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Effect of Multi-Strain Probiotics on Constipation and Quality of Life in Menopausal Women: A double-blind, Randomized, Placebo-controlled, Single-center trial

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ABSTRACT

Objectives: To evaluate the short-term efficacy of a multi-strain probiotic supplement (*Bifidobacterium longum*, *B. breve*, *B. lactis*, *B. animalis* TA1, *Lactobacillus paracasei* MSMC 39-1, *L. rhamnosus*, *L. reuteri* TF314, and *L. gasseri*) in improving bowel movement frequency, stool consistency, and menopause-related quality of life in women with functional constipation.

Materials and Methods: A double-blind, randomized, placebo-controlled trial was conducted at the gynecology outpatient clinic of a tertiary care hospital in Bangkok, Thailand, between August 2024 and April 2025. For four weeks, 46 women with functional constipation, as defined by Rome IV, were randomized to receive a probiotic or placebo capsule every day. Simple randomization was carried out by a third party, and the allocation was hidden from the participants and researchers. Pretest and posttest questionnaires were used to measure menopause-specific quality of life (MENQOL) and symptoms associated with constipation. Data were analyzed using the intention-to-treat approach.

Results: In the probiotics group, the median weekly defecation frequency increased significantly (3.0 to 5.0, $p = 0.003$). Hard stools slightly declined from 32% to 9.1%, although not statistically significant ($p = 0.200$). There were minimal changes in the placebo group. The total MENQOL score, and physical domain improved from 55.1 ± 31.2 to 40.7 ± 22.4 ($p = 0.012$) and from 34.2 ± 21.5 to 24.4 ± 14.1 ($p = 0.014$), respectively, while vasomotor, psychosocial, and sexual domains showed no significant changes. No significant changes occurred in the placebo group. Subgroup analysis of participants over 60 years old showed similar improvements in total score ($p = 0.041$) and physical domain ($p = 0.029$). One participant (4.3%) in the probiotic group discontinued due to bloating.

Conclusion: In menopausal women experiencing constipation, a 4-week multi-strain probiotic treatment demonstrated improvements in the frequency of bowel movements, physical domain and total score of menopause-related quality of life. Probiotics may serve as an adjunctive, non-pharmacological approach to support physical well-being in menopausal women.

Keywords: functional constipation, menopausal women, probiotic supplementation, menopause-specific quality of life, randomized controlled trial.

ผลของโพรไบโอติกต่ออาการท้องผูกและคุณภาพชีวิตในสตรีวัยหมดประจำเดือน: การศึกษาแบบสุ่ม มีกลุ่มควบคุมด้วยยาหลอกในลักษณะปกปิดสองทาง ณ ศูนย์เดียว

นทิตา นาคพันธุ์, ปองรัก บุญญานุรักษ์

บทคัดย่อ

วัตถุประสงค์: เพื่อประเมินประสิทธิภาพในระยะสั้นของผลิตภัณฑ์เสริมอาหารที่มีโพรไบโอติกหลายสายพันธุ์ (*Bifidobacterium longum*, *B. breve*, *B. lactis*, *B. animalis* TA1, *Lactobacillus paracasei* MSMC 39-1, *L. rhamnosus*, *L. reuteri* TF314 และ *L. gasseri*) ในการเพิ่มความถี่ของการขับถ่าย, ลักษณะของอุจจาระ และปรับปรุงคุณภาพชีวิตของสตรีวัยหมดประจำเดือนที่มีอาการท้องผูกจากการทำงานผิดปกติของลำไส้

