวิเคราะห์ ดังนั้น มีผู้เข้าร่วมวิจัยทั้งหมด 101 รายที่นำมาวิเคราะห์ อัตราการรอดชีวิตของผู้ป่วย LMS ในช่วง 2, 5 และ 10 ปี คือ ร้อยละ 74.0, 59.8, 41.9 ตามลำดับ อัตราการรอดชีวิตของผู้ป่วย ESS ในช่วง 2, 5 และ 10 ปี คือร้อยละ 80.8, 80.8, 64.7 ตามลำดับ อัตราการรอดชีวิตของผู้ป่วย CS ในช่วง 2, 5 และ 10 ปี คือร้อยละ 59.6, 49.8, 49.8 ตามลำดับ ปัจจัยที่มีผลต่ออัตราการรอดชีวิตของผู้ป่วย CS คือ น้ำหนักมดลูกตั้งแต่ 400 กรัม ขึ้นไป (hazard ratio (HR) 5.65, 95% confidence interval (CI) 1.34-23.82, p = 0.018) และปัจจัยที่มีผลต่อระยะเวลาปลอดโรคในผู้ป่วย LMS คือ การกระจายไปยังต่อมน้ำเหลือง (HR 8.92, 95% CI 1.09-72.97, p = 0.041)*

สรุป: *ในผู้ป่วย LMS และ CS ที่สามารถอยู่รอดได้ถึง 5 ปี เพียงร้อยละ 50 ในขณะที่ร้อยละ 80 ของผู้ป่วย ESS อยู่ได้นานเกิน 5 ปี ปัจจัยที่มีผลต่ออัตราการรอดชีวิตในผู้ป่วย CS คือ น้ำหนักของมดลูก และ การกระจายไปยังต่อมน้ำเหลืองในแง่ของระยะเวลาปลอดโรคในผู้ป่วย LMS*

คำสำคัญ: *มะเร็งมดลูกชนิดซาร์โคมา, ปัจจัยพยากรณ์โรค, ระยะเวลาปลอดโรค, อัตราการรอดชีวิตของผู้ป่วย*

Introduction

Uterine sarcoma is a rare cancer which accounts for approximately 1-3% of gynecological cancer[1] and 3-8% of uterine cancer[2,3]. The majority of uterine sarcoma consists of leiomyosarcoma (LMS) and endometrial stromal sarcoma (ESS). Previously, carcinosarcoma (CS) or malignant mixed mullerian tumor (MMMT) was classified as uterine sarcoma. Recently, it has been reclassified as dedifferentiated or metaplastic form of endometrial carcinoma[4]. However, in most retrospective studies of uterine sarcoma, CS is still included in the review[4].

LMS is an aggressive tumor with poor prognosis. The most common presenting symptom is palpable mass, which is similar to that of leiomyoma. Pre-operative diagnosis is difficult; therefore, definite diagnosis is usually obtained after surgery. The factors affecting prognosis are conflicting among previous studies[5]. ESS is also a rare tumor which abnormal uterine bleeding is the most common presenting symptom in both premenopausal and postmenopausal age[6]. CS usually occurs in older age groups with similar risk factors to endometrial carcinoma, such as obesity and exposure of exogenous estrogen. CS often presents with postmenopausal bleeding[7].

The primary treatment of uterine sarcoma includes hysterectomy and tumor removal. Oophorectomy and lymphadenectomy are standard surgical treatments in ESS and CS. Nevertheless, benefits of oophorectomy and lymphadenectomy in LMS are still unclear[8, 9]. For adjuvant treatment, chemotherapy is used in advanced or recurrent disease[8,10-12]. Radiotherapy may be useful in reducing local recurrence without significant impact on overall survival[13].

The data of uterine sarcoma is limited and controversial especially in Asia[5, 14]. Therefore, we decided to conduct a study to identify the disease-free survival (DFS), overall survival (OS), and prognostic factors of LMS, ESS and CS[15,16].

The main objective of this study aimed to identify OS of LMS, ESS and CS. The secondary objective were to study the clinical characteristics, DFS and prognostic factors associated with disease outcome and modalities of treatment in these patients.

Materials and Methods

Study population

This retrospective study was conducted after receiving approval from the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB number 220/63). Data were collected from the medical records of patients who were treated at King Chulalongkorn Memorial Hospital (KCMH) from 1st January 2002 to 31st December 2019. Inclusion criteria were patients diagnosed as LMS, CS, or ESS and received primary treatment at KCMH. To confirm the diagnosis, the pathological specimens were reviewed. Exclusion criteria were patients who had insufficient medical records or those whose specimens were not available for pathology review.

Data was retrieved by searching the ICD10 (C541, C542, and C549) which concluded the diagnosis of LMS, CS, and ESS. The collected data consisted of personal data, clinical characteristics, operative data, and pathology data. Staging data before 2009 was restaged using FIGO 2009 criteria. Pathology specimens were reviewed and confirmed the diagnosis by our gynecological pathologists. Data including adjuvant treatment after surgery, location of recurrence, DFS, and OS were retrieved. This study collected every case of LMS, ESS and CS over an 18-years period. All the patients who met the inclusion criteria and did not have exclusion criteria were enrolled in this study. Patients who were lost to follow-up were contacted via telephone. If the patients could not be contacted directly, calls were made to their families to inquire about the patients' status. If both patients and their family members could not be contacted, their survival status was confirmed with the database from The National Health Security Office.

Definitions and statistical analysis

OS was defined as the length of time from the date of diagnosis to either the date of death or the date of the last follow-up[17]. DFS was defined as the duration

from the date of complete treatment to the date when recurrence occurred. Criteria for evaluating of the treatment response was based on the revised response evaluation criteria in solid tumors (RECIST) criteria (version 1.1)[18].

Statistical analyses were performed using STATA version 14.1. Numerical data were presented as mean ± standard deviation (SD) and median ± interquartile range (IQR). Qualitative data were presented as frequency and percentage. Survival analysis was analyzed using the Kaplan-Meier method. A log-rank test was used to compare each survival curve. Univariate and multivariate analyses were performed by using the Cox-regression method. A p value of less than 0.05 was considered statistically significant.

Results

From January 2002 to December 2019, there were 114 cases of LMS, ESS and CS treated at King Chulalongkorn Memorial Hospital. Thirteen cases were excluded due to insufficient data; therefore, 101 cases were analyzed. Thirty-four cases (33.6%) were LMS, 11 cases (10.9%) were ESS, and 57 cases (55.5%) were CS.

Patients' characteristics are shown in Table 1. According to the FIGO staging system, there were 53 (52.5%), 9 (8.9%), 26 (25.7%), and 13 (12.9%) patients in FIGO stages I, II, III and IV, respectively. Twenty-eight (27.7%) patients did not receive adjuvant treatment, and 51 patients (50.5%) had recurrence of the disease.

Table 1. General characteristics of LMS, ESS and CS patients.

	LMS (n = 34)	ESS (n = 11)	CS (n = 56)
Age (mean ± SD) (years)	51.8 ±11.5	49.6±12.2	61.2±12.0
Age			
< 50 years	16 (47.1%)	7 (63.6%)	8 (14.3)
> 50 years	18 (52.9%)	4 (36.4%)	48 (85.7%)
Parity			
Nulliparous	19 (55.9%)	6 (54.5%)	15 (26.8%)
Multiparous	15 (44.1%)	5 (45.5%)	41 (73.2%)
Underlying disease	7 (20.6%)	2 (18.1%)	35 (62.5%)
Previous history of Leiomyoma	3 (8.8%)	1 (9.1%)	0
Previous cancer			
No	34 (100%)	11(100%)	46 (82.1%)
Breast cancer	0	0	8 (14.3%)
* Other	0	0	2 (3.6%)
Presenting symptoms			
No symptom	0	0	1 (1.8%)
Pain	6 (17.6%)	1 (9.1%)	3 (5.4%)
AUB	6 (17.6%)	4 (36.4%)	6 (10.7%)
PMB	5 (14.7%)	3 (27.3%)	37 (66.1%)
Palpable mass	15 (44.1%)	2 (18.2%)	6 (10.7%)
** Other	2 (5.9%)	1 (9.1%)	3 (5.4%)
Pre-op diagnosis			
Benign	14 (41.2%)	6 (54.5%)	4 (7.1%)
Malignancy	9 (26.5%)	4 (36.4%)	50 (89.3%)
Pelvic mass	11 (32.4%)	1 (9.1%)	2 (3.6%)

LMS: leiomyosarcoma, ESS: endometrial stromal sarcoma, CS: carcinosarcoma, AUB: abnormal uterine bleeding, PMB: postmenopausal bleeding

* Other includes gynecological cancer and rectal cancer

** Other includes abdominal distension, pressure effect and pleural effusion

In LMS group, the mean age was 51.8 ± 11.6 years. The most common presenting symptom was palpable mass (44.1%). Twenty-four patients (70.6%) had recurrences. The most common locations of recurrence were the pelvis and lung. In ESS group, the mean age was 49.6 ± 12.2 years. Common presentations

were abnormal uterine bleeding (36.4%) and postmenopausal bleeding (27.3%). Four patients (36.4%) had recurrent disease. The most common location of recurrence was the lung. In CS group, the mean age was 61.2 ± 12.0 years, which was higher than LMS and ESS groups. The most common presenting symptom was postmenopausal bleeding (66.1%). There were 23 patients (41.1%) who had recurrent disease. The most common locations of recurrence were the pelvis and lung. Details of stage, treatment, response of treatment and disease recurrence are shown in Table 2.

Table 2. Surgical treatment, pathologic data, and treatment outcomes of LMS, ESS and CS.

	LMS (n = 34)	ESS (n = 11)	CS (n = 56)
Operation			
Myomectomy	2 (5.9%)	0	1 (1.8%)
TAH	30 (88.2%)	10(90.9%)	50 (89.3%)
TLH	2 (5.9%)	1 (9.1%)	5 (8.9%)
Surgical staging	25 (73.5%)	9 (81.8%)	53 (93%)
Omentectomy	9 (26.5%)	1 (9.1%)	25 (44.6%)
PLND	7 (20.6%)	2 (18.2%)	39 (69.6%)
PAN	3 (8.8%)	1 (9.1%)	15 (26.8%)
Tumor debulking			
Primary surgery	6 (17.6%)	1 (9.1%)	2 (3.6%)
Secondary CRS	4 (11.8%)	0	2 (3.6%)
FIGO			
I	23 (67.6%)	9 (81.8%)	21 (37.5%)
II	2 (5.9%)	1 (9.1%)	6 (10.7%)
III	8 (23.5%)	0	18 (32.1%)
IV	1 (2.9%)	1 (9.1%)	11 (19.6%)
Tumor Size	(n=28)	(n=10)	(n=43)
< 10 cm	18 (64.3%)	3 (30.0%)	9 (20.9%)
≥ 10 cm	10 (25.7%)	7 (70.0%)	34 (79.1%)
Myometrial invasion			
< 50%	N/A	2 (18.2%)	4 (7.1%)
≥ 50%		5 (45.5%)	48 (85.7%)
Unknown		4 (36.4%)	4 (7.1%)
Residual tumor	1 (2.9%)	0	7 (12.5%)
Pelvic LN positive	1 (2.9%)	0	12 (21.4%)
LVSI	1 (2.9%)	2 (18.2%)	20 (35.7%)
Omental metastasis	4 (11.8%)	1 (9.1%)	6 (10.7%)
Omental metastasis/ Omentectomy specimen	4/9 (44.4%)	1/1 (100%)	6/25 (24%)
Surgical margin positive	1 (2.9%)	1 (9.1%)	0
Adjuvant treatment			
No	13(38.2%)	5(45.5%)	10(17.9%)
CMT	16 (47.1%)	1 (9.1%)	22 (39.3%)
RT	4 (11.8%)	3 (27.3%)	11 (19.6%)
CCRT/ CMT+RT	1 (2.9%)	1(9.1%)	13 (23.2%)
Hormone	0	1(9.1%)	0
Response			
Complete	26 (76.5%)	9 (81.8%)	35 (62.5%)
Partial	1 (2.9%)	0	0
Progression	7(20.6%)	2 (18.2%)	21 (37.5%)
Recurrent of disease	24 (70.6%)	4 (36.4%)	23 (41.1%)
Local recurrence	11/24	1/4	10/23
Distant metastasis	13/24	3/4	13/23

LMS: leiomyosarcoma, ESS: endometrial stromal sarcoma, CS: carcinosarcoma, TAH: total abdominal hysterectomy, TLH: total laparoscopic hysterectomy, Surgical staging: TAH with BSO, BSO: bilateral salpingo-oophorectomy, CRS:cytoreductive surgery, PLND: pelvic lymph node dissection, PAN: paraaortic lymph node dissection, LN: lymph node, LVSI: lymphovascular space invasion, CMT: chemotherapy, RT: radiotherapy, CCRT: concurrent chemoradiotherapy, N/A: not applicable.

The 2-year, 5-year, and 10-year DFS and OS are shown in Table 3. DFS curve and OS curve are shown in Fig. 1 and Fig. 2.

Stage, pelvic lymph node status, and lymphovascular space invasion (LVSI) status had significant impact on DFS of LMS in univariate analysis. However, in multivariate analysis, only pelvic lymph node status was an independent prognostic factor (Table 4). No factors had significant effect on DFS of ESS and CS. Therefore, multivariate analysis was not performed for DFS in ESS and CS.

Table 3. General characteristics of LMS, ESS and CS patients.

	LMS (n=34)	ESS (n=11)	CS (N=56)
	% (95%CI)	% (95%CI)	% (95%CI)
Time to recurrent mean (95%CI)	17.4 mo (5.3, 29.5)	107.3 mo (61.7, 153)	6.03 mo (0, 15.4)
2-year DFS	42.5 (25.6, 58.4)	71.6 (35.0, 89.9)	37.2 (24.2, 50.2)
5-year DFS	36.4 (20.6, 52.4)	71.6 (35.0, 89.9)	35.0 (22.2, 48.0)
10-year DFS	15.6 (4.4, 33.2)	57.3 (20.6, 82.2)	19.4 (7.4, 35.7)
Survival mean (95%CI)	105.7 mo (27.5, 183.8)	119.3 mo (76.1, 162.5)	40.16 mo (0, 96.0)
2-year OS	74 (52.9, 86.8)	80.8 (42.4, 94.9)	59.6 (42.8, 73.0)
5-year OS	59.8 (37.5, 76.4)	80.8 (42.4, 94.9)	49.8 (32.8, 64.7)
10-year OS	41.9 (17.3, 64.9)	64.7 (23.0, 87.8)	49.8 (32.8, 64.7)

LMS: leiomyosarcoma, ESS: endometrial stromal sarcoma, CS: carcinosarcoma, DFS: Disease-free survival, OS: overall survival.

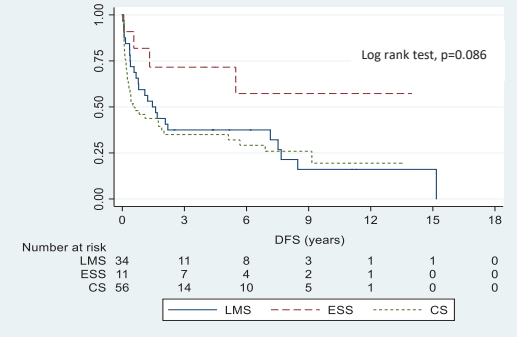

Fig. 1. Kaplan- Meier curves of disease-free survival curves for LMS, ESS and CS.

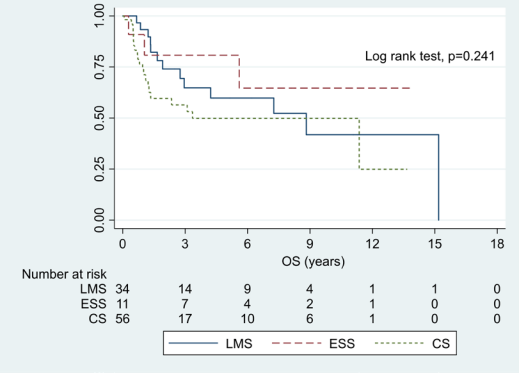

Fig. 2. Kaplan- Meier curves of overall survival curves for LMS, ESS and CS.

Table 4. Univariate and multivariate analysis of DFS in patients with LMS, ESS, CS.

Disease-free survival	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p value[a]	HR (95% CI)	p value[a]
LMS				
Age (years)				
< 50	1		N/A*	N/A*
≥ 50	1.80 (0.69-4.66)	0.228		
Stage				
I-II	1		1	
III-IV	3.99 (1.50-10.58)	0.006	0.39 (0.08-1.80)	0.226
Pelvic LN positive				
No	1		1	
Yes	33.00 (2.06-527.59)	0.013	8.92 (1.09-72.97)	0.041
LVSI				
No	1		1	
Yes	33.00 (2.06-527.59)	0.013	0.39 (0.09-1.60)	0.387
ESS*				
Age (years)				
< 50	1		N/A*	N/A*
≥ 50	1.41 (0.20-10.11)	0.733		
Stage				
I-II	1		N/A*	N/A*
III-IV	>100 (0.00-106)	0.951		
LVSI				
No	1		N/A*	N/A*
Yes	2.48 (0.22-27.77)	0.461		
CS*				
Age (years)				
< 50	1		N/A*	N/A*
≥ 50	1.22 (0.28-5.33)	0.788		
Stage				
I-II	1		N/A*	N/A*
III-IV	1.31 (0.51-3.37)	0.575		
Pelvic LN positive				
No	1		N/A*	N/A*
Yes	2.11 (0.74-6.02)	0.163		
LVSI				
No	1		N/A*	N/A*
Yes	0.73 (0.24-2.26)	0.590		

[a]: Proportional hazards regression, LMS: Leiomyosarcoma, ESS: Endometrial stromal sarcoma, CS: Carcinosarcoma, LN: Lymph node, LVSI: Lymphovascular space invasion, HR: Hazard Ratio

N/A* : Not applicable (Multivariate analysis was not performed due to insignificance in univariate analysis).

*Multivariate analysis was not performed in ESS and CS because there were no significant factors detected from univariate analysis.

Age and abdominal distension were significant for OS of LMS in univariate analysis but not in multivariate analysis. Uterine weight of 400 grams or more, residual tumor and pelvic lymph node status had significant impact on OS of CS in univariate analysis. However, only uterine weight was statistically significant in multivariate analysis. No factor was significant in univariate analysis for OS of ESS. Therefore, multivariate analysis was not performed in this group of patients (Table 5).

Table 5. Univariate analysis and multivariate analysis of OS in patients with LMS, ESS, CS.

Overall Survival	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p value[a]	HR (95% CI)	p value[a]
LMS				
Age (years)				
< 50	1		1	
≥ 50	2.92 (1.14-7.47)	0.025	3.33(0.37-29.61)	0.281
Abdominal distension				
No	1		1	
Yes	32.00 (2.00-511.60)	0.014	3.88(0.11-133.35)	0.455
Uterine Weight (g)				
< 400	1		N/A*	N/A*
≥ 400	1.13 (0.21-6.2)	0.885		
Residual tumor				
No	1		N/A*	N/A*
Yes	4.83 (0.58-40.18)	0.145		
Pelvic LN positive				
No	1		N/A*	N/A*
Yes	4.06 (0.50-33.05)	0.190		
ESS				
Age (years)				
< 50	1		N/A*	N/A*
≥ 50	1.35 (0.19-9.67)	0.768		
Abdominal distension				
No	1		N/A*	N/A*
Yes	0.04 (0.00-12788.4)	0.617		
Uterine Weight (g)				
< 400	1		N/A*	N/A*
≥ 400	105.97 (0.00-106)	0.584		
CS				
Age (years)				
< 50	1		N/A*	N/A*
≥ 50	0.90 (0.35-2.33)	0.824		
Abdominal distension				
No	1.88 (0.25-13.97)	0.537	N/A*	N/A*
Yes				
Uterine Weight (g)				
< 400	1		1	
≥ 400	2.56 (1.05-6.23)	0.038	5.65(1.34-23.82)	0.018
Residual tumor				
No	1		1	
Yes	4.74 (1.94-11.55)	0.001	28.19(0.93-856.28)	0.055
Pelvic LN positive				
No	1		1	
Yes	2.08 (1.02-4.26)	0.045	1.33(0.25-7.03)	0.740

[a]: Proportional hazards regression, LMS: Leiomyosarcoma, ESS: Endometrial stromal sarcoma, CS: Carcinosarcoma, LN: Lymph node, LVSI: Lymphovascular space invasion, HR: Hazard Ratio

N/A*: Not applicable (Multivariate analysis was not performed due to insignificance in univariate analysis).

Discussion

Several retrospective studies have reported that LMS is the most common type of uterine sarcoma. However, some studies have shown that CS is more common than LMS[19-21]. In the present study, 56 of 101 patients (55.4%) were diagnosed with CS, while 34 patients (33.6%) had LMS. The average age of CS (61.2 years) in our study was highest among all groups. Our findings were consistent with those previously reported[13,19,22,23]. Moreover, Park et al demonstrated that the mean age of MMMT or CS, LMS and ESS were 57.1, 47.5, 43.9 years, respectively[22]. The mean age in their series was slightly younger than that of our study. However, patients with CS still had higher mean age than the other groups.

Abnormal vaginal bleeding in both premenopausal and postmenopausal age group was the most common presenting symptoms in CS and ESS in our study (76.8% and 63.7%, respectively). This finding was in line with the results of Park et al. They reported that 68.2% of their patients with CS and 73% of those with ESS presented with abnormal bleeding. However, 44.1% of the patients with LMS in our study had palpable mass as the presenting symptom, while only 21.7% of those in the series of Park et al presented with palpable mass. This may result from the difference in the size of the uterine mass in different studies. Most of the patients in the series of Park et al (82.7%) had uterine masses of less than 10 cm in diameter, while only 37.0% of our participants had less than 10-cm uterine masses[22].