วัสดุและวิธีการ: การทดลองแบบสุ่ม มีกลุ่มควบคุมให้ยาหลอก และปกปิดสองฝ่าย ดำเนินการที่คลินิกโรคเรื้อรัง โรงพยาบาลระดับตติยภูมิ กรุงเทพมหานคร ระหว่างเดือนสิงหาคม พ.ศ. 2567 ถึงเมษายน พ.ศ. 2568 ผู้หญิงวัยหมดประจำเดือนจำนวน 46 คน ที่ได้รับการวินิจฉัยว่ามีอาการท้องผูกจากเกณฑ์ Rome IV ถูกสุ่มแบบ 1:1 ให้ได้รับแคปซูลโพรไบโอติกหรือยาหลอก วันละ 1 เม็ด เป็นเวลา 4 สัปดาห์ การสุ่มดำเนินการโดยบุคคลที่สาม และผู้เข้าร่วมกับผู้วิจัยไม่ทราบกลุ่มที่ได้รับการจัดสรร ประเมินอาการเกี่ยวกับระบบขับถ่ายและคุณภาพชีวิตจำเพาะต่อวัยหมดประจำเดือน (MENQOL) โดยทำแบบสอบถามก่อนและหลังการทดลอง วิเคราะห์ข้อมูลตามหลักการวิเคราะห์ตามเจตนาการรักษา (intention-to-treat)

ผลการศึกษา: ในกลุ่มโพรไบโอติก ความถี่ในการขับถ่ายต่อสัปดาห์เพิ่มขึ้นอย่างมีนัยสำคัญจาก 3.0 เป็น 5.0 ครั้ง ($p = 0.003$) สัดส่วนของอุจจาระแข็งลดลงจากร้อยละ 32 เหลือ 9.1 ($p = 0.200$) ขณะที่กลุ่มยาหลอกมีการเปลี่ยนแปลงเล็กน้อย คะแนนรวม MENQOL และด้านกายภาพดีขึ้นจาก 55.1 ± 31.2 เป็น 40.7 ± 22.4 ($p = 0.012$) และจาก 34.2 ± 21.5 เป็น 24.4 ± 14.1 ($p = 0.014$) ตามลำดับ ในขณะที่ด้านหลอดเลือดและการควบคุมอุณหภูมิ (vasomotor), ด้านจิตสังคม (psychosocial) และ ด้านเพศสัมพันธ์ (sexual) ไม่พบการเปลี่ยนแปลงอย่างมีนัยสำคัญ และกลุ่มยาหลอกก็ไม่มี การเปลี่ยนแปลงอย่างมีนัยสำคัญเช่นกัน การวิเคราะห์กลุ่มย่อยในผู้ที่มีอายุอย่างน้อย 60 ปี พบแนวโน้มการดีขึ้นเช่นเดียวกัน ผู้เข้าร่วมหนึ่งราย (ร้อยละ 4.3) ในกลุ่มโพรไบโอติกหยุดทดลองเนื่องจากอาการท้องอืด

สรุป: ในสตรีวัยหมดประจำเดือนที่มีภาวะท้องผูก การเสริมโพรไบโอติกหลายสายพันธุ์เป็นระยะเวลา 4 สัปดาห์ ช่วยเพิ่มความถี่ในการขับถ่ายอุจจาระและปรับปรุงคุณภาพชีวิตโดยรวมและด้านกายภาพของสตรีวัยหมดประจำเดือนที่มีอาการท้องผูกได้อย่างมีนัยสำคัญ โพรไบโอติกจึงอาจเป็นทางเลือกที่มีประสิทธิภาพโดยไม่ต้องพึ่งพายา เพื่อส่งเสริมสุขภาพทางกายในสตรีวัยหมดประจำเดือน

คำสำคัญ: ภาวะท้องผูกจากการทำงาน, สตรีวัยหมดประจำเดือน, การเสริมโพรไบโอติก, คุณภาพชีวิตเฉพาะวัยหมดประจำเดือน, การทดลองแบบสุ่มและมีกลุ่มควบคุม

Introduction

Menopause, defined as the absence of menstruation for 12 consecutive months, is a natural process resulting from ovarian failure and declining estrogen levels. Most women experience menopause between the ages of 45 and 55. Hot flashes, sleeplessness, mood swings, vaginal dryness, osteoporosis, and gastrointestinal issues are just a few of the symptoms that can seriously lower quality of life during this transition. Constipation is common and can significantly affect day-to-day functioning. It is probably caused by estrogen's effects on gastrointestinal motility⁽¹⁾. These clinical manifestations affect up to 80% of menopausal women, and it is estimated that by 2030, over 1.2 billion women worldwide will be transitioning into menopause⁽²⁾.

About 50% of older people suffer from constipation, a common gastrointestinal illness that is acknowledged as a global health concern because of its substantial effects on both physical and psychological well-being⁽³⁾. Its prevalence rises with age, and it is significantly higher in women, where 33.5% of people over 60 are affected^(4, 5). In addition to hormonal changes, several factors, such as chronic illnesses, consuming medications, and physical inactivity, can lead to constipation in older adults⁽³⁾. Moreover, constipation can lead to issues such as rectal prolapse, fecal impaction, hemorrhoids, and abdominal pain⁽⁴⁾.

In the United States, annual over-the-counter laxative expenditures are estimated at \$821 million⁽⁶⁾. However, up to 47% of patients express worries about the taste, expense, inconvenience, safety, and adverse effects of these drugs⁽⁷⁾. Probiotics have recently drawn interest as an alternate constipation

remedy. According to the World Health Organization (WHO), probiotics are “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host”⁽⁸⁾. The most studied strains include *Lactobacilli* and *Bifidobacterium*, such as *Lactobacillus acidophilus* LA11-Only, *Lactocaseibacillus rhamnosus* LR22, *Limosilactobacillus reuteri* LE16, *Lactiplantibacillus plantarum* LP-Only, and *Bifidobacterium animalis subsp. lactis* BI516, which significantly increased gastrointestinal transit rate, reduced time to first defecation, and improved stool frequency and weight. According to systematic reviews, certain probiotic strains can decrease gastrointestinal transit time by up to 12 hours, increase the frequency of bowel movements by about 1.5 times per week, and relieve several symptoms associated with constipation when taken at doses ranging from 10^8 to 3×10^{10} CFU/day⁽⁹⁾.

Menopausal symptoms are associated with gut and vaginal dysbiosis. The estrobolome, a community of microorganisms that control circulating estrogen levels, can be negatively impacted by gut dysbiosis. The beta-glucuronidase enzyme of some probiotics, such as *Bifidobacterium longum*, *Lactobacillus rhamnosus*, *L. reuteri*, and *L. gasseri*, aids in boosting phytoestrogen and estrogen reactivation, which restores estrobolome action. Additionally, these probiotics enhance immunological modulation and lessen systemic inflammation, which may help with hot flashes and other symptoms⁽¹⁰⁾.

Constipation and menopausal symptoms significantly impair both the physical and psychological well-being of menopausal women. This trial aimed to evaluate the short-term impact of an eight-strain probiotic supplement on bowel movement frequency

and stool consistency in menopausal women, because no studies have specifically investigated the use of probiotics for the treatment of constipation in menopausal women. Evaluating the effects of probiotic supplementation on constipation-related symptoms and well-being in these populations was a secondary goal. According to this study, probiotics are a viable non-pharmacological therapeutic option that may help this population become less dependent on pharmaceutical interventions.

Materials and Methods

This study was a double-blind, randomized, placebo-controlled trial conducted at the gynecology outpatient department of Phramongkutklo Hospital, Bangkok, Thailand, a tertiary care hospital, between August 2024 and April 2025. The Royal Thai Army Medical Department (R091h/67) granted ethical approval. The trial was designed and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010 guidelines to ensure the completeness and quality of the randomized controlled trial methodology.

Participants were menopausal women who met Rome IV criteria for functional constipation⁽¹¹⁾. Menopause was defined as the permanent cessation of menstruation for at least 12 consecutive months⁽¹⁾. Posters were used for recruitment in the gynecology outpatient department, and trained research assistants completed screening. Menopausal women who have gastrointestinal cancers, thyroid conditions being treated, post-radiation intestinal strictures, have used antibiotics, probiotics, prebiotics, or laxatives within the previous two weeks, take more than 1,500 mg of calcium per day, or are unable to communicate in Thai were excluded. All participants provided written informed consent after receiving study information.