Pre-operative diagnosis of LMS is quite difficult. Nearly half of the patients with LMS in our study were diagnosed as benign and the other 32.4% were diagnosed pre-operatively as pelvic mass of uncertain nature. Half of ESS also had preoperative diagnoses as benign condition. However, surgical staging in the initial operation was performed in 73.5% of LMS and 81.8% of ESS (Table 2). Intraoperative specimen opening may be crucial for proper management. However, preoperative diagnosis is important in situations where a gynecologic oncologist is not available. Ultrasonogram is commonly used in gynecologic patients. However, the diagnostic accuracy of this technique for differentiating benign uterine mass from uterine sarcoma is lower than that of magnetic resonance imaging (MRI)[24]. Sensitivity, specificity, negative predictive value, positive predictive value and accuracy of ultrasonogram are inferior to those of MRI (35.1% vs 94.6%, 88.4% vs 92.3%, 48.9% vs 92.3%, 81.2% vs 94.6% and 57.1% vs 93.7%, respectively)[24, 25]. Therefore, MRI may be helpful in suspicious cases[24].

Vanichtantikul et al[26] reported 40.5% of 5-year DFS and 56% of 5-year OS in all uterine sarcoma. They found that factors such as age, histology, tumor size, lymph node dissection, or adjuvant treatment did not have a significant effect on OS. In the present study, the 5-year DFS and the 5-year OS of all participants were 39.3% and 57.6%, respectively. Our findings were quite similar to those previously reported. However, the 5-year DFS and the 5-year OS in our study were somewhat higher than those reported by Park et al, which had 5-year DFS and 5-year OS of 30% and 48%, respectively[22]. These differences may result from different proportions of the initial disease staging at diagnosis. Fifteen percent of the patients in Park et al were in stage IV, while 12.9% of our patients had stage IV[22].

In our study, ESS group had the most favorable prognosis with 5-year OS of 80% and median survival time of 119.3 months, followed by LMS group with 5-year OS of 59.8% and median survival time of 105.7 months. Patients with CS had the worst prognosis with 5-year OS of 49.8% and median survival time of 40.2 months. 5-year OS of ESS group in our study was worse than that reported by Munoz et al, which had 5-year OS of 100%. This difference may result from subgroup analysis. Munoz et al analyzed patients with undifferentiated endometrial stromal sarcoma (UES) separately from patients with ESS[27],while we analyzed both UES and ESS as one group. However, 5-year OS of patients with LMS in their study was consistent with that of our study (61.6% VS 59.8%).

Park et al found that the significant factors affecting DFS were FIGO stage, depth of myometrial

invasion, and complete cytoreduction[22]. Furthermore, some studies also found that prognostic factors associated with the OS of patients with LMS were age, clinical stage, and tumor size. The results of those previous studies were quite different from our study. We found pelvic lymph node status to be the significant prognostic factor for PFS in patients with LMS, while uterine weight of 400 grams or more was an independent prognostic factor for OS in CS group.

The strength of this study was the long data collection period of up to 18 years (from 2002 to 2019) with a 10-year OS report. However, this study still had some limitations due to the retrospective nature of the study. Therefore, some information could not be obtained from the medical record. Moreover, the sample size in ESS group was too small (11 cases) to perform subgroup analysis of high-grade and low-grade ESS. Further prospective study with larger sample size in these certain groups may be warranted. Furthermore, some data such as uterine weight and cervical invasion could not be completely obtained. For example, uterine weight records were only available in 18 of 34 cases with LMS, 6 of 11 cases of ESS and 40 of 56 cases of CS. However, the significance of having uterine weight more than 400 grams was found in CS group. Therefore, the association uterine weight and prognostic significance in CS group can be used for patient counselling and we may need further study to determine the significance of uterine weight on the prognosis of patients with LMS and ESS.

Regarding omental metastasis, 4 patients with LMS, 1 with ESS and 6 with CS had omental metastasis. Due to the limitation of this retrospective study, omentectomy may be performed only in suspicious cases based on the surgeon's decision. Therefore, the percentage of omental metastasis could not reflect the true incidence of omental metastasis as shown in Table 2.

Conclusion

In conclusion, two-thirds of patients with LMS and CS had disease recurrence within 5 years, while most of those with ESS had late recurrence. Only half of LMS and CS could survive to 5 years, while 80% of ESS survived longer. Significant prognostic factors for PFS in LMS group and OS in CS group were pelvic lymph node status and uterine weight of 400 grams or more, respectively. The information from our study would be useful for general gynecologists and gynecologic oncologists to counsel the patients about the course of the disease and prognosis of uterine sarcoma.

Potential conflicts of interest

The authors declare no conflicts of interest.

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OBSTETRICS

Enhanced Recovery after Surgery versus Standard Care for Elective Cesarean Deliveries in the Tertiary Care Center, Rajavithi Hospital, Thailand

Kamaitorn Tientong, M.D.*,***,
Thanyarat Chotikawanich, M.D.**,***,
Peepan Theptong, M.D.*,

** Department of Obstetrics and Gynecology, Rajavithi Hospital, Bangkok, Thailand*
*** Department of Anesthesiology, Rajavithi Hospital, Bangkok, Thailand*
**** Faculty of Medicine, Rangsit University, Bangkok, Thailand*

ABSTRACT

Objectives: To compare the length of stay (LOS), pain score, opioid use, and complications of cesarean deliveries (CD) between an enhanced recovery after surgery (ERAS) and standard care protocol.

Materials and Methods: A total of 80 pregnant women with elective CD were enrolled in a prospective cohort study between January and May 2020. Forty patients were assigned to ERAS protocol, and the remaining 40 were determined under standard care. The ERAS protocol is composed of preoperative, intraoperative, and postoperative care. In addition, the ERAS was modified, including drinking water instead of carbohydrate because of serious aspiration concerns. The primary objective was the length of stay, and the secondary objectives were pain score, opioid use, and complications of CD.

Results: There was a significantly shorter LOS in patients under ERAS protocol (3.0 and 1.9 days, $p < 0.001$), reduced opioid use ($p < 0.001$), and pain score ($p < 0.001$) compared to standard care. Moreover, a shorter time to flatus was found (20 and 40 hours after CD). However, we found no difference in complications between the two groups.

Conclusion: ERAS protocol in elective CD was an effective method to reduce LOS, opioid use, pain score, and improve bowel function without significant complications.

Keywords: ERAS, standard care, elective cesarean delivery.

Correspondence to: *Kamaitorn Tientong, M.D., Department of Obstetrics and Gynecology, Rajavithi Hospital, Bangkok 10400, Thailand. E-mail: tulkamaitorn@gmail.com*

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การส่งเสริมการฟื้นตัวหลังผ่าตัดเปรียบเทียบกับการรักษาแบบมาตรฐานสำหรับการผ่าท้องทำคลอดแบบไม่ฉุกเฉินในศูนย์ตติภูมิ โรงพยาบาลราชวิถี ประเทศไทย

กมัยธร เทียนทอง, ธัญรัตน์ โชติกวณิชย์, พีร์พรรค์ เทพทอง

บทคัดย่อ

วัตถุประสงค์: *เพื่อเปรียบเทียบระยะเวลานอนโรงพยาบาล ระดับความเจ็บปวด การใช้ยากลุ่มโอปิออยด์ และภาวะแทรกซ้อนจากการผ่าท้องทำคลอดระหว่างหญิงตั้งครรภ์ที่ได้รับการส่งเสริมการฟื้นตัวหลังผ่าตัดและการรักษาแบบมาตรฐาน*

วัสดุและวิธีการ: *การศึกษาข้อมูลของหญิงตั้งครรภ์ที่ได้รับการผ่าท้องทำคลอดแบบไม่ฉุกเฉินแบบไปข้างหน้า จำนวน 80 คน ระหว่างเดือนมกราคมถึงพฤษภาคม พ.ศ. 2563 โดยหญิงตั้งครรภ์จำนวน 40 คนได้รับการรักษาในกลุ่มส่งเสริมการฟื้นตัวหลังผ่าตัด ในขณะที่อีก 40 คนได้รับการรักษาแบบมาตรฐาน ในกลุ่มส่งเสริมการฟื้นตัวหลังผ่าตัดประกอบไปด้วยการดูแลก่อนผ่าตัด ขณะผ่าตัดและหลังผ่าตัด มีการปรับเปลี่ยนการดูแลในกลุ่มส่งเสริมการฟื้นตัวหลังผ่าตัดจากการดื่มอาหารเหลวที่มีคาร์โบไฮเดรตเป็นการดื่มน้ำเปล่าเพื่อลดความเสี่ยงของการสำลักอาหารเข้าปอด การศึกษานี้มีวัตถุประสงค์หลักเพื่อเปรียบเทียบระยะเวลานอนโรงพยาบาล วัตถุประสงค์รองได้แก่ระดับความเจ็บปวด การใช้ยากลุ่มโอปิออยด์ และภาวะแทรกซ้อนจากการผ่าท้องทำคลอด*

ผลการศึกษา: *หญิงตั้งครรภ์ที่ได้รับการรักษาแบบส่งเสริมการฟื้นตัวหลังผ่าตัดมีระยะเวลาในการนอนโรงพยาบาลสั้นกว่า (3 วันและ 1.9 วัน, $p < 0.001$) การใช้ยากลุ่มโอปิออยด์น้อยกว่า ($p< 0.001$) ระดับความเจ็บปวดหลังผ่าตัดต่ำกว่า ($p< 0.001$) เมื่อเปรียบเทียบกลุ่มที่ได้รับการรักษาแบบมาตรฐานอย่างมีนัยสำคัญทางสถิติ นอกจากนี้ยังพบว่ามีระยะเวลาในการผายลมครั้งแรกเร็วกว่าในกลุ่มการรักษาแบบส่งเสริมการฟื้นตัวหลังผ่าตัดอีกด้วย (20 และ 40 ชั่วโมงหลังผ่าท้องทำคลอด) แต่อย่างไรก็ตามไม่พบว่ามีความแตกต่างกันของภาวะแทรกซ้อนระหว่างหญิงตั้งครรภ์ทั้งสองกลุ่ม*

สรุป: *การส่งเสริมการฟื้นตัวหลังผ่าท้องทำคลอดแบบไม่ฉุกเฉินเป็นวิธีที่มีประสิทธิภาพในการลดระยะเวลาในการนอนโรงพยาบาล การใช้ยากลุ่มโอปิออยด์ การลดระดับความเจ็บปวด และทำให้การทำงานของลำไส้เร็วยิ่งขึ้น โดยไม่พบว่ามีภาวะแทรกซ้อนที่แตกต่างกัน*

คำสำคัญ: *การส่งเสริมการฟื้นตัวหลังผ่าตัด การรักษาแบบมาตรฐานหลังผ่าตัด การผ่าท้องทำคลอดแบบไม่ฉุกเฉิน*

Introduction

Cesarean delivery (CD) is a life-saving procedure that is essential for the mother and fetus. The rate of CD is globally increasing in both developed and developing countries. In the same way, over the past three years, the CD rate at Rajavithi hospital, the tertiary care center, has increased by more than 50%. Sequelae of the increasing rate of CD increases risks of intraoperative and postoperative complications, length of hospital stay (LOS), postoperative opioid use, and the cost of the health care system.

Enhanced recovery after surgery (ERAS) is an evidence-based recommendation that standardizes perioperative care, patient safety, and health outcomes. It has been used worldwide in colorectal, urologic, gynecologic, and hepatobiliary surgery. ERAS comprises preoperative, intraoperative, and postoperative elements. The main elements of ERAS in CD primarily emphasize the clinical process for maternal care by a multidisciplinary team to guide preadmission information, education, counseling, and maternal comorbidities[1]. The intraoperative and postoperative elements pathways start 30 to 60 minutes before the cesarean incision and end at maternal discharge from the hospital[2]. The results have shown reductions in LOS, complications, readmissions, and health system costs[3].

However, ERAS in CD protocol is not routinely practiced in our hospital, and it is not consistent with the national guideline. Furthermore, in a developing country, there are few well-designed studies about ERAS in CD[4]. Therefore, we conduct this study to determine the primary objective of whether ERAS protocol can shorten LOS. The secondary objective was pain score, time to bowel function after surgery, the dosage of opioids, and bowel function after surgery compared to standard care.

Materials and Methods

This prospective cohort study included 80 pregnant women undergoing elective CD at the Department of Obstetrics and Gynecology, Rajavithi hospital, Thailand, between January and May 2020. The pregnant women were assigned to either ERAS protocol or standard care in a ratio of 1 to 1. Forty patients at ward A were assigned to ERAS protocol, and the remaining 40 at ward B were determined under standard care. The ERAS protocol composes of preoperative, intraoperative, and postoperative elements. We omitted venous thromboprophylaxis from this protocol. Pregnant women with complications as follow: preeclampsia with a severe feature, uncontrolled diabetes mellitus, severe medical disease, morbid obesity, chorioamnionitis, and postpartum hemorrhage, which more than or equal to 1,500 mL were excluded. Only those who could communicate in Thai participated in the study, and written informed consent was obtained from all pregnant women. The group assignments were disclosed to the surgeon and staff in the operative room, while the assessors were blinded during the study. This study was approved by the institutional review board of Rajavithi hospital (IRB number: 62099).

The preoperative ERAS element

Informing the patient about procedures before, during, and after CD and giving the medication (intravenous ranitidine and metoclopramide) to prevent aspiration pneumonitis were performed. Encouraging pregnant women to drink water 30 mL instead of a clear carbohydrate liquid diet until two hours before CD was modified from traditional ERAS. Oral or mechanical bowel preparation was not used before CD.

The intraoperative ERAS element

Prophylactic antibiotics were given within 60 minutes before skin incision, and the vagina was clean with povidone-iodine. Spinal anesthesia with morphine was administered. For all pregnant women, both ERAS and standard care, chlorhexidine-alcohol was used for abdominal skin cleansing and a warming device to prevent hypothermia. Regarding the cesarean section technique in our hospital, blunt expansion of a transverse uterine incision and closure of the incisional wound in two layers was performed in both groups. In ERAS protocol, only patients with subcutaneous tissue thick more than and equal to 2 cm were reapproximated,

and all patients received local wound anesthesia with bupivacaine.

The postoperative ERAS element

An antiemetic agent (ondansetron) was administered to prevent nausea and vomiting, and multimodal anesthesia that included ibuprofen and acetaminophen was used. The postoperative prescription of the type of opioid, whether meperidine, tramadol, and morphine, depended on the surgeon or anesthesiologist's preference. The pain scores equal to and more than four are the indications for giving opioids according to WHO pain management guidelines. Furthermore, early step diet, mobilization, intravenous fluid, and urinary catheter removal were also included in the ERAS group. On the other hand, in the standard care, patients were fed when bowel function was detected, intravenous fluid and urinary catheter were removed 24 hours after CD. The hospital discharge criteria were afebrile, tolerating a soft diet, no nausea, flatus, well-controlled pain, and good mobilization. Post-discharge follow-up was performed within six weeks at the postpartum clinic. All elements are shown in Table 1.

Table 1. Comparison of preoperative, intraoperative, and postoperative elements between the standard care and ERAS.

Elements	Contents	Standard care	ERAS
Preoperative	Patient education about the procedure of CD	Yes	Yes
	NPO at least 8 hours before CD	Yes	No
	Drinking water 30 mL until 2 hours before CD	No	Yes
	Bowel preparation (unison enema)	Yes	No
	Prevention of aspiration (H2 antagonist and Metoclopramide)	No	Yes
Intraoperative	Prophylactic antibiotics	At operative room	Within 60 minutes before CD
	Vaginal cleansing with Povidone-iodine	No	Yes
	Abdominal skin cleansing chlorhexidine-alcohol	Yes	Yes
	Regional (spinal) anesthesia	Depending on indication of CD	Yes
	Prevent hypothermia (a warming device)	Yes	Yes
	Re-approximation of subcutaneous tissue	Yes	Thickness ≥ 2 cm
	Local wound anesthesia	No	Yes
Postoperative	Pain control	Acetaminophen	Acetaminophen and NSAIDs
	Prevent nausea with 5-HT3 antagonist	No	Yes
	Early feeding	No	Yes
	Early ambulation	No	Yes
	Early IV catheter removal	No	Yes
	Early urethral catheter removal	No	Yes

CD: cesarean deliveries, ERAS: enhanced recovery after surgery, NPO: nothing per mouth, IV: intravenous, NSAIDs: non-steroidal anti-inflammatory drugs

The primary objective was LOS. The LOS was defined as the duration from the surgery to hospital discharge. The secondary objectives were pain score, a dosage of opioids, time to bowel function after surgery, and complications of CD compared between the ERAS and standard group. The pain score at 6 hours, the first and the second day after CD was evaluated using a visual analog scale. Time to flatus reflected bowel function recovery. Fever, wound dehiscence, and readmission were recorded as complications. Patient characteristics and operative factors were recorded. The LOS, pain score, the dosage

of opioids, time to bowel function, and complications were also retrieved.

The sample size was estimated based on a pilot study that revealed the mean LOS ± standard deviation (SD) after ERAS protocol, and the standard care were 2 ± 1 and 3 ± 1.75 days. Two independent means with an alpha error of 5%, 80% power, and a ratio of 1:1 were tested with a dropout rate of 25%. Therefore, the number of participants was 40 in each group. All statistical calculations were done using the SPSS statistics software package, version 22.0. Continuous variables were shown as mean and SD and compared by a student's t-test. Categorical variables were expressed as a number and a percentage, compared by a Fisher's exact and Pearson's chi-squared test. A p value less than 0.05 was considered statistical significance.

Results

According to 80 pregnant women who underwent elective CD. Table 2 shows pregnant women's baseline characteristics compared standard care and the ERAS. No significant differences were found in the two groups regardless of age, body mass index, nationality, fetal presentation, gestational age, maternal disease, antenatal complication, and surgeon level.

Table 2. Baseline characteristics of pregnant women comparing between the standard care and ERAS.

Characteristic	Standard care	ERAS	p value
Age (mean ± SD)	30.3 ± 5.2	30.4 ± 6.4	0.156
Body mass index (median) (min-max)	27.6 (19.2 - 35.1)	28.3 (20.4 - 36.1)	0.456
Nationality			0.166
Thai	29 (72.5%)	28 (70%)	
Other	11 (27.5%)	12 (30%)	
Fetal-presentation			0.456
Vertex	32 (80%)	36 (90%)	
Breech	6 (15%)	3 (7.5%)	
Vertex/breech	2 (5%)	1 (2.5%)	
Gestational age (median) (min-max)	39 (34 - 40)	39 (37 - 40)	0.901
Underlying disease			0.547
None	38 (95%)	35 (87.5%)	
Hypertension	1 (2.5%)	1 (2.5%)	
Autoimmune disease	0 (0%)	1 (2.5%)	
Other	1 (2.5%)	3 (7.5%)	
Antenatal complication			0.685
None	32 (80%)	35 (87.5%)	
Gestational Diabetes Mellitus	4 (10%)	3 (7.5%)	
Gestational hypertension	1 (2.5%)	1 (2.5%)	
Preeclampsia without severe feature	2 (5%)	0 (0%)	
Other	1 (2.5%)	1 (2.5%)	
Surgeon			0.576
Resident	31 (77.5%)	33 (82.5%)	
Staff	9 (22.5%)	7 (17.5%)	

ERAS: enhanced recovery after surgery, SD: standard deviation

Table 3. reveals the operative factors of pregnant women. There were no significant differences in intraoperative fluid, operative time, and intraoperative blood loss. However, there were unbalanced indications

of CD between the two groups. In the ERAS group, there were more CD due to previous cesarean section (77.5% vs 32.5%), but less fetal macrosomia and short maternal stature (5% vs 37.5%) compared to the standard group ($p < 0.001$). Additionally, in ERAS protocol, the goals were early step diet and intravenous catheter removal, so postoperative fluid was smaller than the standard care (2,250 ± 577 mL vs 500 ± 0 mL, $p < 0.001$).

Table 3. Comparison of the operative factors of pregnant women between the standard care and ERAS.

Operative factors	Standard care	ERAS	p value
Intraoperative fluid (mL) (mean ±SD)	1423 ± 312	1456 ± 261	0.175
Operative time (minute) (mean ± SD)	73.3 ± 25.4	71.9 ± 14.7	0.764
Indications			< 0.001
Twin	3 (7.5%)	1 (2.5%)	
Abnormal position	2 (5%)	3 (7.5%)	
Fetal macrosomia/ short maternal stature	15 (37.5%)	2 (5%)	
Previous cesarean delivery	13 (32.5%)	31 (77.5%)	
Placenta previa	2 (5%)	0 (0%)	
Other	5 (12.5%)	3 (7.5%)	
Blood loss (mL) (median) (min-max)	300 (100-800)	300 (100-600)	0.704
Postoperative fluid (mL) (mean ± SD)	2,250 ± 577	500 ± 0	< 0.001

ERAS: enhanced recovery after surgery, mL: milliliters, SD: standard deviation

Table 4 identifies the outcomes of the study. In the ERAS group, the LOS was statistically significantly shorter (1.9 vs 3 days, $p < 0.001$). This study also showed the statistical significance of decreasing time to flatus in the ERAS protocol (20 hours vs 40 hours, $p < 0.001$). The complication of CD was comparable between the two groups. In the standard group, one patient had an unknown cause of fever and was discharged without an uneventful event.

Table 4. The outcomes comparing between the standard care and ERAS.