Simple randomization, created by a third party using Statistical Applet, was used to assign eligible individuals to receive either a probiotic supplement or a placebo in a 1:1 ratio. Sequentially numbered, opaque, sealed envelopes were used to guarantee

allocation concealment. Healthcare professionals and participants were both blinded to group assignments.

The nutritional supplement product contained eight probiotic strains, prebiotics, and inert excipients totaling 10 billion CFU in each capsule and served as the probiotic in this investigation. The formulation per capsule was as follows: active ingredients consisted of *Bifidobacterium longum* (10 mg), *Bifidobacterium breve* (10 mg), *Bifidobacterium lactis* (10 mg), *Bifidobacterium animalis* TA1 (20 mg), *Lactobacillus paracasei* MSMC 39-1 (20 mg), *Lactobacillus rhamnosus* (10 mg), *Lactobacillus reuteri* TF314 (10 mg), *Lactobacillus gasseri* (10 mg), xylo-oligosaccharides (100 mg), and resistant maltodextrin (100 mg). Among the inactive components were silicon dioxide (20 mg), magnesium stearate (20 mg), and maltodextrin (110 mg). The probiotic capsule and the placebo capsule both contained the same inactive substances. Hard gelatin capsules of size 0 were used to enclose probiotic and placebo capsules. Their looks, packaging, and methods of administration were all the same. For four weeks, participants were told to take one capsule every day before bed. Every participant received behavioral modification counseling, which included eliminating tea intake, maintaining a regular bowel schedule, exercising frequently, eating a high-fiber diet, and drinking two liters of water every day.

Participants who had a widespread rash, tightness in the chest from an allergic reaction, or severe gastrointestinal symptoms such as vomiting or diarrhea that persisted, together with indications of dehydration, had to be excluded from the research.

To assess the frequency of weekly bowel movements, stool consistency, bowel-related symptoms, and menopause-specific quality of life (MENQOL) at baseline and four weeks following supplementation, all participants were asked to fill out questionnaires. The Thai bowel-related symptoms questionnaire, including the Bristol stool form scale⁽¹²⁾ adapted and permitted by Narathip

Wiwekplern and colleagues⁽¹³⁾, was used to evaluate bowel movement frequency, stool consistency, and bowel-related symptoms. Cronbach's alpha coefficient was used to evaluate internal consistency reliability, and the result was 0.87.

The Bristol Stool Form Scale (BSFS) is a validated seven-category scale to classify stool consistency and form, correlating with gut transit time. Type 1 constipation is characterized by distinct, firm lumps that resemble nuts and is a sign of severe constipation. Type 2 constipation is characterized by a lumpy texture and a sausage-like appearance, indicating mild constipation. Type 3 stools have surface cracks and resemble sausages; they are regarded as being within the normal range. Type 4, which is also normal, is soft, smooth, and shaped like a snake or sausage; it is frequently regarded as the perfect form. Type 5 is borderline normal, characterized by soft blobs with distinct borders, and frequently manifests with a propensity for diarrhea. Type 6 is categorized as moderate diarrhea and manifests as fluffy bits with jagged edges. Type 7, which indicates severe diarrhea, is completely liquid and lacks any solid shape. Clinically, types 1 and 2 suggest constipation, types 3 to 5 are regarded as normal, and types 6 and 7 are associated with diarrhea⁽¹²⁾.

To measure the quality of life, the Menopause-Specific Quality of Life Questionnaire (MENQOL), a validated self-administered tool designed to evaluate the effect of menopausal symptoms on women's quality of life, was used. It consists of 29 items grouped into four domains: vasomotor (3 items), psychosocial (7 items), physical (16 items), and sexual (3 items). Each item asks whether the symptom was experienced in the past month, and if present, how bothersome it was on a scale from 0 (not bothersome) to 6 (extremely bothersome). The Cronbach's alpha values for the vasomotor, psychosocial, physical, and sexual domains and overall MENQOL score were 0.75, 0.89, 0.93, 0.92, and 0.94, respectively⁽¹⁴⁾. In many domains, the Thai version of the MENQOL showed Cronbach's alpha values between 0.75 and

0.93, indicating acceptable to excellent reliability⁽¹⁵⁾.

The MENQOL questionnaire was selected because it comprehensively evaluates menopause-related quality of life. The physical domain includes items such as fatigue, sleep disturbance, joint stiffness, and bloating — symptoms that may be influenced by changes in bowel function and thus relevant to this study's objectives.

Ghfar et al's study was used to calculate the sample size. 46 individuals (23 in each group) were required to compare two distinct groups using a formula with an 80% likelihood of finding a result and a significance threshold of 0.05, while also accounting for a 30% dropout rate. To compare two independent proportions, researchers used a formula that required a total of 46 participants (23 per group), with a power of 80%, a significance level of 0.05, and accounting for a 30% dropout rate.

For all statistical analyses, R 4.4.1 was used. For categorical data, participant characteristics were expressed as frequency and percentage. For continuous data, they were expressed as mean with standard deviation (SD) or median with interquartile range (IQR), as applicable. The Shapiro-Wilk test was used to evaluate the distribution of quantitative variables. The Wilcoxon signed-rank test for non-parametric distributions and the dependent t-test for parametric distributions were used to compare continuous data across the two groups. The Fisher's exact test or the chi-square test, if applicable, was used to evaluate categorical variables. The same statistical tests were used to perform subgroup analysis for participants who were 60 years of age and older. Two-tailed statistical analyses were performed, and p values less than 0.05 were deemed statistically significant. No missing data were reported during the study. All analyses followed the intention-to-treat principle.

Results

In this study, 46 volunteers were recruited, including 23 participants in each group, and they were

randomly randomized to receive either a probiotic or a placebo. Due to bloating, one probiotic group participant had to be excluded. The study details are shown in Fig. 1. Baseline characteristics of eligible participants are presented in Table 1. In general, the majority of clinical, dietary, exercise, and demographic factors were similar between the intervention and

placebo groups. Nevertheless, the median age was significantly lower in the intervention group (61 years, IQR 55, 68) compared to the placebo group (67 years, IQR 60, 78) ($p = 0.036$). Other demographic data showed no significant differences between groups. Thus, the two groups' initial characteristics were identical overall, with the exception of age.