The outcomes	Standard care	ERAS	p value
Length of stay (days) (median) (min-max)	3.0 (1.9 - 4.9)	1.9 (1.8 - 3.0)	< 0.001
Opioids use			< 0.001
None	5 (12.5%)	39 (97.5%)	
Meperidine	8 (20%)	0 (0%)	
Tramadol	20 (50%)	0 (0%)	
Morphine	7 (17.5%)	1 (2.5%)	
Complications			1.000
None	39 (97.5%)	40 (100%)	
Fever	1 (2.5%)	0 (0%)	
Time to flatus (hours) (median) (min-max)	40 (30 - 49)	20 (15 - 26)	< 0.001
Pain score (Median) (Min-Max)			
6 hours post-operation	8 (5-10)	5 (0-10)	< 0.001
The first day	4 (0 - 8)	1 (0-3)	< 0.001
The second day	3 (0 - 5)	0 (0-2)	< 0.001

ERAS: enhanced recovery after surgery

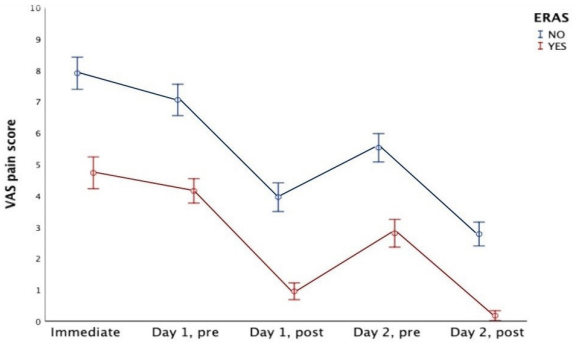

Fig. 1. Repeated measure ANOVA showed the difference of pain score.
ANOVA: analysis of variation, VAS: visual analog scale, ERAS: enhanced recovery after surgery,
Pre: before take analgesic pill, Post: after take analgesic pill.

For pain control, a significant reduction in opioid use was found in the ERAS group ($p < 0.001$). Only one patient (2.5%) in the ERAS group asked for morphine, while 17.5%, 50%, and 20% of the patients in the standard care requested pain killers such as morphine, tramadol, and meperidine consequently. As shown in Fig.1, the pain score at six hours after the operation, the first and the second day significantly reduced in the ERAS group (8 vs 5, 4 vs 1, and 3 vs 0, $p < 0.001$). No evidence of hospital readmission was found in our study.

Discussion

ERAS is a perioperative care program that has been shown to provide clinical benefits (reductions in LOS, complications of CD, and readmission) and health system benefits (reduced hospital cost)[3, 5]. Initially, ERAS was implemented in colorectal surgery nearly 15 years ago, and now there is more widespread use in different surgical specialties, including gynecologic surgery[6].

Several studies demonstrated a reduction of the LOS in ERAS planned CD without increasing readmission and complication rates[6-10]. In the same way, a randomized controlled trial from low-income countries also reported a shorter LOS when using ERAS protocol in emergency CD and a lower incidence of severe pain[4]. In the aspect of opioid use, a retrospective cohort study, implementing ERAS protocol can decrease opioid consumption[10, 11]. Consistent with the previous studies, there was also a statistically significant shorter LOS and reduced opioid use under ERAS protocol compared to standard care in this study. Moreover, a shorter time to flatus and reduced postoperative pain score were found among patients with ERAS protocol. However, in another randomized controlled trial that compared ERAS and the standard care in nonemergent CD, ERAS protocol was not associated with postoperative narcotic use[6]. However, the implementation of ERAS CD in another retrospective study was no statistical change in the LOS outcome, but there was decrease mean of inpatient opioid exposure[11].

Due to the physiology of pregnancy, pregnant women tend to have a risk of aspiration. In the present study, we are seriously concerned about aspiration pneumonitis after preoperative drinking a clear carbohydrate liquid diet in CD. For this reason, we modified the ERAS protocol from a preoperative carbohydrate liquid diet to water. The use of modified ERAS CD, according to our study, has many clinical benefits, including shortening the LOS, reducing pain score, fasten bowel function recovery. For pain control, implementation of ERAS can diminish unnecessary opioid exposure shift to other pain killers such as Acetaminophen and NSAIDs. There was no difference in adverse outcomes after ERAS implementation. Eventually, these interventions may lessen healthcare costs and hospital resources.

The study's main strengths were a prospective cohort study, and the original ERAS was modified to

suit the hospital context. Furthermore, ERAS protocol was anticipated with a multidisciplinary team such as anesthesiologists and nurses. In addition, this is the first study that modified the ERAS protocol using preoperative water instead of a clear carbohydrate liquid diet. On the other hand, there were several limitations in this study. First, there were unbalanced indications for CD between the two groups that may affected the outcomes. Second, we did not enroll the pregnant women who had conditions for the emergency CD because of the difficulty of controlling in preoperative element. Third, information about breastfeeding was not included in the study's objective. Last, cost-effective analyses in ERAS were not evaluated.

Conclusion

ERAS protocol in elective CD effectively reduces LOS, opioid use, pain score and improves bowel function without significant complications.

Acknowledgment

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Potential conflicts of interest

The authors declare no conflicts of interest.

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OBSTETRICS

Knowledge, Attitude, and Practice towards Oral Health among Pregnant Women Attending Antenatal Care at Siriraj Hospital

Chatkoew Boriboonhirunsarn, D.D.S., M.Sc.*,
Dittakarn Boriboonhirunsarn, M.D., M.P.H, Ph.D.**

** Dental Division, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
*** Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

ABSTRACT

Objectives: To evaluate knowledge, attitude, and practice towards oral health of pregnant women, and to compare characteristics between women with different levels of oral health knowledge.

Materials and Methods: A total of 304 low-risk pregnant women, before 20 weeks of gestation, were randomly selected to complete a self-administered questionnaire during their first antenatal care visit. The questionnaire consisted of 4 parts, including baseline characteristics, knowledge, attitude, and questions about personal practice and related information received. Women were further categorized into having lower, medium, and higher knowledge level according to knowledge score tertiles. Various characteristics were compared between the 3 groups.

Results: Overall knowledge score was 7.5 out of 15. Majority of women reported correct answers about oral health care during pregnancy (58.9%-98.4%). Fewer women reported correct answers on relationship between oral health and pregnancy (26.6%-66.1%). Only 14.1% and 15.5% reported that oral and dental surgeries and local anesthetics were safe. Women had misconceptions on many issues including swollen gum, loose tooth, and dental treatments. More than half of the women (56.3%) had ever received information on oral and dental health during pregnancy and 54.9% reported to receive information from medical personnel. Women with higher knowledge scores were more likely to have higher education and income, have dental visits before pregnancy, and receive information from health care personnel.

Conclusion: Pregnant women had relatively limited knowledge on some issues of oral health during pregnancy. Higher level of knowledge was related to higher education and income.

Keywords: oral health, pregnancy, knowledge, attitude, practice.

Correspondence to: *Dittakarn Boriboonhirunsarn, M.D., M.P.H, Ph.D., Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand. E-mail: dittakarn.bor@mahidol.ac.th*

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ความรู้ ทัศนคติ และการปฏิบัติตัว เกี่ยวกับสุขภาพช่องปากในสตรีตั้งครรภ์ที่มาฝากครรภ์ที่โรงพยาบาลศิริราช

ฉัตรแก้ว บริบูรณ์หิรัญสาร, ดิฐกานต์ บริบูรณ์หิรัญสาร

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความรู้ ทัศนคติ และ การปฏิบัติตัว เกี่ยวกับสุขภาพช่องปากในสตรีตั้งครรภ์ และเปรียบเทียบลักษณะต่างๆ ของสตรีตั้งครรภ์ที่มีความรู้เกี่ยวกับสุขภาพช่องปากในระดับที่ต่างกัน*

วัสดุและวิธีการ: *ทำการสุ่มเลือกในสตรีตั้งครรภ์ที่มีความเสี่ยงต่ำ จำนวน 340 ราย ที่มีอายุครรภ์น้อยกว่า 20 สัปดาห์ โดยให้สตรีตั้งครรภ์ตอบแบบสอบถามด้วยตนเองในระหว่างการมาฝากครรภ์ครั้งแรก แบบสอบถามประกอบด้วย 4 ส่วน ได้แก่ ข้อมูลพื้นฐาน ความรู้ ทัศนคติ และการปฏิบัติตัว และการได้รับข้อมูล สตรีตั้งครรภ์จะถูกแบ่งเป็น 3 กลุ่ม ตามคะแนนของความรู้ เป็นกลุ่มที่มีความรู้ น้อย ปานกลาง และมาก จากนั้นทำการเปรียบเทียบลักษณะต่างๆ ของสตรีตั้งครรภ์ ระหว่างสตรีตั้งครรภ์ 3 กลุ่ม ดังกล่าว*

ผลการศึกษา: *คะแนนความรู้โดยรวมเท่ากับ 7.5 จากคะแนนเต็ม 15 คะแนน สตรีตั้งครรภ์ส่วนใหญ่ตอบคำถามได้ถูกต้องเกี่ยวกับการดูแลสุขภาพช่องปากระหว่างตั้งครรภ์ (ร้อยละ 58.9-98.4) ในขณะที่สตรีตั้งครรภ์จำนวนน้อยกว่าตอบคำถามได้ถูกต้องเกี่ยวกับความสัมพันธ์ระหว่างสุขภาพช่องปากกับการตั้งครรภ์ (ร้อยละ 26.6-66.1) สตรีตั้งครรภ์เพียงร้อยละ 14.1 และ 15.5 ให้คำตอบว่าการทำหัตถการเกี่ยวกับช่องปากและฟัน และการใช้ยาระงับความรู้สึกเฉพาะที่ มีความปลอดภัย พบว่าสตรีตั้งครรภ์ยังมีความเข้าใจไม่ถูกต้องในหลายประเด็น เช่น การมีเหงือกบวม ฟันโยก และการรักษาทางทันตกรรม เป็นต้น สตรีตั้งครรภ์ร้อยละ 56.3 เคยได้รับข้อมูลเกี่ยวกับสุขภาพช่องปากในระหว่างตั้งครรภ์ และร้อยละ 54.9 ได้รับข้อมูลดังกล่าวจากบุคลากรทางการแพทย์ สตรีตั้งครรภ์ที่มีคะแนนระดับความรู้สูง ได้แก่ กลุ่มที่มีระดับการศึกษาและรายได้สูงกว่า ได้รับการตรวจทางทันตกรรมก่อนการตั้งครรภ์ และได้รับข้อมูลจากบุคลากรทางการแพทย์*

สรุป: *สตรีตั้งครรภ์มีความรู้เกี่ยวกับสุขภาพช่องปากขณะตั้งครรภ์ค่อนข้างจำกัด ระดับคะแนนความรู้ที่สูง สัมพันธ์กับการมีระดับการศึกษาและรายได้สูง*

คำสำคัญ: *สุขภาพช่องปาก ตั้งครรภ์ ความรู้ ทัศนคติ การปฏิบัติตัว*

Introduction

The World Health Organization has recognized that oral health, which includes health of the gum, teeth, and jawbone, is among important indicators of overall health, well-being and quality of life. It is estimated that oral diseases affect as many as 3.5 billion people worldwide[1]. Among others, oral health is considered as an important health agenda that could improve quality of life[2, 3]. Oral health problems during pregnancy are of concern and have been recognized by many organizations, including the World Health Organization[3], the American College of Obstetricians and Gynecologists[4], the American Dental Association[5], and the American Academy of Pediatric Dentistry[6].

It is evident that there are considerable changes in oral health status due to normal physiologic alterations that occur during pregnancy. Therefore, pregnant women are at increase vulnerability to oral health problems. Gingivitis, gingival lesions, tooth mobility, tooth erosion, dental caries, and periodontitis are commonly reported during pregnancy with varying prevalence[4-8]. A previous Thai study reported as many as 58.5% of pregnant women had some form of oral health problems, including plaque, gingivitis, and periodontitis[9]. Another study reported that as many as 74.0% of Thai pregnant women had dental caries and 86.2% had gingivitis[10]. Periodontal disease, including gingivitis and periodontitis, can commonly occur in pregnant women[11], and it has been associated with various adverse pregnancy outcomes[4-7]. Although a causal relationship has not been established, periodontitis has consistently reported to be associated with many adverse pregnancy outcomes including preterm delivery, low birth weight, gestational diabetes, and preeclampsia[8, 12, 13]. Exact mechanisms are not clear but these were possibly due to chronic inflammation and interactions with inflammatory cytokines. These important issues signify the importance of appropriate oral health care during pregnancy.

Awareness of changes in oral health during pregnancy and possible relationship with adverse outcomes should be raised among both pregnant women and health care providers. In many settings, the knowledge is still limited and many misconceptions are still perceived by both pregnant women and care providers. Some health care providers are unaware of the importance of oral health in pregnant women. Some tend to avoid dental evaluation and treatment during pregnancy were possibly due to misbelief that some dental procedures are unsafe for the fetus, etc. A previous study reported that pregnant women have some oral health knowledge and it varied by race or ethnicity, and maternal education[14]. Another study showed that pregnant minority (African and Hispanic American) had only limited knowledge on oral health during pregnancy[15]. A recent study also reported that most of the pregnant women reported that they were unaware about gingivitis, its cause, effects, treatment, and preventive measures[16]. A Thai study reported that low education, inadequate oral health care, poor oral hygiene, and lack of knowledge were important risk for oral health problems during pregnancy[10]. A Study in Muslim Thai pregnant women reported that the majority of pregnant women had fair oral hygiene, improper self-oral hygiene care, and inadequate knowledge of the importance of oral-systemic health relationships[17]. Another study reported that only 41.5% of Thai pregnant women had normal oral health and 60.6% incorrectly identified their oral health status[9]. This can infer that knowledge on oral health during pregnancy is limited and more oral health education should be additionally provided, awareness on this important issue should be raised, and related misconceptions should be clarified.

Siriraj Hospital is a university-based tertiary care hospital with over 6,000 deliveries a year. Its antenatal care clinic serves pregnant women who seek antenatal care from all parts of Thailand who live or work in Bangkok and vicinity areas. However, information on knowledge, attitude, and practice on oral health during pregnancy are limited and the issues are rarely evaluated in Thailand as well as in Siriraj Hospital. Therefore, the objective of this study was to evaluate knowledge on oral health during pregnancy. Attitude of the women on this specific issue and related practice were also assessed. In addition, various baseline characteristics, attitude, and personal practice were compared between different knowledge levels to evaluate possible

associated factors. As relating evidence is limited with only a few studies in Thailand regarding the issue and application of results from previous studies might not be appropriately applied to Thai population, the information from this study would help in better understanding of various aspects of oral health issues during pregnancy and awareness and concerns could be raised among health care providers. In addition, this could also help in providing better care of the pregnant women in the future.

Materials and Methods

This cross-sectional study was conducted after approval from Siriraj Institutional Review Board. Eligible pregnant women were those who had singleton pregnancy, were ≥ 18 years, and less than 20 weeks of gestation. Exclusion criteria included multiple pregnancy, women with fetal anomalies or fetal deaths, and those who were considered having high-risk pregnancies. High-risk pregnancies were those with underlying medical diseases such as diabetes, hypertension, autoimmune disease, etc., or those who developed complications during pregnancy, such as gestational diabetes, preeclampsia, etc. During January to June 2021, a total of 304 pregnant women who met inclusion were randomly selected and asked to participate in the study during their first visit at antenatal care clinic.

After informed consent, the women were asked to complete a self-administered questionnaire confidentially in a private room. The questionnaire consisted of 4 parts as follows. 1) Baseline characteristics, including age, parity, occupation, education, and family income. 2) Knowledge about oral and dental health during pregnancy which consisted of 15 items regarding oral and dental health care during pregnancy (5 items), relationship between oral and dental health and pregnancy (5 items), and dental procedures during pregnancy (5 items). 3) Questions about attitude towards oral health during pregnancy which consisted of 10 statements that the women were asked to report if they agreed with each statement. 4) Questions about practice, advice and information received regarding oral and dental health care during pregnancy. After the questionnaire was returned, a brief counseling regarding oral and dental health during pregnancy were provided to all women. Further appointments at antenatal care clinic and dental department were scheduled as appropriate.

The questionnaire was developed by the investigators and was initially verified for content validity by experts in obstetrics and dentistry. All items were developed from discussion between experts in both fields. For knowledge items, basic knowledge pregnant women should know were selected. For attitude statement, common attitude and perception of pregnant women on oral health during pregnancy were discussed and chosen based on expert opinions and experiences. For practice questions, items were chosen based on expert opinions. For knowledge part of the questionnaire, there were 3 possible answers for each question sentence (correct, incorrect, and not sure) and a score of 1 was given if the women answered "correct" for positive (true) or "incorrect" for negative (false) sentences. Total possible scores were 15. For the attitude part, there were 2 possible answers for each sentence, i.e., agree, and disagree. The reliability of the questionnaire was tested and the results showed Chronbach's alpha of 0.89, 0.84, and 0.8 for knowledge, attitude, and practice part. A sample size was calculated from an estimated 60% of pregnant women had good knowledge on oral and dental health during pregnancy. At 95% significance level and 6% acceptable error, at least 285 women were required, including 10% loss[18].

Various characteristics, including responses from the questionnaire were described using descriptive statistics, such as mean, standard deviation, number, and percentage. The women were further classified into 3 groups by knowledge score tertiles, i.e., having lower, medium, and higher knowledge. Various characteristics and responses on attitude and practice were compared between these 3 subgroups. One-way analysis of variance (ANOVA) and chi square were used in comparisons of various characteristics, attitude, and practice as appropriate. IBM SPSS Statistics for Windows®, Version 24.0 (IBM Corp., Armonk, N.Y., USA) was used for statistical analyses. A p value of < 0.05 was considered statistically significant.

Results

A total of 304 pregnant women were included in this study. Mean age was 30.7 years, mean gestational age was 14.2 weeks of gestation, and 37.5% were nulliparous. Majority (56.3%) of the women were employee, 49.7% graduated bachelor degree or higher, and almost 60% had family income of > 30,000 Baht.

Knowledge about oral health during pregnancy was evaluated and the results are shown in Table 1. In terms of oral health care during pregnancy, the mean knowledge score was 3.9 of 5. For relationship between oral and dental health and pregnancy, fewer women reported correct answers, especially regarding effects of oral and dental health on pregnancy. Mean score for this domain was 2.1 of 5. With regard to dental procedures during pregnancy, the mean score was only 1.4 of 5. While 56.6% reported scaling is safe, less than 40% reported that other procedures were safe. Only 14.1% and 15.5% reported that oral and dental surgeries and local anesthetics were safe, respectively. Mean overall knowledge score was 7.5 out of 15 possible scores.

Table 1. Knowledge about oral health during pregnancy of pregnant women in the study (N = 304).

Knowledge about oral health during pregnancy questions	Correct answer n (%)
1. Oral health care during pregnancy	
During pregnancy, you should	
Brush your teeth at least twice a day	299 (98.4)
Use fluoride-based toothpaste	265 (87.2)
Use dental floss or interdental brush regularly	189 (62.2)
Avoid sugary and sweet food	263 (86.5)
You can receive dental care and treatment as usual, similar to non-pregnant women	179 (58.9)
Mean score ± SD (total score = 5)	3.9 ± 1.0
2. Relationship between oral health and pregnancy	
The followings are oral and dental changes during pregnancy	
Increase risk of dental caries	201 (66.1)
Increase risk of gingivitis and periodontitis	140 (46.1)
Increase risk of tooth loss	130 (42.8)
The followings are the effects of oral health on pregnancy	
Poor oral health, especially periodontitis, may be related to adverse pregnancy outcomes, such as preterm birth and low birth weight.	95 (31.3)
Poor oral health in the mothers is associated with increased risk of poor oral health of the children	81 (26.6)
Mean score ± SD (total score = 5)	2.1 ± 1.0
3. Dental procedures during pregnancy	
The followings are safe during pregnancy	
Scaling	172 (56.6)
Tooth extraction	92 (30.3)
Oral and dental surgery, such as gingival surgery, wisdom teeth removal, etc.	43 (14.1)
Dental X-ray	88 (28.9)
Local anesthetics	47 (15.5)
Mean score ± SD (total score = 5)	1.4 ± 1.6
Overall mean score ± SD (total score = 15)	7.5 ± 3.2

SD: standard deviation

Attitudes towards oral health during pregnancy are shown in Table 2. While swollen gum and loose tooth were thought to be normal during pregnancy in 16.8% and 12.8%, respectively, 30.9% thought that gum bleeding during tooth brushing is also normal. The women reported that dental treatment is contraindicated in 28.9%. And 38.2% and 41.4% reported that X-ray and local anesthetics are contraindicated. Majority of the women (69.4%) reported that dental caries or loose tooth are caused by maternal transfer of calcium to the

baby. As many as 77.6% agreed that women should have dental visit before pregnancy and 60.5% agreed that women should have a dental visit at least once during pregnancy. However, 59.9% thought that pregnant women should visit a dentist only when there is a problem.

Table 2. Attitude towards oral health during pregnancy of pregnant women in the study (N = 304).

Attitude towards oral health during pregnancy questions	Agree n (%)
1. Swollen and reddened gum are normal during pregnancy	51 (16.8)
2. Gum bleeding during tooth brushing is normal during pregnancy	94 (30.9)
3. Loose tooth is normal during pregnancy	39 (12.8)
4. Dental treatment is contraindicated during pregnancy	88 (28.9)
5. Dental X-ray is contraindicated during pregnancy	116 (38.2)
6. Local anesthetics is contraindicated during pregnancy	126 (41.4)
7. Dental caries or loose tooth are caused by transfer of maternal calcium to the baby	211 (69.4)
8. Women should visit a dentist for oral health evaluation before pregnancy	236 (77.6)
9. Women should visit a dentist at least once during pregnancy	184 (60.5)
10. Pregnant women should visit a dentist only when there is a problem	182 (59.9)

Negative items: 1-7, 10

Results on practice, advice, and information regarding oral health care during pregnancy are displayed in Table 3. Before pregnancy, majority of the women had last dental visit in the past year (57.8%) and 53.3% were regular check up. Most of the women (64.1%) reported they did not have any dental problems and 26.3% reported to have dental caries. More than half of the women (56.3%) had ever received information on oral and dental health during pregnancy and 54.9% reported to receive information from medical personnel.