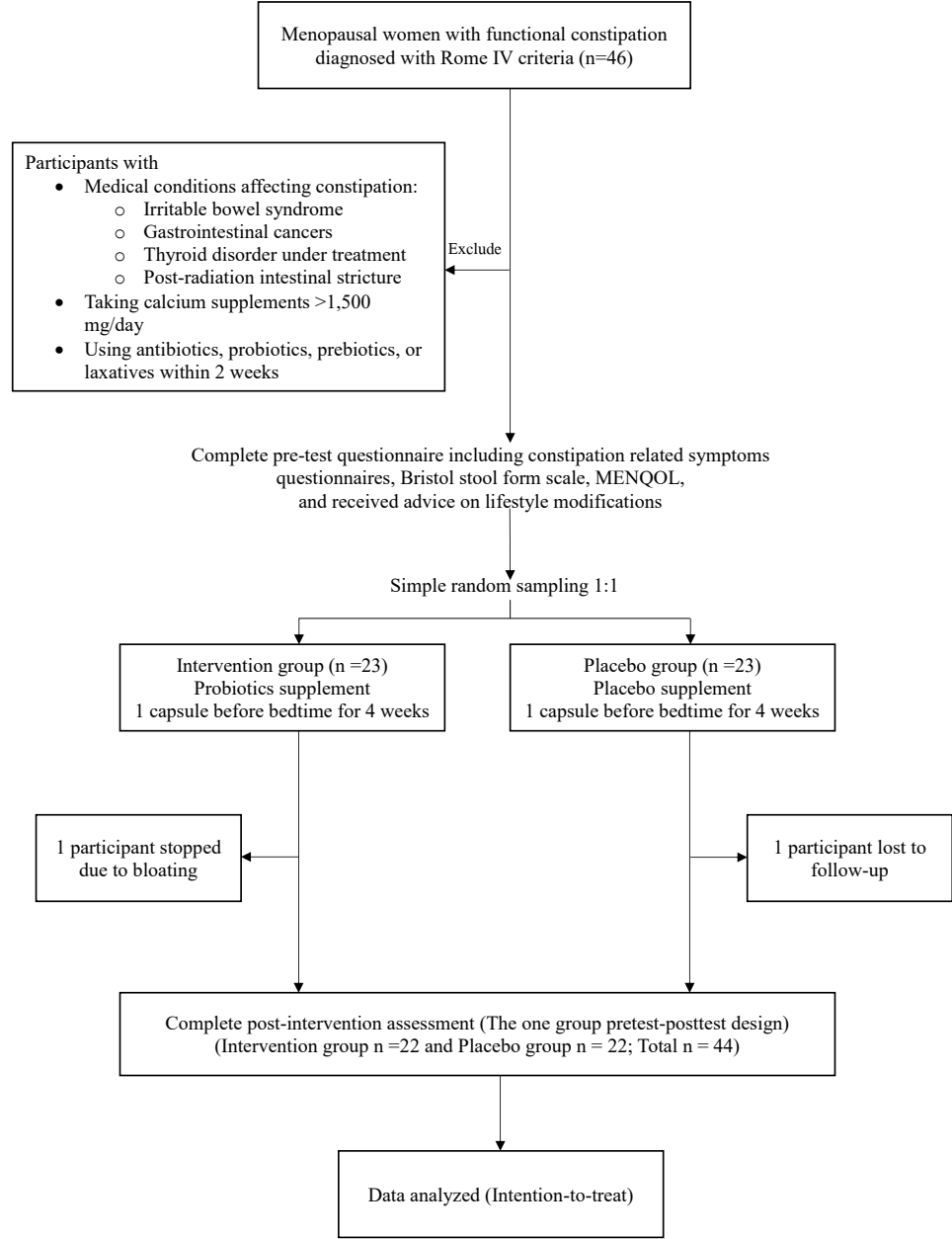


Fig. 1. Flow of participant enrollment.

Table 1. Baseline characteristics of participants.