Table 3. Practice, advice, and information regarding oral health care during pregnancy of pregnant women in the study (N = 304).

Questions	n (%)
Time of last dental visit	
< 6 months	94 (30.8)
6 months – 1 year	82 (27.0)
> 1 year	128 (42.2)
Reasons of last dental visit	
Check up	162 (53.3)
Dental problems	90 (29.6)
Not remembered	52 (17.1)
Current dental problems*	
Caries	80 (26.3)
Pain	12 (3.9)
Swollen gum	20 (6.6)
Others	6 (2.0)
Report no problem	195 (64.1)
Received any advice or information	171 (56.3)
Sources of advice or information*	
Medical personnel	167 (54.9)
Family and friends	32 (10.5)
Internet	74 (24.3)
Others	36 (11.8)

* Multiple answers

All the women were further categorized into 3 subgroups according to knowledge score tertiles. Women with scores in 1st, 2nd, and 3rd tertile were those with knowledge score of < 6, 6-8, and > 9. They were considered as having lower, medium, and higher knowledge, respectively. General characteristics, attitude towards oral health during pregnancy, and practice, advice, and information regarding oral and dental health care during pregnancy were compared between women with different knowledge levels and the results are shown in Table 4.

Table 4. Comparison of various characteristics, attitude, and practice between different knowledge scores regarding oral health during pregnancy of pregnant women in the study.

Characteristics	Knowledge scores			p value
	Lower (n = 88)	Medium (n = 109)	Higher (n = 107)	
Age	30.0 + 5.7	30.9 + 5.8	31.0 + 5.1	0.438
Nulliparous	32 (34.1%)	43 (39.4%)	39 (36.4%)	0.884
Occupation				0.004
Civil service	8 (9.1%)	23 (21.1%)	30 (28.0%)	
Employee	56 (63.6%)	67 (61.5%)	48 (44.9%)	
Others	24 (27.3%)	19 (17.4%)	29 (27.1%)	
Education				0.012
Less than Bachelor degree	56 (63.6%)	49 (44.9%)	48 (44.9%)	
Bachelor degree or higher	32 (36.3%)	60 (55.1%)	59 (55.1%)	
Family income				0.014
< 30,000 Baht	47 (53.4%)	36 (33.0%)	42 (39.3%)	
> 30,000 Baht	41 (46.6%)	73 (67.0%)	65 (60.7%)	
Attitude questions		**Agree with the statement**		
Swollen and reddened gum are normal during pregnancy	30 (34.1%)	12 (11%)	9 (8.4%)	< 0.001
Gum bleeding during tooth brushing is normal during pregnancy	35 (39.8%)	34 (31.2%)	25 (23.4%)	0.048
Loose tooth is normal during pregnancy	17 (19.3%)	12 (11%)	10 (9.3%)	0.091
Dental treatment is contraindicated during pregnancy	22 (25%)	37 (33.9%)	29 (27.2%)	0.338
Dental X-ray is contraindicated during pregnancy	24 (27.3%)	47 (43.1%)	45 (42.1%)	0.001
Local anesthetics is contraindicated during pregnancy	27 (30.7%)	55 (50.5%)	44 (41.1%)	0.020
Dental caries or loose tooth are caused by transfer of maternal calcium to the baby	41 (46.6%)	82 (75.2%)	88 (82.2%)	< 0.001
Women should visit a dentist for oral and dental health evaluation before pregnancy	53 (60.2%)	87 (79.8%)	96 (89.7%)	< 0.001
Women should visit a dentist at least once during pregnancy	33 (37.5%)	69 (63.3%)	82 (76.6%)	< 0.001
Pregnant women should visit a dentist only when there is a problem	37 (42%)	72 (66.1%)	73 (68.2%)	< 0.001
Practice questions				
Time of last dental visit before pregnancy				0.04
< 6 months	16 (18.2%)	37 (33.9%)	41 (38.3%)	
6 months – 1 year	28 (31.8%)	29 (26.6%)	25 (23.4%)	
> 1 year	44 (50.0%)	43 (39.5%)	41 (38.3%)	
Reasons of last dental visit				0.04
Check up	36 (40.9%)	61 (56%)	65 (60.8%)	
Dental problems	30 (34.1%)	30 (27.5%)	30 (28%)	
Not remembered	22 (25.0%)	18 (16.5%)	12 (11.2%)	
Received any advice or information	43 (48.9%)	51 (46.8%)	77 (72%)	< 0.001
Sources of advice or information				
Medical personnel	36 (40.9%)	55 (50.5%)	76 (71%)	< 0.001
Family and friends	7 (8.0%)	7 (6.4%)	18 (16.8%)	0.029
Internet	14 (15.9%)	27 (24.8%)	33 (30.8%)	0.053
Others	6 (6.8%)	9 (8.3%)	21 (19.6%)	0.008

Women with lower knowledge level were significantly less likely to work as civil service (p = 0.004), more likely to graduate less than bachelor degree (p = 0.012), and more likely to have family income of < 30,000 Baht (p = 0.014). Women with lower knowledge level were significantly more likely to agree with incorrect statements. These include swollen gum and bleeding during tooth brush are normal during pregnancy, dental X-ray and local anesthetics are contraindicated, caries and loose tooth are from calcium depletion, and dental visit schedule. Women with low knowledge level were significantly more likely to have last dental visit of > 1 year and less likely to visit for regular check up. On the other hand, women with high knowledge level were significantly more likely to receive any advice or information regarding oral health during pregnancy and more likely to receive such information from medical personnel.

Discussion

The results of this study showed that, from knowledge scores, pregnant women had relatively inadequate knowledge on oral health during pregnancy. The knowledge score was lowest in the domain of dental procedures during pregnancy. Only 15% of the women correctly knew that, during pregnancy, local anesthetics and dental surgeries are safe and only 30% stated that dental X-ray and tooth extraction are safe. In terms of the relationship between oral health and pregnancy, approximately 30% correctly knew about adverse effects of oral health on pregnancy. Almost 70% believed that dental caries or loos tooth are caused by maternal calcium transfer to the fetus. Moreover, approximately 30-40% of the women perceived that dental treatments are unsafe. This was similar to the results of previous studies that pregnant women still had inadequate knowledge on oral health during pregnancy and some misconceptions regarding oral care and dental treatments[14-16]. Although routine dental care and treatments are safe, pregnant women often voluntarily avoid or postpone them for the duration of pregnancy, which might be due to limited knowledge and such misconceptions.

The results also revealed that lower socio-economic status was related to having lower level of knowledge as shown by lower educational level and family income compared to those with higher level of knowledge. This was similar to other studies that lower educational level was among important factors for having inadequate knowledge and inappropriate practice regarding oral health during pregnancy[14, 15, 19]. A Thai study also reported that, in addition to inadequate oral health care and poor oral hygiene, lower educational status and lack of knowledge were significant factors for oral health problems during pregnancy[10]. A study in Muslim Thai pregnant women reported that gingival inflammation was found to be decrease as educational level increased[17]. It was also found that the majority of pregnant women had fair oral hygiene, improper self-oral hygiene care, and inadequate knowledge.

In this study, women with higher level of knowledge were more likely to receive advice and information on oral health from medical personnel. Dental visits when not pregnant has been reported to be an important determinant of receiving dental care during pregnancy[15, 20]. Having regular dental visits could help improving knowledge on oral health in various aspects possibly from receiving regular oral health education and counseling by dentists and related health care providers.

Despite the importance of oral health during pregnancy is well-established, many health care providers in many settings rarely address it during antenatal care. Large public hospitals usually have relatively busy obstetric and dental services in terms of large number of general and complicated cases that might not be easy to integrate appropriate dental care into routine service for pregnant women. This might also possibly due to the unawareness of recommended guidelines, their reluctance on assessing oral health due to lack of skills, misconceptions about safety issue of dental procedures, and even their lack of knowledge to

address the issue with the women[21]. A previous study reported that more than half of the obstetricians did not ask about oral health issues and did not provide information on oral health during antenatal care visits, even though majority of them aware of its importance[22]. Another study found that obstetricians had high degree of knowledge with respect to the adverse pregnancy outcomes related to periodontal disease and majority recommended dental visits during pregnancy. However, they still had some misconceptions regarding dental treatment during pregnancy, especially on dental X-ray and the use of local anesthetics[23].

The strengths of this study might include that current study is among a few studies regarding this important issue in Thailand. The questionnaire was not only developed based on scientific knowledge, but also from common beliefs among Thai population which should be suitable for the study population. Pregnant women were randomly selected and enrolled during antenatal care visit that they were naïve from routine advice and counseling before completion of the questionnaire. This could help in minimizing bias in assessing baseline knowledge and attitude of the women. However, some limitations should be mentioned. Oral and dental health examinations were not performed and prevalence of actual abnormalities were not evaluated. In addition, knowledge and attitude of obstetricians and related health care providers were not evaluated. In addition to differences in cultural contexts, characteristics of the population also differed between studies, even among Thai studies, that generalization of the results might be limited.

Adequate knowledge about oral health during pregnancy could lead to better oral hygiene practice and awareness of the importance of oral health care during pregnancy. These results of this study reflect that knowledge on oral health during pregnancy is probably still inadequate and more oral health educations are needed among pregnant women in Thailand. Further studies are needed to elucidate how to improve oral health education among pregnant women as well as its barriers. In the midst of some misconceptions of both health care providers and pregnant women especially on dental procedures during pregnancy, dental evaluation visits before pregnancy should be strongly encouraged. Due to variations in background characteristics and cultural differences, a context-specific health promotion program related to oral health during pregnancy should be developed and implemented in each setting, including oral health education and appropriate preconception and antenatal oral health care. Appropriate interventions could help improve knowledge, attitude, and practice on oral health during pregnancy among Thai pregnant women. Pregnancy should be considered as an opportune time to offer preventive oral health services to improve maternal and neonatal health in the future.

Future researches are needed especially on care improvement process on appropriate oral health care during pregnancy, evaluation of future interventions of preventive oral health services, and other related issues. In addition, whether or not the improvement in oral health care could further improve pregnancy outcomes is also to be evaluated in the future as well.

Conclusion

In conclusion, knowledge on oral health was relatively inadequate in some specific issues among pregnant women. Incorrect understandings regarding many dental procedures were common. Women with higher level of knowledge on oral health during pregnancy were more likely to be in higher socio-economic status, have regular dental visits before pregnancy, and receive advice and information from health care personnel.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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GYNAECOLOGY

Metoclopramide for Preventing Ileus after Benign Gynecologic Surgery: A randomized controlled trial

Chainarong Sillapasa, M.D.*,
Rungruedee Jeerasap, M.D.*,
Thumwadee Tangsiriwatthana, M.D.*

** Department of Obstetrics and Gynecology, Khon Kaen Hospital, Khon Kaen, Thailand*

ABSTRACT

Objectives: To assess the efficacy of metoclopramide in preventing ileus after benign gynecologic surgery.

Materials and Methods: Participants included were diagnosed with benign gynecologic conditions and scheduled for abdominal hysterectomy at Khon Kaen Hospital between October 2021 and May 2022. Participants were randomly allocated into two groups: the metoclopramide group (n=25) received an injection of 2 ml (10 mg) of intramuscular metoclopramide, while the control group (n=25) received an injection of normal 2 ml of intramuscular saline at 2 h after surgery.

Results: The metoclopramide group had significantly less time to first passage of flatus than the control group (placebo) (1,785.3 ± 125.7 vs. 2,186.3 ± 103.0 min, mean difference 401.0 min (95% CI 73.1 to 728.9, p=0.02)). The incidence of ileus symptoms was significantly lower in the metoclopramide group than in the control group (28% vs 68%, p<0.01). Although not statistically significant, the metoclopramide group compared to the control group experienced (a) a shorter time to first defecation and time to tolerate a solid diet, (b) less need for additional antiemetics and additional analgesics, and (c) a shorter length of hospital stay. There were no adverse effects related to the use of metoclopramide in this study.

Conclusion: Postoperative intramuscular metoclopramide enhanced the recovery of bowel function after benign gynecologic surgery.

Keywords: metoclopramide, benign gynecologic surgery, postoperative ileus.

Correspondence to: *Chainarong Sillapasa, M.D., Department of Obstetrics and Gynecology, Khon Kaen Hospital, Khon Kaen, 40000, Thailand. E-mail: Chainarong.s@kkumail.com*

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การใช้ยาเมโทโคลพราไมด์ในการป้องกันการเกิดภาวะลำไส้อืดหลังการผ่าตัดโรคทางนรีเวชที่ไม่ใช่มะเร็ง : การศึกษาแบบสุ่ม

ชัยณรงค์ ศิลปษา, รุ่งฤดี จีระทรัพย์, ทุมวดี ตั้งศิริวัฒนา

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพของยาเมโทรโคลพลาไมด์ในการป้องการเกิดภาวะลำไส้อืดหลังการผ่าตัดโรคทางนรีเวชที่ไม่ใช่มะเร็ง*

วัสดุและวิธีการ: *อาสาสมัครผู้เข้าร่วมที่ได้รับการวินิจฉัยโรคทางนรีเวชที่ไม่ใช่มะเร็ง และมีกำหนดการผ่าตัดมดลูกทางหน้าท้องที่โรงพยาบาลขอนแก่น ระหว่างเดือน ตุลาคม พ.ศ.2564 ถึง พฤษภาคม พ.ศ. 2565 ได้รับการสุ่มแบ่งอาสาสมัครเป็นสองกลุ่ม คือกลุ่มเมโทโคลพราไมด์จำนวน 25 คน ได้รับยาเมโทโคลพราไมด์ ปริมาณ 2 มิลลิลิตร (ขนาด 10 มิลลิกรัม) แบบฉีดทางกล้ามเนื้อ ในขณะที่กลุ่มควบคุมจำนวน 25 คน ได้รับน้ำเกลือปริมาณ 2 มิลลิลิตร แบบฉีดทางกล้ามเนื้อ ที่สองชั่วโมงหลังผ่าตัด*

ผลการศึกษา: *กลุ่มเมโทโคลพราไมด์มีระยะเวลาการผายลมครั้งแรกหลังการผ่าตัดน้อยกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (1,785.3 ± 125.7 vs. 2,186.3 ± 103.9 นาที, mean difference 401.0 นาที (95% CI 73.1 to 728.9; p = 0.02) อุบัติการณ์ผู้ป่วยที่มีภาวะลำไส้อืดหลังการผ่าตัดลดลงอย่างมีนัยสำคัญในกลุ่มที่ได้ยาเมโทโคลพราไมด์เมื่อเทียบกับกลุ่มควบคุม (ร้อยละ 28% vs. 68; p < 0.01) กลุ่มเมโทโคลพราไมด์มีระยะเวลาในการเริ่มขับถ่ายอุจจาระ, การสามารถเริ่มรับประทานอาหารที่เคี้ยวได้, การใช้ยาแก้คลื่นไส้อาเจียน, การใช้แก้ปวดเพิ่ม และระยะเวลาในการพักรักษาตัวโรงพยาบาลน้อยกว่ากลุ่มควบคุม แต่ไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ ไม่พบผลข้างเคียงที่สัมพันธ์กับการใช้ยาเมโทโคลพราไมด์ในการศึกษานี้*

สรุป: *การได้รับยาเมโทโคลพราไมด์แบบฉีดทางกล้ามเนื้อหลังผ่าตัดช่วยกระตุ้นการทำงานของสำไส้หลังการผ่าตัดโรคทางนรีเวชที่ไม่ใช่มะเร็ง*

คำสำคัญ: *ยาเมโทโคลพราไมด์, การผ่าตัดโรคทางนรีเวชที่ไม่ใช่มะเร็ง, ภาวะลำไส้อืดหลังการผ่าตัด*

Introduction

Postoperative ileus (POI) is a transient impairment of gastrointestinal function[1]. POI usually presents with nausea, vomiting, abdominal pain, abdominal distention, bloating, and constipation[1,2] and may be followed by aspiration, dehydration, electrolyte imbalance, and hospital-acquired infection[1,2]. POI is a public health problem that often occurs after abdominal surgery. The respective incidence of POI in abdominal surgery and gynecological cancer surgery was 10-30%[1] and 51.8%[3]. If POI is longer than the presumed normal duration, it is assumed that a pathological or prolonged POI has occurred[1], increasing the cost of treating complications and the length of hospital stay.

The pathophysiology of POI is complex, which may result from the stimulation of the autonomic nervous system during surgical procedures and the release of various neurotransmitters or cytokines that activate inflammatory processes, resulting in the cessation of intestinal function. After surgery, the gastrointestinal system resumes normal function by reducing the inflammatory process and stimulating a cholinergic effect through the vagus nerve[1,2,4]. Based on the pathophysiology that occurs in the intestines during surgery, there are multiple methods to prevent POI, such as bowel preparation, prophylactic nasogastric tube insertion, minimally invasive surgery, maintenance of euvolemia during operation, multimodal analgesia, alvimopan (opioid μ-receptor antagonist), prokinetics, coffee, gum chewing, and early postoperative feeding[1,2,4,5].

Metoclopramide is classified as a prokinetic—part of a group discovered in the 1950s[6,7]. It acts as a dopamine D2 receptor antagonist, a 5-hydroxytryptamine 4 receptor agonist (serotonin) and muscarinic receptor agonist[4, 6, 7]—all of which facilitate cholinergic activity within the enteral nervous system or the vagus nerve. The effects on the digestive system include reducing nausea and vomiting, increasing contraction of the esophageal sphincter, increasing peristalsis, and reducing gastric emptying time[4,7]. According to its effects on the gastrointestinal system, several trials studied the effect of metoclopramide on preventing POI; however, its efficacy remains uncertain[1]. Previous studies found positive and negative results vis-à-vis preventing the occurrence of POI[1, 8, 9, 10, 11], so the current study aimed to evaluate the efficacy of metoclopramide in preventing POI after benign gynecologic surgery.

Materials and Methods

This randomized controlled study was conducted at the Department of Obstetrics and Gynecology, Khon Kaen Hospital. Before the commencement of the research, its protocol was reviewed and approved by the Khon Kaen Hospital Institutional Review Board for Human Research (reference number: KEF64019).

Recruited patients included those diagnosed with benign gynecological conditions and scheduled for abdominal hysterectomy with or without adnexal surgery. Patients were excluded if they (a) had conditions that might influence gastrointestinal motility (including previous bowel surgery, previous abdominal irradiation, chronic constipation, pancreatitis, peritonitis, hypothyroidism, and chronic use of drugs that impact intestinal peristalsis), (b) used oral or mechanical bowel preparation before surgery, (c) had a history of serious side effects due to metoclopramide, (d) underwent a procedure with entry into the gastrointestinal tract or bowel anastomosis, and/or (e) needed intensive care after surgery or nasogastric tube drainage. The patients were informed about the study at the gynecological ward before undergoing surgery. Written informed consent was obtained from each participant before enrollment. Postoperative hysterectomy women who met the eligibility criteria were randomly assigned into two groups using a computer-generated list and allocation concealment using sequentially opaque envelopes: the metoclopramide group and the control group. Baseline characteristics were recorded: age, body mass index (BMI), comorbid diseases, indications for surgery, previous abdominal surgery, and preoperative hemoglobin (Hb) level. The participants were informed

about the outcomes that they had to observe and record, including: time to first passage of flatus after surgery, time to first defecation, and ileus symptoms. A digital clock was set up as the standard time for recording the outcomes. Before the operation, all patients received the same preoperative care, anesthetic protocol, intravenous antibiotic prophylaxis after induction of anesthesia, and transverse abdominis plane (TAP) block. The surgical procedures were performed by staff or senior residents under supervision by staff not involved in the study.

After the operation, the nurse on the ward opened the envelope that contained a 3-ml syringe. Each identical syringe had 2 ml of clear liquid of metoclopramide or normal saline prepared by a pharmacologist. The metoclopramide group received 2 ml (10 mg) of intramuscular metoclopramide (MET-SIL®, T.P. DRUG LABORATORIES (1969) CO., LTD), while the control group received 2 ml of intramuscular normal saline (placebo) 2 h after surgery. The surgeon and ward nurses did not know which agent the participants received.

The postoperative care protocol was intravenous administration of an opioid agent (2 mg of morphine for body weight < 50 kg or 3 mg for body weight ≥ 50 kg) every 4 h for 24 h. In addition, a single dose of 4 mg intravenous ondansetron was administered to prevent nausea and vomiting. Prophylactic antibiotics were administered for 24 h after surgery. Ambulation was promoted the day after surgery. The postoperative feeding regimen was standardized; a liquid/soft diet was begun on the first postoperative day, followed by a solid/regular diet over the next 24 h, as tolerated.

When the patients began postoperative feeding, additional analgesics were provided according to the patient numeric pain score (1-10). For example, oral paracetamol 500 mg or Ibuprofen 400 mg were provided when the pain score was 4 – 6 out of 10, while intravenous morphine was provided when the pain was ≥ 7 out of 10.

All primary and secondary outcomes were recorded. The primary outcome was time to first passage of flatus after surgery. The secondary outcomes were time to first defecation, time to tolerate a solid diet (defined as eating any food that requires chewing without vomiting or nausea within 4 h after the meal), additional antiemetic requirements, additional analgesic requirements, ileus symptoms (defined by the I-FEED scoring system[5] divided into three categories: normal or mild [score 0-2], moderate or postoperative gastrointestinal intolerance [score 3-5], severe or postoperative gastrointestinal dysfunction [score > 6]), adverse effect of metoclopramide (e.g., drowsiness, restlessness, extrapyramidal reaction, and/or rash)[11], and length of hospital stay. After the patients became conscious, the outcomes were reviewed and then recorded in the record form by the ward nurse every 4 h after surgery until the patient was discharged. Patients could be discharged when they could tolerate a solid diet and urinate and defecate normally, had no bleeding per vagina, had no abdominal pain, could ambulate without assistance, had stable vital signs without fever for at least 24 hours, and had no postsurgical complications. After discharge, the length of hospital stay was recorded.