Characteristic	Placebo (n = 22)	Intervention (n = 22)	p value
	n (%)	n (%)	
Age (years)			0.116 ^d
< 60	5 (22.7)	11 (50.0)	
≥ 60	17 (77.3)	11 (50.0)	
Median (IQR)	67 (60, 78)	61 (55, 68)	0.036 ^b
Body mass index ^a (kg/m ²)	25.5 (22.4, 27.3)	24.4 (22.9, 26.4)	0.898 ^b
Marital status			0.630 ^c
Single	5 (22.7%)	3 (13.6%)	
Married	14 (63.6%)	14 (63.6%)	
Widowed	3 (13.6%)	3 (13.6%)	
Divorce	0 (0.0%)	2 (9.1%)	
Underlying diseases			
Hypertension	7 (31.8%)	5 (22.7%)	0.498 ^d
Diabetes mellitus	2 (9.1%)	3 (13.6%)	1.000 ^c
Dyslipidemia	6 (27.3%)	8 (36.4%)	0.517 ^d
Other	7 (31.8%)	2 (9.1%)	0.132 ^c
Occupation			0.347 ^c
Government	6 (27.3%)	3 (13.6%)	
Self employed	0 (0.0%)	1 (4.5%)	
Trading	2 (9.1%)	5 (22.7%)	
Unemployed	14 (63.6%)	13 (59.1%)	
Educational level			0.724 ^d
Primary school	4 (18.2%)	8 (36.4%)	
Secondary/vocational school	8 (36.4%)	6 (27.3%)	
Bachelor's degree or higher	10 (45.5%)	8 (36.4%)	
Beverage intake ^a			
Tea (cup per week)	0.00 (0.00, 2.00)	0.00 (0.00, 0.00)	0.522 ^b
Coffee (cup per week)	5.0 (0.0, 7.0)	7.0 (0.0, 7.0)	0.245 ^b
Water (glass a day)	8.00 (6.00, 10.00)	6.00 (5.00, 8.00)	0.225 ^b
Consumed dietary fiber intake frequency per day			0.701 ^c
Everyday	7 (31.8%)	10 (45.5%)	
Frequently (5-6 times a week)	5 (22.7%)	5 (22.7%)	
Occasionally (3-4 times a week)	4 (18.2%)	4 (18.2%)	
Rarely (1-2 times a week)	6 (27.3%)	3 (13.6%)	
Consumed dietary fiber per meal			0.680 ^c
Half	8 (36.4%)	9 (40.9%)	
Less than half	8 (36.4%)	7 (31.8%)	
More than half	4 (18.2%)	6 (27.3%)	
None	2 (9.1%)	0 (0.0%)	
Exercise ^a (minutes/week)	55 (0, 140)	33 (0, 210)	0.942 ^b

IQR: interquartile range

^a Median (Q1, Q3)^b Wilcoxon rank sum test; ^c Fisher's exact test; ^d Pearson's Chi-squared test

Table 2 displays the bowel-related symptoms before and after the 4-week intervention for the

intervention and placebo groups. The median (IQR) defecation frequency per week significantly increased

in the intervention group from 3.0 (2.0, 3.0) to 5.0 (4.0, 7.0) ($p = 0.003$). The placebo group also showed an improvement from 2.0 (2.0, 3.0) to 3.5 (2.0, 4.0) ($p = 0.049$). The proportion of participants requiring enemas decreased from 14% to 4.5% in the placebo group and from 4.5% to 0% in the intervention group. Additionally, in the intervention group, the number of participants who no longer delayed bowel movements increased from 14 (64%) to 20 (91%) ($p = 0.080$), without significant difference.

In terms of stool consistency, the number of participants with hard stools (BSFS types 1–2) went

down from 32% to 9.1% in the intervention group, while it stayed the same in the placebo group. Normal stools (BSFS types 3–5) increased from 55% to 64% in the intervention group and from 41% to 50% in the placebo group. Despite the fact that these modifications benefited the intervention group, there was no statistically significant difference between the pre- and post-treatment groups ($p = 0.200$). Although they did not approach statistical significance, other symptoms such as straining, incomplete evacuation, bloating, feeling of obstruction, and gas showed numerical improvements in the intervention group.

Table 2. Bowel-related symptoms before and after treatment between the placebo and intervention groups.