The sample size was calculated based on a pilot study of 30 patients with a power of 90%, an α level of 0.05, and a dropout rate of 15%. Fifty participants (25 in each group) were thus required. Data were analyzed using Stata version 14 based on an intention-to-treat analysis. The normality of continuous data was tested using histogram plots and/or the Kolmogorov-Smirnov test of normality. Student's t-test (or the Mann-Whitney U test) and the chi-squared test (or Fisher's exact test) were used to analyze continuous and categorical data, respectively. The Kaplan Meier survival analysis was used to analyze time to first passage of flatus after surgery. A p value < 0.05 was considered statistically significant.

Results

Between October 2021 and May 2022, 53 eligible women scheduled for abdominal hysterectomy, with or without adnexal surgery, were enrolled in the

study. Three of them were excluded from the study: one because the surgery was canceled due to covid-19 infection and two because of postoperative complications requiring intensive care. So, a total of 50 eligible women were randomly assigned: 25 to the metoclopramide group and 25 to the control group. There were no dropouts (Fig. 1). Preoperative baseline characteristics were similar between groups, including age, body mass index (BMI), comorbid diseases, indications for surgery, previous abdominal surgery, and pre-operative hemoglobin (Hb) level (Table 1).

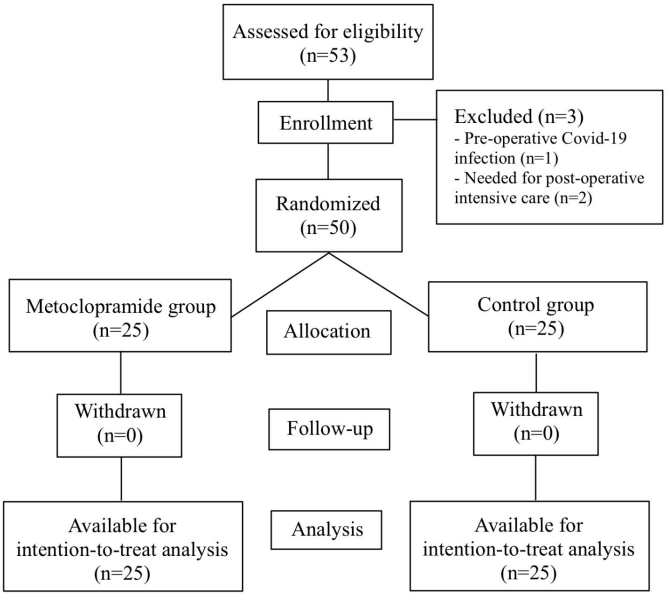

Fig. 1. Study flow.

Table 1. Baseline characteristics of participants undergoing abdominal hysterectomy for benign gynecologic condition.

Baseline characteristic	Metoclopramide group (n=25)	Control group (n=25)	p value
Age (years), mean (SD)	47.3 (5.8)	49.2 (7.2)	0.30[a]
Body mass index (kg/m^2), mean (SD)	26.7 (5.8)	25.9 (4.7)	0.59[a]
Comorbid diseases, n (%)	6 (24.0)	6 (24.0)	1.00[b]
Indication for surgery, n (%)			0.08[c]
Myoma uteri	23 (92.0)	15 (60.0)	
Adenomyosis	1 (4.0)	5 (20.0)	
Cervical intraepithelial neoplasia III	0 (0.0)	1 (4.0)	
Endometrial hyperplasia	0 (0.0)	2 (8.0)	
Ovarian tumor	1 (4.0)	2 (8.0)	
Previous abdominal surgery, n (%)	13 (52.0)	14 (56.0)	0.77[b]
Pre-operative hemoglobin level (g/dL), mean (SD)	10.2 (2.4)	11.6 (1.9)	0.28[a]

[a] Student T-test, [b] Chi-square test, [c] fisher's exact test. SD: standard deviation.

Operative outcomes were also similar between groups, including operative procedure, type of incision, length of incision, operative time, duration of anesthesia, estimated blood loss, provisional diagnosis, and post-operative hemoglobin (Hb) level (Table 2).

Table 2. Operative outcomes of participants undergoing abdominal hysterectomy for benign gynecological condition.

Operative outcome	Metoclopramide group (n=25)	Control group (n=25)	p value
Operative procedure, n (%)			0.10[b]
Total abdominal hysterectomy with bilateral salpingectomy	9 (36.0)	4 (16.0)	
Total abdominal hysterectomy with bilateral salpingo-oophorectomy	16 (64.0)	21 (84.0)	
Type of incision, n (%)			
Low Midline	9 (36.0)	13 (52.0)	0.25[b]
Pfannenstiel	15 (60.0)	12 (48.0)	0.39[b]
Maylard	1 (4.0)	0 (0.0)	0.50[c]
Length of incision (cm), mean (SD)	11.3 (1.2)	11.8 (1.6)	0.25[a]
Operative time (min), mean (SD)	86.2 (25.8)	91.1 (22.6)	0.48[a]
Duration of anesthesia (min), mean (SD)	106.0 (36.6)	109.2 (22.3)	0.71[a]
Estimated blood loss (ml), mean (SD)	165.6 (27.8)	147.2 (26.0)	0.63[a]
Post-operative diagnosis, n (%)			0.08[c]
Myoma uteri	23 (92.0)	15 (60.0)	
Adenomyosis	1 (4.0)	5 (20.0)	
Cervical intraepithelial neoplasia III	0 (0.0)	1 (4.0)	
Endometrial hyperplasia	0 (0.0)	2 (8.0)	
Ovarian tumor	1 (4.0)	2 (8.0)	
Post-operative hemoglobin level (g/dL), mean (SD)	9.8 (1.9)	11.2 (1.6)	0.07[a]

[a] Student T-test, [b] Chi-square test, [c] fisher's exact test. SD: standard deviation.

The respective time to first passage of flatus after surgery was 1,785.3 ± 125.7 min and 2,186.3 ± 103.9 min in the metoclopramide group and control group, respectively. The mean difference was 401.0 min (95% confidence interval (CI) 73.1 to 728.9, p = 0.02). The respective proportion to first passage of flatus within 48 h after surgery in the metoclopramide and control group was 100% and 88%, respectively. The respective mean difference in minimum and maximum time to first passage of flatus was 815 and 145 min (Table 3). The Kaplan-Meier survival analysis of time to first passage of flatus between groups is presented in Fig. 2. The respective median survival time to first passage of flatus after surgery (50%) in the metoclopramide group and control group was 1,530 min (95% CI: 1,435 to 2,365) vs. 2,085 min (95% CI: 1,715 to 2,640, p = 0.02).

Table 3. Postoperative ileus (POI), additional drug requirement and length of hospital stay of participants undergoing abdominal hysterectomy for benign gynecological condition.

Outcomes	Metoclopramide group (n=25)	Control group (n=25)	Mean Difference (min)	95% CI	p value
Time to first passage of flatus (min), mean (SD)	1,785.3 (125.7)	2,186.3 (103.9)	401.0	73.1 to 728.9	0.02[a]*
Minimum time (min)	610	1425	815		
Maximum time (min)	2880	3025	145		
At 12 h, n (%)	2 (8)	0 (0)			
At 24 h, n (%)	8 (32)	1 (4)			
At 36 h, n (%)	16 (64)	13 (52)			
At 48 h, n (%)	25 (100)	22 (88)			
More than 48 h, n (%)		25 (100)			
Time to first defecation (min), mean (SD)	1,767.0 (322.1)	1,949.0 (435.4)	182.0	-35.8 to 399.8	0.09[a]
Time to tolerate a solid diet (min), mean (SD)	4,022.7 (928.9)	4,077.4 (1,202.9)	54.7	-556.4 to 665.9	0.85[a]
Additional antiemetic requirements, n (%)	2 (8.0)	3 (12.0)			0.63[b]
Additional analgesic requirements, n (%)	10 (40.0)	11 (44.0)			0.77[b]
Ileus symptoms, n (%)	7 (28.0)	17 (68.0)			< 0.01[b]*
Severe	0 (0.0)	1 (4.0)			0.50[c]
Moderate	1 (4.0)	6 (24.0)			0.04[b]*
Mild	6 (24.0)	10 (40.0)			0.22[b]
Length of hospital stay (hrs.), mean (SD)	99.8 (8.4)	100.6 (6.7)			0.74[a]

[a] Student T-test, [b] Chi-square test, * significant p<0.05. SD: standard deviation, CI: confidence interval.

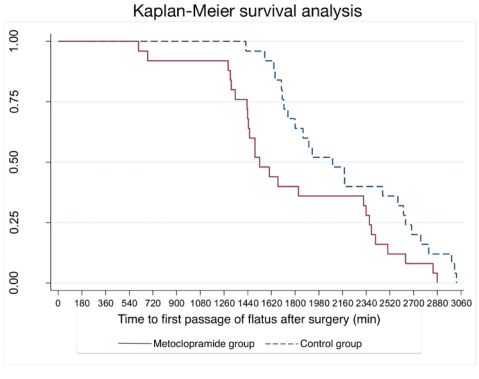

Fig. 2. Kaplan-Meier survival analysis of the time to first passage of flatus

Kaplan-Meier survival estimated the time to first passage of flatus. Median time to first flatus (50%) of metoclopramide group was 1,530 min (95% CI: 1,435 to 2,365) and control group was 2,085 min (95% CI: 1,715 to 2,640). Log-rank test for survivor functions (p = 0.02)

In addition, ileus symptoms were significantly less frequent in the metoclopramide group (n = 7, 28%) than in the control group (n = 17, 68%). The ileus symptoms were categorized using the I-FEED scoring system. Moderate symptoms were defined as postoperative gastrointestinal intolerance (POGI), and these increased significantly in the control group compared to the metoclopramide group (24% vs. 4%, p = 0.04). None of the patients with ileus symptoms had any clinicals indicating mechanical obstruction or peritonitis and responded to supportive treatment. Whereas time to first defecation, time to tolerate a solid diet, additional antiemetic requirements, additional analgesic requirements, and length of hospital stay were less in the metoclopramide group than in the control group, albeit without statistical significance. We found no adverse effects related to the use of metoclopramide (Table 3).

Discussion

Our study showed that, compared to placebo, intramuscular metoclopramide at 2 h after surgery promoted the recovery of gastrointestinal function by significantly shortening the time to first passage of flatus. The metoclopramide group was significantly faster (401.0 min) than the control group (1,785.3 ± 125.7 vs. 2,186.3 ± 103.9 min). About one-third (32%) of women in the metoclopramide group experienced first passage of flatus within 24 hours after surgery compared to only 4% of women in the control group. The average time to first passage of flatus in the metoclopramide group was 13.5 h faster than in the control group, supporting the hypothesis that metoclopramide is effective in preventing POI.

Notwithstanding, the results of our study indicated a longer time to first passage of flatus compared to that reported by Agah et al[11] (viz., 1,098.2 min), which might be explained by the different types of surgery and anesthesia. Our study used a total transabdominal hysterectomy under general anesthesia, while Agah et al[10] used cesarean section, with most patients receiving regional anesthesia. The type of surgical procedure and anesthesia have a significant impact on the recovery of the gastrointestinal system. The procedure of cesarean is less associated with direct bowel manipulation than hysterectomy. Surgical procedures require more bowel manipulation, which induces the inflammatory process, the main mechanism of POI[1]. In 2016, a Cochrane review[12] showed the benefit of epidural analgesia added to general anesthesia in abdominal surgery, accelerating the return of flatus and bowel movement faster than systemic opioid-based regimens plus general anesthesia. In addition, the regional analgesic technique decreased opioid consumption, lessening the impact on gastrointestinal motility.

A meta-analysis[8] of five clinical trials showed the beneficial effect of metoclopramide on ileus symptoms, as in our study that showed a reduction in POI symptoms after benign gynecologic surgery, especially postoperative gastrointestinal intolerance (POGI). Metoclopramide is widesly used as an antiemetic and effective in reducing postoperative nausea and/or vomiting[7] which is one of POI symptoms. Thus, postoperative metoclopramide injection decreased time to first passage of flatus and reduced ileus symptoms by enhancing bowel function. We assume that such a positive outcome might also increase patient satisfaction and reduce the costs of medical care.

Our results showed that time to first defecation, time to tolerate a solid diet, additional antiemetic requirements, additional analgesic requirements, and length of hospital stay trended to be less in the metoclopramide group than in the control group, albeit not statistically significant. These results differ from those of a meta-analysis[8] and Agah et al[11], who reported that metoclopramide significantly addressed these issues, perhaps explained by differences in types of operation and time to a step diet. Our study confirmed no adverse effects of metoclopramide as reported in the meta-analysis[9] vis-à-vis preventing POI.

The study's strengths included that it was a prospective, double-blind RCT design with an adequate sample size and used the I-FEED scoring

system to categorize POI symptoms. Limitations included (a) the use of a subjective measure of time to first passage flatus, which is a clinical parameter requiring patient self-observation for evaluating restoration of bowel function, and (b) the patients received food according to the hospital meal schedule regardless of the time duration after surgery, which might affect the evaluation of time to first defecation and time to tolerate a solid diet.

Conclusion

In summary, compared with placebo, postoperative intramuscular metoclopramide significantly enhanced the recovery of bowel function after benign gynecologic surgery and decreased the development of POI.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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GYNAECOLOGY

Overactive Bladder Symptom Score Changes after Pessary Insertion in Women with Pelvic Organ Prolapse and Overactive Bladder

Sucharee Yaranun, M.D.*,
Keerati Chiengthong, M.D.*,
Purim Ruanphoo, M.D., PhD*,
Suvit Bunyavejchevin, M.D., MHS*

** Female Pelvic Medicine and Reconstructive Surgery Division, Departments of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

ABSTRACT

Objectives: To determine the overactive bladder symptom score (OABSS) change after pessary insertion in patients with symptomatic pelvic organ prolapse and overactive bladder at 3 months after treatment.

Materials and Methods: During May 2020 and May 2021, 27 patients diagnosed as having pelvic organ prolapse with overactive bladder and treated by vaginal pessary were recruited in the study. The Thai-version Overactive Bladder Symptom Scores (OABSS) Questionnaire was used to assess the overactive bladder symptom before and after pessary treatment at 3 months follow-up.

Results: The mean total OABSS scores at pre- and post- treatment were 6.9 ± 3.3 and 4.4 ± 3.1, with significant difference at $p < 0.05$. The patients with improved OABSS score were 85.2% (23/27) after pessary insertion. OABSS significantly improved in all subcategories including frequency, nocturia, urgency, and incontinence. After performing the univariate analysis, there was no significant relationship between OABSS outcome and various factors such as age, weight, height, BMI, parity, and POP-Q stages.

Conclusion: The overactive bladder symptom score (OABSS) changed significantly after pessary treatment in women diagnosed with symptomatic pelvic organ prolapse and overactive bladder.

Keywords: pelvic organ prolapse, overactive bladder, overactive bladder symptom score (OABSS), pessary .

Correspondence to: *Suvit Bunyavejchevin, M.D., MHS. Departments of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. Email: suvit.b@chula.ac.th*

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อาการกระเพาะปัสสาวะไวเกินในผู้ป่วยที่มีภาวะอุ้งเชิงกรานหย่อน ภายหลังการรักษาด้วยห่วงพยุงช่องคลอด

สุชารีย์ ยะระนันท์ กีรติ เชียงทอง ปุริม เรือนภู่ สุวิทย์ บุณยะเวชชีวิน

บทคัดย่อ

วัตถุประสงค์: *เพื่อประเมินคะแนนของแบบสอบถามอาการโรคกระเพาะปัสสาวะไวเกิน (OABSS) ที่เปลี่ยนแปลงไปหลังจากการรักษาผู้ที่มีภาวะอุ้งเชิงกรานหย่อนและภาวะกระเพาะปัสสาวะไวเกินด้วยห่วงพยุงช่องคลอด*

วัสดุและวิธีการ: *ระหว่างเดือน พฤษภาคม พ.ศ. 2563 ถึง พ.ศ.2564 สตรีไทยจำนวน 27 ราย ที่ได้รับการวินิจฉัยว่ามีภาวะอุ้งเชิงกรานหย่อนและภาวะกระเพาะปัสสาวะไวเกินและได้รับการรักษาด้วยห่วงพยุงช่องคลอดได้คัดเลือกเข้ามาในการศึกษา โดยมีการประเมินอาการของกระเพาะปัสสาวะไวเกินก่อนและหลังการรักษาด้วยห่วงพยุงช่องคลอดที่ระยะเวลา 3 เดือน ด้วยแบบสอบถามอาการโรคกระเพาะปัสสาวะไวเกินฉบับภาษาไทย (Thai-version OABSS)*

ผลการศึกษา: *ค่าเฉลี่ย ± ค่าเบี่ยงเบนมาตรฐานของคะแนนของแบบสอบถามอาการโรคกระเพาะปัสสาวะไวเกิน (OABSS) ก่อน และ หลัง การรักษาคือ 6.9 ± 3.3 และ 4.4 ± 3.1 ตามลำดับ โดยค่า $p < 0.05$ แสดงถึงความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ในงายวิจัยนี้ผู้ป่วยทั้งหมดร้อยละ 85.2 (23/27) มีคะแนนของแบบสอบถามลดลง (อาการกระเพาะปัสสาวะไวเกินดีขึ้น) หลังจากการรักษาด้วยห่วงพยุงช่องคลอด ซึ่งคะแนนของแบบสอบถาม OABSS ลดลงอย่างมีนัยสำคัญทางสถิติในทุกหัวข้อของแบบสอบถาม ซึ่งได้แก่ อาการปัสสาวะบ่อย ปัสสาวะตอนกลางคืน ปัสสาวะเร่งรีบ รวมไปถึงอาการกลั้นปัสสาวะไม่ได้ จากการศึกษาแบบ Univariate analysis ของปัจจัยที่อาจจะส่งผลต่อคะแนนของแบบสอบถาม OABSS ที่ไม่ดีขึ้น พบว่าไม่มีความสัมพันธ์ระหว่างผู้ป่วยที่อาการไม่ดีขึ้นและปัจจัยเหล่านี้ได้แก่ อายุ น้ำหนัก ส่วนสูง ค่าดัชนีมวลกาย จำนวนการคลอด และ POP-Q stage*

สรุป: *คะแนนของแบบสอบถามอาการโรคกระเพาะปัสสาวะไวเกิน (OABSS) เปลี่ยนแปลงไปในทางที่ดีขึ้นอย่างมีนัยสำคัญทางสถิติ เมื่อเปรียบเทียบก่อนและหลังการรักษาผู้ที่มีภาวะอุ้งเชิงกรานหย่อนและภาวะกระเพาะปัสสาวะไวเกินด้วยห่วงพยุงช่องคลอด*

คำสำคัญ: *อวัยวะอุ้งเชิงกรานหย่อน, ภาวะกระเพาะปัสสาวะบีบตัวไวเกิน, ความเที่ยงตรงของแบบสอบถามอาการโรคกระเพาะปัสสาวะไวเกิน, ห่วงพยุงทางช่องคลอด*

Introduction

The prevalence of pelvic organ prolapse (POP) increased with age and it doubled in women aged 80 years and older[1]. Overactive bladder (OAB) is a symptom often seen in women who experienced pelvic organ prolapse. These were confirmed in several studies that the incidence of overactive bladder was significantly higher in patients with symptomatic POP. Furthermore, many factors such as bladder outlet obstruction, bladder distension and prominent cystocele were found to be the significant risk factors of OAB in women with POP[2, 3].

Vaginal pessary is a treatment of choice for POP. There was the evidence that the three-day micturition/ incontinence diary and the urgency and urge incontinence improved in women diagnosed as having OAB with POP after pessary treatment[4, 5]. Using standard questionnaires for the diagnosis and follow-up for the response of treatment was introduced as the instrument for the patient reported outcome measurement[6]. The standard questionnaires such as overactive bladder symptoms score (OABSS) questionnaire is recommended by the International Consultation on Incontinence[7] for the assessment of changes in overactive bladder symptoms. The OABSS questionnaire had already been translated and validated into Thai language[8]. Although there were evidences of clinical OAB symptom improvement in POP patients after pessary treatment, no studies regarding the utilization of standard symptom questionnaire to assess and compare clinical improvement after different treatment modalities for future research were reported. In order to fill this research gap, this research was primarily designed to evaluate overactive bladder symptoms before and after treating patients having symptomatic POP with vaginal pessary by applying the Thai version of OABSS. The secondary objective was to identify the risk factors in the cases that OABSS were not improved after pessary management.

Materials and Methods

This study was carried out as the before and after study at the Female Pelvic Medicine and Reconstructive Surgery clinic of King Chulalongkorn Memorial Hospital, Bangkok, Thailand, between May 2020 and May 2021. The research protocol was approved by the Institutional Review Board of the hospital. This study followed the STROBE guideline for prospective and observational study[9].

Participants were women aged more than 18 years old with (1) symptomatic POP diagnosed by clinical symptoms, pelvic examination and POP-Q staging classification (2) overactive bladder symptoms, and (3) vaginal pessary as the treatment of choice for prolapse. The exclusion criteria were women with undiagnosed vaginal discharge, abnormal uterine bleeding, vaginal or cervical cancer, impaired mental capacity, noncompliance in follow-up, infection, and intermittent catheter usage. Information regarding demographic data, patient characteristics, and OABSS were extracted for analysis. POP was defined as the descent of one or more of the anterior vaginal wall, posterior vaginal wall, the uterus (cervix), or the apex of the vagina (vaginal vault or cuff scar after hysterectomy), correlated with symptoms[10]. Overactive bladder (OAB) is diagnosed primarily by symptoms such as urgency with or without urge incontinence, usually with frequency and nocturia, and other causes such as infection or other pathology needed to be ruled out[11]. Clinical risk factors that were evaluated in this study included age, weight, height, body mass index (BMI), parity, and POP-Q stage. At 0 and 3 months of pessary treatment, the participants were asked to self-complete the Thai version of OABSS questionnaires. The clinical data including the side effect or complications of pessary were recorded at 3 months follow-up.

The OABSS questionnaire is the self-reported questionnaire to quantify OAB symptoms[12]. It consists of 4 questions, including daytime frequency, night-time frequency, urgency, and urgency incontinence. The severity of each symptom is rated on the Likert scale from 0-2 for day time frequency, from 0-3 for night-time frequency, from 0-5 for urgency incontinence, respectively. The total score of the OABSS ranges from 0 to 15, indicating the higher the score, the more severe

the symptoms. Patients were defined as improved if the post-treatment score of OABSS decreased more than or equal to 1, and were defined as not improved if the score did not change.

The sample size was calculated from the mean difference of the pre- and post-treatment OABSS scores obtained during the 10-case pilot study with add on drop out of 20%. Thus, the formula for sample size calculation for two dependent means study was $(Z_{1-\alpha/2}+Z_{1-\beta})^2 * \sigma^2 / d^2$. The pool variance ($\sigma$) was 3.4 and the delta (mean difference of OABSS score = d) was 2.0 (α = 0.05 and β = 0.2). $N = (1.96 + 0.84)^2 \times (3.4)^2 / (2)^2 = 23$. With the add on drop out of 4 cases, 27 participants were required.

The numbers and percentages were used for categorical data presentation. The mean and standard deviation were used for the continuous data presentation. The difference between pre- and post-treatment OABSS was analyzed by the paired t-test. The univariate analysis by independent t-test and multivariate analysis by logistic regression analysis were used for the factors affecting the OABSS outcomes in this study. Statistical analysis was carried out by IBM SPSS Statistics for Windows, version 22.0 with statistical significance at p value less than 0.05.

Results

Of 27 women, the mean age was 71.8 ± 8.7 years. Most women demonstrated advanced stage (stage III-IV) POP in both anterior (70.3%) and apical (59.2%) compartments, except posterior compartment (29.6 %) (Table 1). Successful pessary fitting was achieved at the first visit and pessary use was continued without complications until the 3-month follow-up. No treatment failure, such as pessary change and switching to another treatment modality, was reported.

Table 1. Patients' Characteristics (n = 27).

Characteristics	Mean ± SD
Age (yr)	71.8 ± 8.7
Weight (kg)	58.3 ± 7.9
Height (cm)	151.3 ± 4.8
BMI (kg/m^2)	24.6 ± 3.7
Parity	3.0 ± 1.6
POP-Q stage	**n (%)**
Anterior compartment	
Stage 0	2 (7.4)
Stage I	2 (7.4)
Stage II	4 (14.8)
Stage III	12 (44.4)
Stage IV	7 (25.9)
Apical compartment	
Stage 0	2 (7.4)
Stage I	4 (14.8)
Stage II	5 (18.5)
Stage III	4 (14.8)
Stage IV	12 (44.4)
Posterior compartment	
Stage 0	4 (14.8)
Stage I	8 (29.6)
Stage II	7 (25.9)
Stage III	5 (18.5)
Stage IV	3 (11.1)

SD: standard deviation, BMI: body mass index, POP-Q: Pelvic Organ Prolapse Quantification system, OABSS: overactive bladder symptom score

The majority of women (48.1%) demonstrated the total OABSS between 6-11 prior to treatment, whereas 40.7% showed lower scores between 3-5 after treatment (Table 2).

Table 2. Pre and Post treatment of the OABSS score (n = 27).

OABSS score	Pre-treatment OABSS score n (%)	Post-treatment OABSS score n (%)
Pre-treatment OABSS: total score		
Less than 3	2 (7.4)	7 (25.9)
3 to 5	9 (33.4)	11(40.8)
6 to 11	13 (48.1)	7 (25.9)
12 or more	3 (11.1)	2 (7.4)
Pre-treatment OABSS: frequency score		
0	13 (48.1)	20 (74.2)
1	13 (48.1)	6 (22.2)
2	1 (3.7)	1 (3.7)
Pre-treatment OABSS: nocturia score		
0	1 (3.7)	2 (7.4)
1	5 (18.5)	8 (29.6)
2	9 (33.4)	12 (44.5)
3	12 (44.4)	5 (18.5)
Pretreatment OABSS: urgency score		
0	0 (0)	12 (44.5)
1	9 (33.4)	3 (11.1)
2	7 (25.9)	6 (22.2)
3	0 (0)	1 (3.7)
4	7 (25.9)	4 (14.8)
5	4 (14.8)	1 (3.7)
Pretreatment OABSS: incontinence score		
0	13 (48.1)	16 (59.3)
1	0 (0)	3 (11.1)
2	9 (33.4)	5 (18.5)
3	0 (0)	1 (3.7)
4	3 (11.1)	1 (3.7)
5	2 (7.4)	1 (3.7)

OABSS: overactive bladder symptom score

When statistically comparing, the mean OABSS between pre- and post-pessary treatment, significant improvement was observed in both total scores (6.9 ± 3.3 vs 4.4 ± 3.1, $p < 0.05$) and all subcategories (Table 3).

Table 3. The Mean ± SD of the Pre and Post treatment OABSS (n = 27).

	Pre-treatment		Post-treatment		p value
	mean ± SD	min-max	mean ± SD	min-Max	
OABSS items					
Frequency	0.6 ± 0.6	0-2	0.3 ± 0.5	0-2	0.017*
Nocturia	2.2 ± 0.9	0-3	1.7 ± 0.9	0-3	0.020*
Urgency	2.6 ± 1.5	1-5	1.4 ± 1.6	0-4	0.001*
Incontinence	1.5 ± 1.7	0-5	0.9 ± 1.4	0-5	0.037*
Total	**6.9 ± 3.3**	**2-14**	**4.4 ± 3.1**	**1-12**	**< 0.001***

*statistically significant at p-value < 0.05. SD: standard deviation, OABSS: overactive bladder symptom score

There were 23 cases with OABSS score improvement and 4 cases of non-improvement. For women with OABSS improvement (n = 23), the mean total scores prior to and after pessary treatment were 7.3 ± 3.3 and 4.1 ± 3.2, respectively, whereas those with no improvement (n = 4) demonstrated similar outcomes between pre-and post-treatment scores (4.2 ± 1.7 vs 5.8 ± 2.1). By using univariate analysis, there was no difference in terms of the age, weight, height, BMI, parity, and POP-Q stage when compared between women with and without improved OABSS (Table 4).

Table 4. Univariate analysis of the factors affecting the OABSS outcome (n = 27).

Factors	Improved OABSS group (n = 23)	Not improved OABSS group (n = 4)	p value
	mean ± SD	mean ± SD	
Age (yr)	72.0 ± 8.2	69.5 ± 12.2	0.573
Weight (kg)	58.0 ± 7.9	59.7 ± 9.3	0.700
Height (cm)	151.5 ± 3.8	150.3 ± 9.3	0.653
BMI (kg/m^2)	25.5 ± 3.9	26.5 ± 3.3	0.630
Parity	3.3 ± 1.3	3.0 ± 2.0	0.961
	n (%)	n (%)	p value
POP-Q stage			
1 and 2	5 (18.5)	0 (0)	0.320
3 and 4	18 (66.7)	4 (14.8)	0.320

SD: standard deviation, BMI: body mass index, POP-Q: Pelvic Organ Prolapse Quantification system, OABSS: overactive bladder symptom score

Discussion

Results from our study have confirmed that POP-related OAB symptoms, which were quantified by the OABSS questionnaire, significantly improved after ring pessary treatment. There were many similar reports showing that OAB symptom significantly improved after using a pessary as the treatment for POP[5, 13, 14]. Clemons et al reported that 73 women with successful pessary fitting had the urge incontinence improvement by 46% after 2 months of treatment[13]. Fernando et al demonstrated that 79 patients had significant improvement in both urgency (38%, $p < 0.001$) and urge urinary incontinence (29%, $p < 0.015$)[14]. According to Kuhn et al, 73 women evaluated by the Sheffield POP symptom questionnaires were also found to have significant OAB improvement after the pessary treatment[5]. Using the OABSS to measure the OAB symptom improvement is considered beneficial due to the quantitative measurement which makes it easy for objective comparison of OAB symptoms before and after treatment. The use of OABSS questionnaire required more time in the outpatient clinic for both medical personnel and the patients. This might limit the use of OABSS in clinical practice. Because the major symptom for the diagnosis of OAB is the urgency, the use of urgency questionnaire such urgency distress inventory (U-UDI) is advocated for future research[15].

The pessary can improve symptoms of overactive bladder in POP patients by the reduction of bladder outlet obstruction/bladder distension which occurred as a consequence of the prominent cystocele[3]. We noticed that OAB symptoms improved in 85.2%, (23 out of 27) of the patients, whereas the remaining 14.8% reported unchanged or worsened symptoms. Among patients whose symptoms were not improved after the pessary use, the mean total OABSS were relatively low before treatment with the average score of 4.3. Fortunately, no patient required any additional treatments. This can be assumed that pessary can significantly relieve OAB symptoms in patients with more severity (higher OABSS scores).

From our results, the use of pessary was found to significantly improve OAB symptoms. With the advantages of low cost and low complication rates, vaginal pessary should be recommended as a first-line treatment option for women with POP-related OAB

symptoms. If symptoms do not improve after pessary insertion, additional treatments for OAB may be considered.

Strengths of this study

This study used the validated Thai-version OABSS as the standard questionnaire with proper selection criteria. The good compliance in the pessary treatment and follow-up were noted in this study.

Limitations of this study

The sample size calculation for the secondary outcome was not carried out. The future studies with larger sample size with longer follow-up period are advocated. Further comparative studies of OAB symptoms between different treatment modalities, such as pessary only vs pessary with vaginal estrogen, pessary vs surgery, and pessary vs other conservative management should be considered.

Conclusion

The prolapse-related OAB symptoms can be significantly improved after pessary treatment for prolapse as quantified by the validated Thai-version OABSS.

Potential conflicts of interest

The authors declare no conflicts of interest.

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GYNAECOLOGY

Practice of Antibiotic Prophylaxis in Abdominal Hysterectomy at King Chulalongkorn Memorial Hospital

Gunta Prawai, M.D.*,
Surasith Chaithongwongwatthana, M.D., M.Sc.*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand*

ABSTRACT

Objectives: To evaluate the rate of adherence to the guidelines for antibiotic prophylaxis using in elective abdominal hysterectomy.

Materials and Methods: Retrospective descriptive study was conducted by reviewing medical records of women underwent elective abdominal hysterectomy at King Chulalongkorn Memorial Hospital (KCMH) from January to December 2019. Cases who having bacterial infection, surgical procedures on gastrointestinal or urinary tract, operative time longer than 3 hours, blood loss more than 1,500 milliliters, immunosuppression, or receiving immunosuppressive agents were excluded. Logistic regression analysis was used to determine factors associated with appropriate use of antibiotics prophylaxis.

Results: A total of 588 women underwent elective abdominal hysterectomy in the study period. Among 391 eligible patients with a mean age of 48.7 years, 326 cases (83.4%) had benign diseases on final diagnosis. Most of the operations used transverse skin incision and a median operative time and blood loss were 90 minutes and 200 milliliters, respectively. Use of antibiotics prophylaxis that adherent to the guidelines was demonstrated in 63 cases (16.1% of all cases, 19.3% of cases without staging procedures). Among cases without staging procedures, operation by residents was the only factor that significantly increased appropriate use of antibiotics prophylaxis with adjusted odds ratio of 6.84 (95% confidence interval 3.40-13.74).

Conclusion: Uses of antibiotic prophylaxis for abdominal hysterectomy at KCMH were mostly not adherent to the guidelines. An antibiotic stewardship program needs to be implemented to improve the practice.

Keywords: antibiotic prophylaxis, hysterectomy, practice.

Correspondence to: *Surasith Chaithongwongwatthana, M.D., M.Sc., Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. E-mail: iamsurasith@gmail.com*

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การใช้ยาปฏิชีวนะป้องกันการติดเชื้อสำหรับการตัดมดลูกทางหน้าท้องในทางปฏิบัติในโรงพยาบาลจุฬาลงกรณ์

กันตา พระไวย์, สุรสิทธิ์ ชัยทองวงศ์วัฒนา

บทคัดย่อ

วัตถุประสงค์: *เพื่อประเมินอัตราการปฏิบัติตามแนวทางการใช้ยาปฏิชีวนะป้องกันการติดเชื้อสำหรับการตัดมดลูกทางหน้าท้องที่ไม่เร่งด่วน*

วัสดุและวิธีการ: *การศึกษาเชิงพรรณนาย้อนหลังโดยการทบทวนเวชระเบียนของสตรีที่ได้รับการตัดมดลูกทางหน้าท้องที่ไม่เร่งด่วนในโรงพยาบาลจุฬาลงกรณ์ ตั้งแต่เดือนมกราคมถึงธันวาคม ค.ศ. 2019 ผู้ป่วยที่ถูกคัดออกจากการศึกษา ได้แก่ มีการติดเชื้อแบคทีเรีย, ได้รับการผ่าตัดในระบบทางเดินอาหารหรือทางเดินปัสสาวะ, ระยะเวลาการผ่าตัดนานกว่า 3 ชั่วโมง, ปริมาณการเสียเลือดมากกว่า 1,500 มิลลิลิตร, ภูมิคุ้มกันบกพร่อง หรือ ได้รับยากดภูมิคุ้มกัน การประเมินปัจจัยที่สัมพันธ์กับการใช้ยาปฏิชีวนะเพื่อป้องกันการติดเชื้อที่เหมาะสมใช้การวิเคราะห์การถดถอยโลจิสติค*

ผลการศึกษา: *จำนวนสตรีที่ได้รับการตัดมดลูกทางหน้าท้องที่ไม่เร่งด่วนในช่วงระยะเวลาการศึกษาทั้งหมด 588 ราย มีผู้ป่วยที่เข้าเกณฑ์การศึกษาทั้งสิ้น 391 ราย ซึ่งมีอายุเฉลี่ย 48.7 ปี และ 326 ราย (ร้อยละ 83.4) ได้รับการวินิจฉัยขั้นสุดท้ายเป็นโรคที่ไม่ใช่มะเร็ง แผลผ่าตัดส่วนใหญ่เป็นแผลในแนวขวาง มีค่ามัธยฐานของระยะเวลาการผ่าตัด และปริมาณการเสียเลือดเท่ากับ 90 นาที และ 200 มิลลิลิตรตามลำดับ พบการใช้ยาปฏิชีวนะป้องกันการติดเชื้อที่ดำเนินตามตามแนวทางปฏิบัติ 63 ราย (ร้อยละ 16.1 ของผู้ป่วยทั้งหมด, ร้อยละ 19.3 ของผู้ป่วยที่ไม่ได้รับการผ่าตัดเพื่อกำหนดระยะโรคมะเร็ง) ในรายที่ไม่ได้รับการผ่าตัดเพื่อกำหนดระยะโรคมะเร็ง พบว่า การผ่าตัดโดยแพทย์ประจำบ้านเป็นปัจจัยเดียวที่เพิ่มการใช้ยาปฏิชีวนะที่เหมาะสมอย่างมีนัยสำคัญ โดยมีค่า odds ratio เท่ากับ 6.84 (ช่วงความเชื่อมั่นร้อยละ 95 เท่ากับ 3.40-13.74)*

สรุป: *การใช้ยาปฏิชีวนะป้องกันการติดเชื้อสำหรับการตัดมดลูกทางหน้าท้องในโรงพยาบาลจุฬาลงกรณ์ ส่วนใหญ่ไม่เป็นไปตามแนวทางปฏิบัติ จำเป็นต้องดำเนินการตามระบบการส่งเสริมการใช้ยาปฏิชีวนะอย่างสมเหตุผลเพื่อนำไปสู่การปรับปรุงการปฏิบัติอย่างเหมาะสมต่อไป*

คำสำคัญ: *ยาปฏิชีวนะป้องกันการติดเชื้อ, การตัดมดลูก, การปฏิบัติ*

Introduction

Surgical-site infection is one of the common complications of gynecologic surgery. Risk of the infection is increased when patients have any predisposing factors that included poor-controlled diabetes, smoking, obesity, malnutrition, thick subcutaneous tissue, concomitant urinary tract or skin infections, bacterial vaginosis, or immunodeficiency[1]. Besides other preventive measures, antibiotic prophylaxis given before an abdominal hysterectomy has demonstrated an effectiveness in reducing the incidence of postoperative infection[2] and is widely recommended globally[1,3,4].

The guidelines on antibiotic prophylaxis for abdominal hysterectomy have recommended giving a single dose of cefazolin intravenously within 1 hour before surgery[1]. In patients allergic to cephalosporins, clindamycin, erythromycin, or metronidazole should be used instead[1,3]. No additional doses are recommended except when the procedure is longer than 3 hours, or the estimated blood loss is more than 1,500 milliliters (mL)[3]. Continuation of antibiotic prophylaxis after completion of the operation is discouraged because it may increase cost and risk of adverse events, but no additional benefit is demonstrated[5]. In addition, the overuse of antibiotics can contribute to development of drug-resistant bacteria[6].

There has been practice variation among countries in the use of surgical antibiotic prophylaxis; however, adherence to guideline recommendations should be emphasized[7]. The present study was conducted to assess a proportion of cases underwent elective abdominal hysterectomy at King Chulalongkorn Memorial Hospital (KCMH) that was adherent to the practice guidelines for antibiotic prophylaxis.

Materials and Methods

This retrospective descriptive study was approved by The Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. Medical records of patients who underwent elective abdominal hysterectomy at KCMH from January to December 2019 were reviewed. The study population were women between 18 and 60 years of age who admitted for elective abdominal hysterectomy. Cases having bacterial infection required antibiotic treatment, undergoing surgical procedure on gastrointestinal or urinary tract in the same operation, operative time longer than 3 hours, blood loss more than 1,500 mL, being immunocompromised, or receiving immunosuppressive agents or chemotherapy were excluded.

Data were retrieved from the medical records that coded with ICD-9-CM number 68.39 (other and unspecified subtotal abdominal hysterectomy) or 68.49 (other and unspecified total abdominal hysterectomy) and recorded in the case report form. Baseline characteristics including age, weight, height, body mass index, menopausal status, and underlying medical diseases were collected. Information on operation and antibiotic use that were retrieved including surgical indications, surgeon's status, incision types, procedure details, duration of operation, estimated amount of intraoperative blood loss, number and type of prophylactic antibiotics, timing to administer antibiotic prophylaxis and duration of antibiotic use. Adherence to the guidelines for antibiotic prophylaxis was determined by three aspects. First, whether to use recommended antibiotics. Cefazolin is the first line recommended antibiotic while either clindamycin or metronidazole is used in cases with allergy to cephalosporin. Second, whether used only a single dose of intravenous antibiotic. Lastly, whether the drug was administered within 60 minutes prior to incision.

The sample size was calculated by using the formula for a binary outcome in single population[8]. According to Sae-Tia et al study[9], the proportion of cases with appropriate use of antibiotic prophylaxis was 0.752. A total of 316 cases were needed when an alpha error was 0.05, an acceptable error was 0.05, and 10% cases with missing data. Statistical analysis was performed with SPSS software package version 22.0 (IBM Corp., Armonk, NY, USA). Data were presented as mean and standard deviation (SD) or median and interquartile range (IQR) for quantitative measurement. Numbers and percentages were used to describe

qualitative data. The association between various factors and appropriate antibiotic administration was assessed by calculating odds ratio (OR) and 95% confidence interval (CI). Logistic regression analysis was used to determine adjusted OR and 95% CI for each factor.

Results

There were 588 women who underwent an elective abdominal hysterectomy at KCMH in 2019. After excluding patients who required postoperative antibiotic treatment, the total number of eligible cases was 391 with a mean age of 48.7 years and a mean body mass index of 24.6 kg/m^2 (Table 1). Most of the pathological diagnosis were benign conditions (326 cases, 83.4%) including uterine fibroids, benign ovarian tumors, endometriosis and precancerous lesions. Surgical staging procedures were performed in 65 cases for whom carcinoma were diagnosed in 56 cases while the other 9 cases had benign ovarian tumors. About half of the operations were performed by attending staff and most of the skin incisions were transverse. The median duration of operation was 90 minutes and median intraoperative blood loss was 200 mL.

Table 1. Demographic, clinical and operative data (n = 391).

Characteristics	Values
Age (years)	48.7 ± 9.2
Body mass index (kg/m^2)	24.6 ± 4.4
Menopause	103 (26.3%)
Having medical disease	145 (37.1%)
Final diagnosis	
Myoma/adenomyosis	258 (66.0%)
Benign ovarian tumor	47 (12.0%)
Other benign tumor/endometriosis	10 (2.6%)
CIN/EIN	11 (2.8%)
Endometrial cancer	52 (13.3%)
Ovarian cancer	10 (2.6%)
Other cancer	3 (0.8%)
Surgical staging procedures	65 (16.6%)
Midline incision	120 (30.7%)
Surgeon's status	
Resident	148 (37.9%)
Fellow	42 (10.7%)
Attending staff	201 (51.4%)
Operative time (minute)	90 (75-120)
Estimated blood loss (mL)	200 (100-350)

Data presented as mean ± standard deviation, n (%), median (interquartile range)
CIN: cervical of intraepithelial neoplasia, EIN: endometrial intraepithelial neoplasia

Cefazolin was used for antibiotic prophylaxis in 209 cases (53.5%) (Table 2) while clindamycin was prescribed to all of 4 women who allergy to cephalosporin. Only 86 cases (22.0%) received a single dose of antibiotics while 240 cases (61.4%) got parenteral antibiotics more than 24 hours. Oral antibiotics were noted in 67 cases (17.1%). Regarding timing of antibiotic administration, 338 cases (86.4%) were given within 60 minutes prior to skin incision. Overall, adherence to the guidelines for antibiotic prophylaxis was found in 63 cases (16.1%) which all were benign diseases without staging procedures. The rate of adherence to the guidelines in elective abdominal hysterectomy without staging procedures in this study population were 19.3% (63 in 326 cases).

Table 2. Antibiotic use (n = 391).

Characteristics	Values
Antibiotic use for prophylaxis	
Cefazolin	209 (53.5%)
Ceftriaxone	154 (39.4%)
Clindamycin	26 (6.6%)
Others	2 (0.5%)
Duration of parenteral antibiotic	
Single dose	86 (22.0%)
One day	65 (16.6%)
More than one day	240 (61.4%)
Use of oral antibiotic	67 (17.1%)
Antibiotic administered within 60 minutes prior to skin incision	338 (86.4%)
Adherence to the guidelines	63 (16.1%)

Data presented as n (%)

Among cases without surgical staging, resident as a surgeon was the only factor that significantly increased the adherence to the practice guidelines with an OR (95%CI) of 6.61 (3.47-12.62) and an adjusted OR (95%CI) of 6.84 (3.40-13.74) (Table 3).

Table 3. Factors associated with adherence to the guidelines of antibiotic prophylaxis in cases without staging procedures (n = 326).

Factors	Adherence to the guidelines	OR (95%CI)	Adjusted OR (95%CI)
Menopause			
Yes (n = 55)	7 (12.7%)	0.56 (0.24-1.30)	0.55 (0.21-1.42)
No (n = 271)	56 (20.7%)		
Having medical disease			
Yes (n = 106)	22 (20.8%)	1.14 (0.64-2.04)	0.92 (0.47-1.77)
No (n = 220)	41 (18.6%)		
BMI ≥ 30 kg/m2			
Yes (n = 34)	4 (11.8%)	0.53 (0.18-1.55)	0.38 (0.12-1.19)
No (n = 292)	59 (20.2%)		
Midline incision			
Yes (n = 79)	20 (25.3%)	1.61 (0.88-2.94)	1.02 (0.52-1.99)
No (n = 247)	43 (17.4%)		
Surgeon status			
Resident (n = 140)	49 (35.0%)	6.61 (3.47-12.62)	6.84 (3.40-13.74)
Others (n = 186)	14 (7.5%)		
Operative time ≥ 90 minutes			
Yes (n = 167)	36 (21.6%)	1.34 (0.77-2.34)	1.26 (0.65-2.42)
No (n = 159)	27 (17.0%)		
Estimated blood loss ≥ 200 mL			
Yes (n = 196)	40 (20.4%)	1.19 (0.68-2.11)	0.81 (0.42-1.57)
No (n = 130)	23 (17.7%)		

OR: odds ratio, CI: confidence interval

Discussion

Antibiotic prophylaxis for abdominal hysterectomy is aimed to reduce post-operative surgical-site infection[2]. However, inappropriate use of antibiotic

prophylaxis in terms of timing and type of antibiotics may not serve this intention. Furthermore, overusing antibiotics may increase the risk of harmful adverse effects and promote antibiotic resistant bacteria[6]. According to the KCMH guidelines for antibiotic prophylaxis using in elective abdominal hysterectomy that follows the American College of Obstetricians and Gynecologists recommendation[1], adherent use of antibiotic prophylaxis was found only 16.1% of all cases. Only 54.5% of cases received cefazolin or appropriate alternatives. Grievously, use of a single-dose regimen was found in about one-fifth of cases.

One of reasons for not adhering to the guidelines related to antibiotic choices. Cefazolin, a beta-lactam antibiotic that is mostly recommended for antibiotic prophylaxis in abdominal hysterectomy[1,3], was used only 53.5% of all cases in the present study. Due to broader-spectrum activity, ceftriaxone was the second most prescribed although a randomized controlled trial showed no difference between ceftriaxone and cefazolin in preventing infectious morbidity for hysterectomy[10]. Some physicians believe that broad spectrum antibiotics would have a better result. In fact, when compared to recommended beta-lactam antibiotics, rates of post-hysterectomy surgical site infection were significantly higher among patients who received alternative or non-standard regimens[11].

Previous studies demonstrated that there was no significant difference in the rate of surgical site infections between patients receiving a single dose or multiple doses of prophylactic cefazolin for hysterectomy[5,12]. Nevertheless, prolonged administration of antibiotic prophylaxis was reported to be very common (41- 86%)[13]. To achieve adequate tissue concentrations of the antibiotic at the time of the incision and throughout the procedure, antibiotic prophylaxis is widely recommended to administer within 60 minutes prior to incision[1, 3]. However, poor adherence to recommended timing intervals were noted as the most common problem[14].

Low adherence to the guidelines for antibiotic prophylaxis in the present study were similar to reports from other low- and middle-income countries[15]. Abubaker et al's study assessed compliance with antibiotic prophylaxis for obstetrics and gynecology surgeries in three tertiary hospitals located in Northern Nigeria[16]. Optimal timing of antibiotic prophylaxis was found in 16.5% of cases and all the procedures used prolonged duration of administration with range of 5 to 12 days.

Because all of cases with staging procedures were non-adherent to the guidelines, they were excluded from multivariable analysis to determine factors associated with the adherence. The only significant factor increasing adherence was surgeon status as residents. This finding was comparable with Uppendahl et al's study that resident cases had more adherence to the guidelines compared with others. More aware of the current guidelines and in training quality audit might be an explanation for this circumstance.

The present study provided information regards to practice on antibiotic prophylaxis for abdominal hysterectomy in the tertiary hospital. The study results should increase awareness for both gynecologists and hospital administrators to urgently develop strategies to improve proper use of antibiotic prophylaxis. Although the present study collected data from electronic medical records using in KCMH, there were still some limitations due to its retrospective nature. Some input may not be accurate as prospective data collection, such as timing and blood loss. No detailed information was recorded to explain why some cases were prescribed prolonged use of antibiotics. A prospective study is needed to evaluate the outcomes of the antibiotic stewardship program that should be implemented.

Conclusion

Uses of antibiotic prophylaxis for abdominal hysterectomy at KCMH were mostly not adherent to the guidelines. An antibiotic stewardship program needs to be implemented to improve the practice for reduction of overused antibiotic as well as prevention of antimicrobial resistance.

Potential conflicts of interest

The authors declare no conflicts of interest.

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CASE REPORT

Umbilical Endometriosis in the Absence of Previous Surgery: A case report

Ahmad Akram Omar, M.D.*,**,
Erinna Mohamad Zon, M.D.*,**,
Rahimah Abdul Rahim, M.D.*,**,
Adibah Ibrahim, M.D.*,**,
Noor Adibah Hanum Che Hashim, M.D.*,**,
Faezahtul Arbaeyah Hussain, MBBS.***

** Department of Obstetrics & Gynaecology, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia*
*** Department of Obstetrics & Gynaecology, Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia*
**** Department of Pathology, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia*

ABSTRACT

The abdominal wall is the commonest site of extrapelvic endometriosis, which usually develops with prior surgical scar. An estimated incidence of umbilical endometriosis is around 0.5% - 1%, a rare condition. We illustrate a case of a 41-year-old woman, nulliparous, primary infertility for 15 years, without significant medical or surgical history, had been suffering from an umbilical skin lesion and cyclical bleeding from the umbilicus for 6-month duration. It was associated with pelvic pain and related to menstrual cycle. Physical examination revealed a skin-colored mass measuring around 3 x 2 cm in size, located at the umbilicus. An ultrasonographic examination of the abdomen revealed an ill-defined hypoechoic collection at the umbilical region and a right ovarian cyst measuring around 4 x 3 cm with a ground glass appearance. Laparoscopic surgery and surgical exploration confirmed the presence of these lesions where the umbilical mass did not communicate with the peritoneal cavity. Surgical excision of the umbilical mass was done and histopathology examination confirmed that the lesion was consistent with endometriosis.

Keywords: endometriosis, umbilical endometriosis, cyclical pain, surgical excision.

Correspondence to: *Noor Adibah Hanum Che Hashim, M.D., Department of Obstetrics & Gynaecology, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, 16150, Malaysia. E-mail: adibahanum@usm.my*

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Introduction

Endometriosis is a common gynaecological problem in women of reproductive age that frequently occurs in the pelvic region. Extrapelvic endometriosis, though rare, has been reported in association with prior surgical scars. Umbilical endometriosis is extremely rare in the absence of surgery, and the incidence is reported to be 0.5-1%[1]. The exact pathogenesis remains unknown. However, some theories postulate that the umbilicus may act as a physiological scar explaining the development of spontaneous disease in this area[2].

Patients with umbilical endometriosis may be misdiagnosed with a surgical complaint as they may present with a nonspecific complaint like vague abdominal pain and palpable subcutaneous swelling. A thorough history and physical examination are essential for making the correct diagnosis, and with the aid of imaging can help in assisting the diagnosis.

Case Report

A 41-year-old lady, nulliparous with primary infertility for 15 years, presented to the outpatient clinic with an umbilical skin lesion and cyclical bleeding from the umbilicus for a 6-month duration. She had no significant medical history with no history of abdominal surgery. Abdominal examination revealed a skin-colored mass measuring around 3 x 2 cm in size, located at the umbilicus which was firm and mild tender (Fig. 1). It was associated with pelvic pain and related to the menstrual cycle.

An ultrasonographic examination of the abdomen revealed an ill-defined 14.7 x 19.4 mm hypoechoic mass at the umbilical region (Fig. 2) and a right ovarian cyst measuring around 4 x 3 cm with a ground glass appearance. The patient was offered for surgical intervention as the persistent symptoms disturbed her daily activity. A diagnostic laparoscopic surgery and surgical exploration confirmed these findings of stage 2 endometriosis, where the umbilical mass did not communicate with the peritoneal cavity.

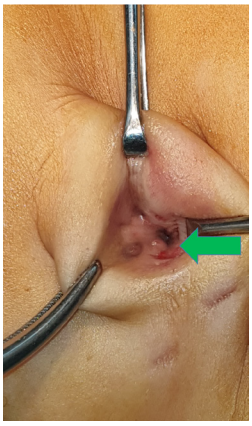

Fig. 1. Clinical appearance of umbilical endometriosis with hyperpigmented area seen (green arrow).

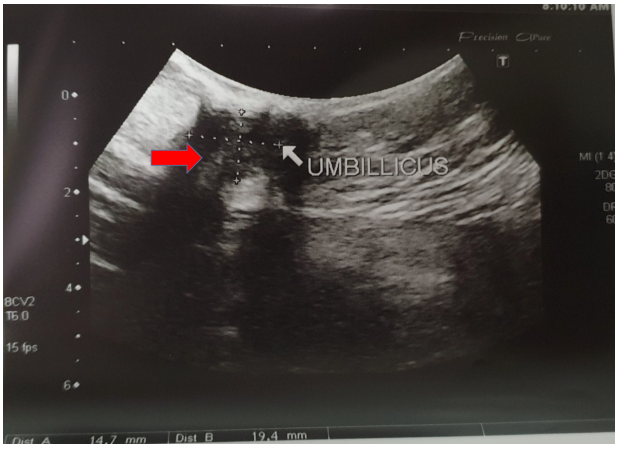

Fig. 2. Transcutaneous ultrasound showed a 14.7 x 19.4 mm umbilical nodule (red arrow).

Surgical excision of the umbilical mass was performed, with the mass about 3 x 2 cm, firm in consistency with wide excision and clear margins (Fig. 3). Histopathology examination confirmed that the mass consisted of multiple endometrial glands surrounded by endometrial stroma, which was consistent with endometriosis (Fig. 4). She was on gonadotropin-releasing hormone analogue for six cycles and had been followed-up six weeks postoperative, and she was found to be an asymptomatic and well-healed scar. She was planned to be seen at six-month postoperative however she defaulted to our follow-up.

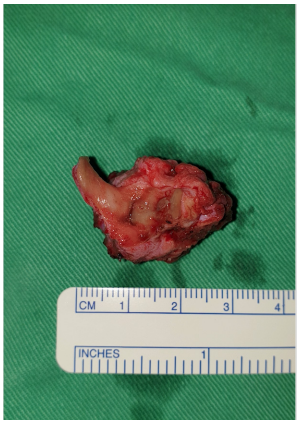

Fig. 3. Surgical excised tissue of umbilical endometriosis.

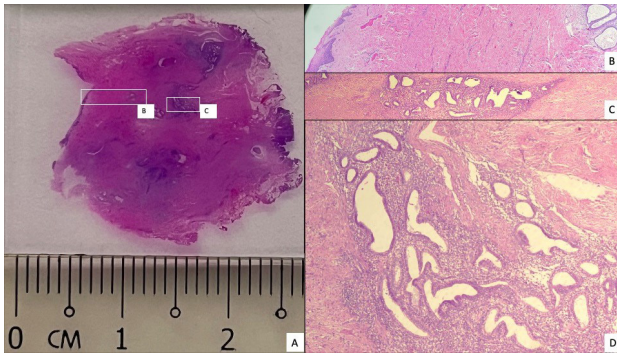

Fig. 4. A Macroscopy of umbilical nodule with measurement of 22 mm greatest diameter (H&E). B Overlying skin with endometriotic cystic glands within the parenchyma (H&E, 40x). C Endometriotic spots in deeper part of the umbilical nodule (H&E,40x). D Endometriosis composed of cystically dilated endometrial glands with its stroma within the fibrocollagenous tissue of the nodule (H&E, 100x).

Discussion

Umbilical endometriosis is most commonly diagnosed in reproductive-age women between the ages of 31 and 38 years[3]. It is defined as the presence of endometrial glands and / or stroma within the umbilicus[4]. It is most commonly seen secondary to surgical scar and rarely found as primary umbilical endometriosis. The exact pathogenesis is still unknown however there are theories postulate the pathogenesis of primary umbilical endometriosis; that the umbilicus may act as a physiological scar[2]; metaplastic changes of urachal remnants5; migration of endometrial cells through the abdominal cavity or the lymphatic system; genetic predisposition; and immunologic defect[4]. In this case, the patient had coexistent pelvic endometriosis, the theory postulated is possible due to hematogenous or lymphatic spread which the shedding endometriotic cells are transported through the lymphatic and vascular system to the umbilicus[6,7].

Umbilical endometriosis should be suspected in patients with complaints of cyclical pain, swelling, discharge and bleeding in relation to menstruation[8]. The most common presenting symptoms are umbilical swelling, cyclical pain and bleeding with or without dysmenorrhea[9,10]. However, patients may present with nonspecific complaints such as cutaneous mass and nonspecific abdominal pain without any association with the menstrual cycle, leading to misdiagnose as a surgical problem, and delay in diagnosis and treatment[5,7]. Based on our patient's presentation, despite patient presenting with a classical complaint of umbilical endometriosis, other differential diagnoses still have to be cautious such as umbilical hernia, pyogenic granuloma, keloid, melanoma, primary or metastatic carcinoma (Sister Mary Joseph's nodule)[9]. Benign nevus and lipoma also have to be considered as the presentation is subcutaneous mass or discoloration of the umbilical skin.

The most common findings may manifest as umbilical mass; a firm consistency nodule varying in colour (i.e., bluish-black to intense red, brown or purpura) or multilobulated depending on the amount of haemorrhage and the depth of penetration of ectopic endometrial tissue[10]. The size of umbilical mass in most of the reported cases is around 0.5 to 2.5 cm[5, 6, 10] and the one case reported to be encounter 4 cm size of umbilical mass in largest dimension[9]. Patients with umbilical endometriosis with no history of abdominal surgery (known as spontaneous cutaneous endometriosis) have a greater risk of coexisting endometriosis in the pelvic region[11]. Similar to our patient, umbilical endometriosis is more likely due to advanced pelvic disease as

compared with those patients who had scar endometriosis.

Radiological investigations are nonspecific but maybe helpful. Ultrasound can be used to assess the size of the nodule and the surrounding tissue's involvement, and to exclude other pelvic pathology to aid in planning for surgical intervention[12]. Ultrasound features may include solid with varied echogenicity lesion, most typically seen as hypoechoic lesion with an anechoic cystic component, with or without vascularity seen in Doppler sonography[5,12]. This is consistent with the ultrasound findings in our patient. For proper delineation of the mass in relation to the subcutis and muscles, computed tomography scans and MRI are useful[12].

The mainstay treatment in all cases of umbilical endometriosis is wide local excision of the mass with clear margins (at least 1 cm) to offer the highest probability of a favorable outcome, as incomplete excision may lead to recurrence[13,14]. The preferred timing for excision of umbilical endometriosis is at the end of menstrual cycle when the glands are smallest, to minimize the complication[15]. When there is coexistent with pelvic endometriosis, laparoscopy surgery is useful in excision of the endometriotic lesions, thus reducing the recurrence rate[5,7]. The use of hormonal therapy with a gonadotropin-releasing hormone may be added in cases of severe pelvic disease to reduce the symptoms or decreasing the size of the mass prior surgical intervention. In this case, the patient was not given preoperative hormonal therapy as the mass of umbilical endometriosis was not large and the umbilical defect after the resection can be repaired directly. However, she did receive postoperative hormonal treatment as the findings were coexistent with pelvic endometriosis as to reduce the rate of recurrence.

Conclusion

Umbilical endometriosis should be considered in a reproductive-age patient who presents with cyclical bleeding and abdominal pain regardless of surgical history. Surgical intervention with complete excision is the optimal treatment, and diagnosis is confirmed by histopathology examination. Hormonal therapy can be considered when there is a coexistent with pelvic endometriosis.

Potential conflicts of interest

The authors declare no conflicts of interest.

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CASE SERIES

Transvaginal Natural Orifice Transluminal Endoscopic Surgery for Hysterectomy in Women with Posterior Cul-de-sac Obliteration: A series of seven cases

Watcharada Uckara, M.D.*,
Kakanang Soimongkol, M.D.*,
Suporn Chanasabaeng**,
Piyathida Sutjaritphong**,
Sawaek Weerakiet, M.D.*

** Division of Obstetrics and Gynecology, Bangkok Hospital Udon, Udonthani, Thailand*
*** Division of Nursing, Bangkok Hospital Udon, Udonthani, Thailand*

ABSTRACT

Objectives: To describe the initial experience and surgical outcomes of the vaginal natural orifice transluminal endoscopic surgery (vNOTES) for hysterectomy (vNOTESH) in women with posterior cul de sac obliteration.

Case series: From December 2019 to February 2021, seven women who had indications of hysterectomy with or without a salpingo-oophorectomy at Bangkok Hospital Udon, Udonthani Province, Thailand, were recruited. All women had evidence of severe pelvic adhesion. Pelvic and recto-vaginal examinations revealed a fixed uterus with posterior cul de sac obliteration. In this type of women a wound retractor was placed within the vaginal flaps, and creation of pneumovagina, followed by an anterior colpotomy and serial steps of adhesiolysis and hysterectomy using an endoscope and endoscopic instruments.

Results: Application of a wound retractor and the anterior colpotomy were successfully done in all cases. The operation was converted to Total laparoscopic hysterectomy (TLH) in one woman because of severe adhesion. The median age and Body Mass Index (BMI) of the remaining six women were 44 years (range of 41-49), and 25.1 kg/m^2 (range of 22-32.5), respectively. The median operative time and estimated blood loss (EBL) were 161 min (range of 116-215) and 350 ml (range of 150-800), respectively. One woman received a blood transfusion. There were no perioperative complications.

Conclusion: This case series demonstrated that the vNOTESH in women with posterior cul de sac obliteration is challenging, but feasible by a skillful surgeon. However, it was an initial experience; a study with a larger population should be conducted to evaluate the feasibility and safety.

Keywords: hysterectomy, pelvic adhesion, posterior cul de sac obliteration, surgical outcomes, vNOTES.

Correspondence to: *Sawaek Weerakiet, M.D., Bangkok Hospital Udon, 111 Thongyai Road, Mueang District, Udonthani 41000, Thailand. Email: sawaekweerakiet@gmail.com*

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การผ่าตัดมดลูกผ่านกล้องทางช่องคลอดในสตรีที่มีพังผืดหนาแน่นที่ cul de sac ด้านหลัง: รายงานผู้ป่วย 7 ราย

วัชรดา อักขระ, คัคนางค์ สร้อยมงคล, สุภรณ์ ชะนะสะแบง, ปิยธิดา สุจริตพงษ์, เสวก วีระเกียรติ

บทคัดย่อ

วัตถุประสงค์: *เพื่อนำเสนอประสบการณ์เบื้องต้นและผลการผ่าตัดมดลูกผ่านกล้องทางช่องคลอดในสตรีที่มีพังผืดหนาแน่นที่ cul de sac ด้านหลัง*

รายงานผู้ป่วย: *เป็นการศึกษาแบบย้อนหลังด้วยการทบทวนเวชระเบียนอิเลคโทรนิกของสตรีที่มีพังผืดหนาแน่นที่ cul de sac ด้านหลัง ที่ได้รับการผ่าตัดมดลูกผ่านกล้องทางช่องคลอด ตั้งแต่ ธันวาคม 2562- กุมภาพันธ์ 2564 จำนวน 7 ราย ในโรงพยาบาลกรุงเทพอุดร จังหวัดอุดรธานี สตรีเหล่านี้มีประวัติที่บ่งว่ามีพังผืดรุนแรงในอุ้งเชิงกราน มดลูกติดแน่นทางด้านหลังจากการตรวจภายในร่วมกับการตรวจทางทวารหนัก เทคนิกการผ่าตัดในสตรีกลุ่มนี้ จะวางตัวถ่างแผลขนาดเล็กภายในเยื่อบุช่องคลอดที่ลอกออกจากปากมดลูก สร้างภาวะขยายช่องคลอดด้วยก๊าซตามด้วยการเปิดช่องเข้าสู่ช่องท้องทางด้านหน้าของช่องคลอด เลาะพังผืด และผ่าตัดมดลูก*

ผลการศึกษา: *การวางตัวถ่างแผลขนาดเล็กภายในเยื่อบุช่องคลอดที่ลอกออกจากปากมดลูก สร้างภาวะขยายช่องคลอดด้วยก๊าซตามด้วยการเปิดช่องเข้าสู่ช่องท้องทางด้านหน้าของช่องคลอดสำเร็จทุกราย แต่สตรี 1 รายถูกต้องเปลี่ยนเป็นการผ่าตัดมดลูกผ่านกล้องทางหน้าท้อง เนื่องจากพบมีพังผืดรุนแรงระหว่างมดลูกกับลำไส้ตรงที่อาจมีภาวะแทรกซ้อนต่อลำไส้ตรงได้ สตรีที่เหลือ 6 รายมีค่ามัธยมฐานของอายุและดัชนีมวลกายเท่ากับ 44 ปี (41-49) และ25.1 กก./ม2 (22-32.5) ระยะเวลาการผ่าตัดและปริมาณเลือดที่ออกเท่ากับ 161 นาที (116-215) และ 350 มล. (150-800) สตรี 1 รายได้รับเลือดระหว่างการผ่าตัด ไม่มีภาวะแทรกซ้อนทั้งระหว่างและหลังการผ่าตัด*

สรุป: *การศึกษานี้แสดงให้เห็นว่า การผ่าตัดมดลูกผ่านกล้องทางช่องคลอดสำหรับสตรีที่มีพังผืดหนาแน่นที่ cul de sac ด้านหลังสามารถประสบความสำเร็จได้ด้วยแพทย์ที่มีประสบการณ์ อย่างไรก็ตามควรมีการศึกษาที่มีจำนวนสตรีที่เข้าร่วมมากกว่าเพื่อประเมินความเป็นไปได้ ความปลอดภัยของการผ่าตัดชนิดนี้*

คำสำคัญ: *การผ่าตัดมดลูก, การผ่าตัดมดลูกผ่านกล้องทางช่องคลอด, ผลการผ่าตัด, พังผืดในอุ้งเชิงกราน, พังผืดหนาแน่น*

Introduction

Transvaginal natural orifice transluminal endoscopic surgery hysterectomy (vNOTESH) has been performed for the last 10 years[1-3]. After the first report from Taiwan[1], many studies done in Asia and Europe have been published[4-10]. The vNOTESH has some advantageous surgical outcomes including short operative time[5, 6, 8], less post-operative pain[5, 8], and shorter hospital stay[5, 6] when compared to those of patients undergoing total laparoscopic hysterectomy (TLH)[5, 7, 8]. It has become more popular and practiced than before. A most recent report showed that there are many experts in many countries have practiced the vNOTESH[11].

There are two surgical phases in the vNOTESH procedure, vaginal and endoscopic. The vaginal phase is aimed to provide access to the peritoneal cavity. The procedure is done much like a conventional vaginal hysterectomy. The important step in this phase is an entry into the peritoneal cavity with performing colpotomy. A wound retractor is applied through the vagina into the peritoneal cavity to establish a pneumoperitoneum. Subsequently, the endoscopic phase is done to carry out hysterectomy step by step from sealing and cut the uterine vessels to the uterine pedicles using an endoscope and endoscopic instruments. Although there are some differences between institutes in the vaginal phase technique[2, 3, 5, 8], the steps are the same almost everywhere. A posterior colpotomy is first done, followed by application of a wound retractor[2, 3, 5, 8]. Therefore, it is necessary that women undergoing vNOTESH have no pelvic adhesion or posterior cul de sac obliteration. In all publications of the vNOTESH, women with severe pelvic adhesion were not eligible[2, 3, 5-8] for inclusion in such studies.

A study by Yantapant and Roekyindee[9] showed a different method of performing the vaginal phase. In their work, after circumcising the cervix and dissecting the anterior and posterior vaginal mucosae upward to the peritoneum, a wound retractor was applied between the mucosal flaps to establish a pneumovagina. Then, anterior and posterior colpotomies were done endoscopically[9].

This technique gave our team an idea to perform the vNOTESH in women with posterior cul de sac obliteration. If an anterior colpotomy can be successfully done after applying the wound retractor, the pelvic organs and adhesion conditions can be assessed. Then, adhesiolysis and hysterectomy can be accomplished. To the best of our knowledge, the vNOTESH in women with posterior cul de sac obliteration has never been reported. Therefore, the aims of this work were firstly to describe the initial experience in the entry into the peritoneal cavity and performing hysterectomy, and secondly to report surgical outcomes of the vNOTESH in women with posterior cul de sac obliteration.

Case Series

cases

From December 2019 to February 2021, seven women presenting indications for hysterectomy with or without a salpingo-oophorectomy at Bangkok Hospital Udon, Udonthani Province, Thailand, were included. All women showed evidence of severe pelvic adhesion, such as a history of pelvic surgery, previous or present pelvic inflammatory disease (PID), or peritoneal and ovarian endometriosis. Pelvic and recto-vaginal examinations revealed a fixed uterus with posterior cul de sac obliteration, but no recto-vaginal mass. The posterior cul de sac obliteration was defined when the anterior rectal wall sticks to the posterior vagina, the posterior upper part of the cervix and the lower segment of the uterus leading to no space of the rectouterine pouch. None of them were virgins. Before the operation, each woman was counseled regarding the surgical procedure, the risks of bleeding during the

operation that may necessitate receiving a blood transfusion, intra- and post-operative complications and a potential conversion to TLH. Written informed consent form was obtained from all women before the surgery. The following data were reported: age, body mass index (BMI), parenthood, the number and type of deliveries, indications for hysterectomy, previous diseases and surgeries, number of conversions to TLH, operative time, estimated blood loss (EBL), number of patients who received blood transfusion, intra- and post-operative complications, post-operative pain assessed with visual analogue scales (VAS), weight of specimens, and the final pathological diagnosis. The study was approved by the Bangkok Hospital Headquarters Institutional Review Board (BHQ-IRB) (COA. 2021-43).

Surgical technique

All hysterectomies were done by the same surgeon (SW). The surgeries were performed under general anesthesia with endotracheal intubation. Each woman was placed in the lithotomy position with both legs supported by elastic bandages. A Foley catheter was indwelled. After 20 ml of 1% xylocaine with 1:200,000 epinephrine was injected into the submucosal space around the cervix, circumcising the cervix, and dissecting the anterior and posterior vaginal mucosae upward to the anterior and posterior peritonea were done. Both cardinal ligaments were sealed and cut using a Curved Large Jaw Open Sealer LigaSureTM system (Covidien, Mansfield, MA, USA). Allis forceps were used to grasp on each of 4 sides of the vaginal flaps. Then the inner ring of a wound retractor (6 cm in diameter, Lagis Enterprise Co., Ltd., Taichung, Taiwan) was applied within the vaginal flaps. The outer rim was covered with a silicone cap. A pneumovagina was established with a pressure of 12 mm Hg. A 10 mm, 3-D laparoscope (Endoeye Flex HD 3D, Olympus Corporation, Japan) was used through one trocar and two endoscopic instruments through another pair of trocars. Fig. 1 shows a process of surgery in woman with adenomyosis and peritoneal endometriosis. An anterior colpotomy was done (Fig. 1A). Then both uterine vessels were dissected, sealed and cut. In cases where the uterine vessels could not be clearly identified, the sealing and cutting were done as close to the uterine surface as possible. A larger wound retractor (8 cm in diameter) was applied in the peritoneal cavity to widen the visual and surgical fields (Fig. 1B). After surveillance of the reproductive organs and assessment of adhesion, an adhesiolysis and hysterectomy were meticulously done. Firstly, the tissue within the broad ligament was separated from the corpus with a blunt dissection technique (Fig. 1C). The process was alternated with sealing and cutting of the anterior broad ligament from the lower to the upper parts of the uterine corpus (Fig. 1D). After the posterior broad ligament was exposed, sealing and cutting the ligament were done (Fig. 1E), followed by sealing and cutting the proximal part of the fallopian tube, the ovarian and round ligaments (Fig. 1 F). An identical procedure was on the other side of the uterus (Fig. 1G). After separation of the adnexa from the corpus, adhesion between the uterus and the rectum could be identified (Fig. 1H). Sealing and cutting the uterosacral ligaments were done (Fig. 1I). Subsequently, with traction of the corpus upward, adhesiolysis of the corpus from the rectum was done using a sharp dissection technique to complete the hysterectomy (Fig. 1J). An energy sealing device LigaSureTM (Covidien, Mansfield, MA, USA) was used for sealing and cutting of all ligaments and vessels. Bipolar coagulation was occasionally used for hemostasis on bleeding points.

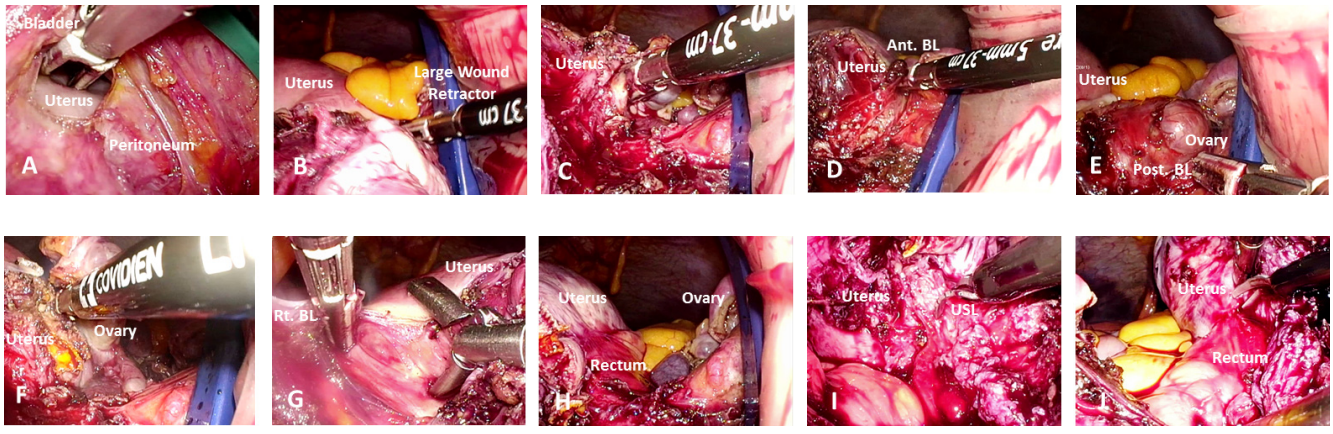

Fig. 1. Procedure of vNOTESH in women with posterior cul de sac obliteration.

Fig. 1A: Anterior colpotomy was performed.

Fig. 1B: A larger wound retractor was placed instead of the small one to widen the visual and surgical fields.

Fig. 1C: The tissue within the broad ligament was separated from the corpus with a blunt dissection technique.

Fig. 1D: The anterior broad ligament was sealed and cut. Ant. BL: Anterior broad ligament.

Fig. 1E: Sealing and cutting the posterior broad ligament were done to expose the adnexum. Post. BL: Posterior broad ligament.

Fig. 1F: Sealing and cutting the proximal part of the fallopian tube, the ovarian and round ligaments were done.

Fig.1 G: Sealing and cutting the broad ligament of the opposite side were performed similarly.

Fig. 1H: After sealing and cutting the broad ligament, and the pedicle, the adhesion between the uterus and the rectum could be seen clearly.

Fig. 1I: The uterosalcral ligaments were cut. USL: uterosacral ligament.

Fig. 1J: Adhesiolysis between the uterus and the rectum was finally done to remove the uterus.

In woman with diagnosis of chronic pelvic inflammation, adhesion between the corpus and other structures was not so dense (Fig. 2A), and was filmy in some areas (Fig. 2B). Adhesiolysis could be performed easily with the energy sealing device and scissors. A bilateral salpingectomy (BS) was routinely carried out. If necessary, a unilateral or bilateral salpingo-oophorectomy was carried out instead. Finally, surveillance and hemostasis of the stumps of ovarian ligaments or the infundibulopelvic ligaments were done. After removal of the wound retractor and the specimens, hemostasis of the stumps of the uterine vessels, as well as the cardinal and uterosacral ligaments was also done. Then, the vaginal vaults were approximated with no. 2/0 coated polyglactin suture.

Pre- and post-operative protocols were quite similar for all women. A prophylactic antibiotic, 2 g of cefazolin, was given before starting the operation, unless the woman had an allergy to this drug. In this case, 600 mg of clindamycin was used instead. Another dose of these medicines was administered 6-8 h later. A dose of 40 mg parecoxib was routinely prescribed during the operation with a second dose 12 h later. An intravenous injection of 25 mg of pethidine or 50 mg of tramadol every

6 h was added within 24 h, if necessary. Additionally, 25 mg of diclofenac was administered orally three times daily. Intravenous fluid and the Foley catheter were both removed around 24 h after the surgery. The patients were discharged 48 h after admission.

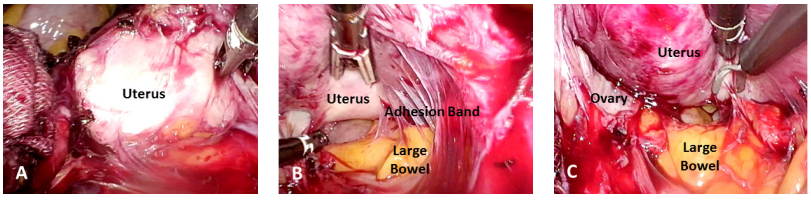

Fig. 2. Adhesion and adhesiolysis in woman with diagnosis of chronic pelvic inflammation.

Fig. 2A: Adhesion at the lateral side of the corpus was not so dense.

Fig. 2B: Filmy adhesion between the uterus and the rectum was seen.

Fig. 2C: Adhesiolysis could be performed using the energy sealing device and scissors.

Results

Table 1 shows clinical characteristics of these seven women. Their median age and BMI were 44 years (range of 41-49), and 25.1 kg/m^2 (range of 22 - 32.5), respectively. Two women were nulliparous. The indications for the operation were adenomyosis in four women, adenomyosis with submucous myoma in one woman, adenomyosis with an ovarian tumor in one woman, and an ovarian tumor in one woman.

Table 1. Women characteristics.

Case no.	Age	BMI	Parity	Normal delivery	Cesarean section	Indications
1	47	22.3	1	0	1	Adenomyosis
2	49	24.0	0	0	0	Adenomyosis
3	41	32.5	2	2	0	Adenomyosis
4	42	25.8	2	2	0	Left ovarian tumor
5	46	22.0	3	3	0	Adenomyosis, submucous myoma
6	42	26.7	1	0	1	Adenomyosis, Right ovarian tumor
7	44	25.1	0	0	0	Adenomyosis

BMI: body mass index

The application of the wound retractor, the pneumovagina creation and performing the anterior colpotomy were successful in all cases. However, in one woman (case no. 6) after the broad ligaments and the uterine pedicles were sealed and cut, a so severe adhesion that it was difficult to discriminate between the uterine corpus and the rectum was found. Considering the risk of the rectal injury, a conversion to TLH was done for this woman. The surgical outcomes of the remaining six women are shown in Table 2. The median of operative time and EBL were 161 min (range of 116-215) and 350 ml (range of 150-800), respectively. One woman received a blood transfusion. The median of VAS assessed at 6, 24 and 48 h after surgery were 3 (range of 2-4), 3 (range of 2-3), and 2 (range of 0-2), respectively. The median weight of specimens was

151.5 g (range of 130.5-332 g). The final pathological diagnosis was adenomyosis in five women. Of these five women, four had the added diagnosis of peritoneal endometriosis with severe pelvic adhesion. One had chronic PID with pelvic adhesion. The final diagnosis of the other woman was a tubo ovarian abscess. There were no perioperative complications. The vaginal stumps revealed good healing in all cases.

Table 2. Surgical outcomes and final diagnosis.

Case no.	Previous disease and surgery	Operative time (min)	EBL (ml)	VAS after 6, 24, 48h	Weight of specimens (g)	Final diagnosis
1	Ovarian Endometrioma, Cystectomy	215	700	3, 3, 2	189.5	Adenomyosis, Peritoneal endometriosis
2	No	158	200	2, 2, 2	131	Adenomyosis, Peritoneal endometriosis
3	Ruptured appendicitis, appendectomy Tubal resection	182	400	3, 3, 0	170	Chronic PID with adhesion, Adenomyosis
4	No	160	300	3, 2, 1	130.5	Tubo-ovarian abscess
5	No	162	800	3, 3, 2	332	Adenomyosis, sub. myoma, Peritoneal endometriosis
7	No	116	150	4, 3, 2	133	Adenomyosis, endometrioma, Peritoneal endometriosis

EBL: estimated blood loss, VAS: visual analogue scale, 6, 24 and 48 h after surgery, PID: pelvic inflammatory disease, Sub. myoma: submucous myoma

Discussion

The vNOTESH is a safe and feasible procedure in experienced hands. It has advantages over the laparoscopic hysterectomy in terms of a shorter operative time, less postoperative pain and a shorter hospital stay[5, 7, 8]. Moreover, it has no risk of trocar related complications and no abdominal scarring results, promoting woman satisfaction[12]. Technically, in the vNOTESH, a colpotomy has to be done to enter the peritoneal cavity to establish a pneumoperitoneum. Therefore, severe pelvic adhesion including posterior cul de sac obliteration and rectovaginal mass presents a contraindication. Nevertheless, some authors[13, 14] have recently reported using the vNOTESH in patients with suspected pelvic adhesion. Nulens et al[14] reported successfully performing the vNOTESH in eleven women with history of vNOTES adnexectomy or vNOTES cystectomy. The current case series indicates that performing the vNOTESH in women with posterior cul de sac obliteration is possible. Additionally, the operation in the women with this type of severe adhesion has never been reported to the best of our knowledge.

The causative factor of the posterior cul de sac obliteration is inflammation in the area of pouch of Douglas leading to adhesion of the posterior surfaces of the cervix and the corpus with the anterior surface of the rectum. The most common causes of the inflammation are peritoneal endometriosis, and pelvic inflammatory disease (PID)[15]. There were the similar

causes, the peritoneal endometriosis in 5 women and the PID in two in the current report.

To diagnose the posterior cul de sac obliteration in the current report, a pelvic examination and recto-vaginal examination were only used. A magnetic resonance imaging (MRI) or computed tomography (CT) scan was not added. The CT scan has been used to diagnose the adhesion of anterior abdominal wall with the uterus in one woman undergoing the vNOTESH[16]. The MRI has been used to identify the posterior cul de sac obliteration with accuracy rates of 56.6-92%[17, 18]. Interestingly, pelvic examination and recto-vaginal examination also have quite high accuracy rate, especially by laparoscopic experts in the diagnosis of posterior cul de sac obliteration[19]. Therefore, these examinations were enough to assess the obliteration with the definition as described. The posterior cul de sac obliteration was found in all women in the current report. In addition, one author only used these pelvic examinations with criteria to define the posterior cul de sac obliteration in women undergoing a vaginal hysterectomy[20]. On the other hand, these two examinations were used to exclude women with posterior cul de sac obliteration with high accuracy rate in all previous publications of vNOTESH[1, 5-8, 21, 22]. Only one out of 137 women was false negative of the obliteration in one study[22].

The vagina phase is the first crucial step for success in the vNOTESH. The technique used in this series to access the peritoneal cavity is not difficult. Placing a small wound retractor within the vaginal flaps before the anterior colpotomy is a modification of the work of Yantapant and Roekyindee and it has a key role in the procedure. With this technique the anterior colpotomy could be done successfully in all cases in the current report. It appears to be a useful application to access into the peritoneal cavity in women with posterior cul de sac obliteration. This means that women with posterior cul de sac obliteration should no longer be an absolute contraindication of the vNOTESH. Furthermore, when the larger wound retractor was used instead of the smaller one, surveillance of the pelvic organs and pelvic adhesion, with the subsequent operation were more feasible.

In the endoscopic phase, the procedure of the hysterectomy in women with severe pelvic adhesion is a painstaking one which is more difficult than those without adhesion. The uterine vessels, the broad ligaments and the uterine pedicles can serially be performed easily in women without adhesion. By contrast, the procedure including the sealing and cutting of all vessels and ligaments, and the adhesiolysis has to be performed with caution of organ injury in women with severe adhesion. Furthermore, it is possible that the operation in this phase may not be successful. A conversion to TLH is needed if there is risk of organ injury which was found in one woman with severe pelvic adhesion in the current study.

The operative time and EBL seemed to be high in the current report. It had twice the operative duration[8] and three times the EBL than for women with no adhesion[8]. Adhesiolysis requires extreme caution to avoid injury to other organs. Therefore, more time was required with a much greater blood loss from the raw surfaces. However, the surgical outcomes for these six women were satisfactory. There were no both intra- and post-operative complications. Furthermore, the postoperative VAS pain scores were quite low and might not be different from those with no pelvic adhesion[5, 8].

A limitation in this current report was that it was a retrospective study with a small number of women included. However, 7 women are not too small and proper for a case series report aiming to describe the technique of the vNOTESH in difficult and specific cases. In fact, a case series report should have more than four or five subjects included according to Abu-Zidan et al[23] and Esene et al[24]. And there were some examples of case series reports in which 6 patients were included[25, 26]. Nevertheless, a prospective study with a larger population and more aspects of surgical outcomes should be conducted as a future study.

Conclusion

This seven-case series demonstrated that the vNOTESH in women with posterior cul de sac obliteration was challenging, but feasible by a skillful

surgeon. The technique that application of a wound retractor before a colpotomy was a key step of successful procedure of the vNOTESH in this type of women. Nevertheless, it was the initial experience, a study with more population is needed to refine the technique and to verify safety.

Potential conflicts of interest

The authors declare no conflicts of interest.

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