Characteristic	Placebo (n = 22)		p value	Intervention (n = 22)		p value
	Pre-treatment	Post-treatment		Pre-treatment	Post-treatment	
	n (%)	n (%)		n (%)	n (%)	
Number of defecations over the past week ^a	2.0 (2.0, 3.0)	3.5 (2.0, 4.0)	0.049 ^b	3.0 (2.0, 3.0)	5.0 (4.0, 7.0)	0.003 ^b
Use of enema in the past month	3 (14%)	1 (4.5%)	0.600 ^c	1 (4.5%)	0 (0%)	1.000 ^c
Frequency of holding defecation per week			1.000 ^c			0.080 ^c
Never	15 (68%)	16 (73%)		14 (64%)	20 (91%)	
Sometimes (1 to 2 times)	1 (4.5%)	0 (0%)		3 (14%)	0 (0%)	
Occasionally (3 to 4 times)	4 (18%)	3 (14%)		4 (18%)	2 (9.1%)	
Frequently (5 to 6 times)	2 (9.1%)	3 (14%)		1 (4.5%)	0 (0%)	
Blood in the stool	1 (4.5%)	1 (4.5%)	1.000 ^c	1 (4.5%)	1 (4.5%)	1.000 ^c
Bristol stool form scale			0.700 ^c			0.200 ^c
Hard (type 1 or 2)	10 (45%)	10 (45%)		7 (32%)	2 (9.1%)	
Normal (type 3,4 or 5)	9 (41%)	11 (50%)		12 (55%)	14 (64%)	
Watery (type 6 or 7)	3 (14%)	1 (4.5%)		3 (14%)	6 (27%)	
Constipation assessment form (out of 10) ^a						
Straining	5.0 (3.0, 7.0)	5.0 (3.0, 7.0)	1.000 ^b	4.0 (0.0, 5.0)	2.0 (0.0, 4.0)	0.600 ^b
Incomplete evacuation	5.0 (3.0, 7.0)	4.0 (3.0, 6.0)	0.700 ^b	3.0 (0.0, 5.0)	0.5 (0.0, 3.0)	0.200 ^b
Obstruction sensation	3.0 (0.0, 7.0)	3.0 (0.0, 6.0)	0.800 ^b	2.0 (0.0, 6.0)	0.0 (0.0, 3.0)	0.065 ^b
Defecation satisfaction	5.0 (4.0, 7.0)	7.0 (6.0, 8.0)	0.006 ^b	7.0 (5.0, 8.0)	8.0 (6.0, 8.0)	0.200 ^b
Bloating	4.0 (0.0, 7.0)	1.0 (0.0, 5.0)	0.300 ^b	1.5 (0.0, 4.0)	0.0 (0.0, 2.0)	0.200 ^b
Belching frequency	1.5 (0.0, 5.0)	2.0 (0.0, 5.0)	1.000 ^b	2.0 (0.0, 5.0)	1.0 (0.0, 2.0)	0.400 ^b
Appetite loss	3.5 (2.0, 5.0)	2.0 (0.0, 5.0)	0.120 ^b	1.0 (0.0, 3.0)	0.0 (0.0, 2.0)	0.200 ^b
Flatulence	4.0 (2.0, 6.0)	4.5 (3.0, 7.0)	0.800 ^b	4.0 (2.0, 5.0)	3.0 (2.0, 6.0)	1.000 ^b

^a median (Q1, Q3)

^b Wilcoxon rank sum test; ^c Fisher's exact test

Table 3 presents the Menopause-Specific Quality of Life (MENQOL) scores for both the placebo and intervention groups before and after the 4-week intervention. The total MENQOL score in the intervention group significantly decreased from

55.1 ± 31.2 to 40.7 ± 22.4 ($p = 0.012$), reflecting an improvement in menopause-specific quality of life. In contrast, no significant change was observed in the placebo group (64.9 ± 40.3 to 65.5 ± 42.7, $p = 0.873$) (Fig. 2). The physical domain in the intervention group

also showed a significant improvement (34.2 ± 21.5 to 24.4 ± 14.1 , $p = 0.014$), indicating reductions in symptoms such as decreased energy, fatigue, muscle or joint stiffness, and difficulty sleeping. The vasomotor

domain showed a pattern toward improvement (5.9 ± 4.5 to 4.2 ± 3.8 , $p = 0.066$). Conversely, the placebo group did not show any significant changes in their MENQOL score.

Table 3. MENQOL scores before and after treatment between the placebo and intervention groups.

Characteristic	Placebo (n = 22)		p value ^a	Intervention (n = 22)		p value ^a
	Pre-treatment	Post-treatment		Pre-treatment	Post-treatment	
	mean $\pm$ SD	mean $\pm$ SD		mean $\pm$ SD	mean $\pm$ SD	
Vasomotor	4.5 $\pm$ 5.0	5.2 $\pm$ 5.4	0.189	5.9 $\pm$ 4.5	4.2 $\pm$ 3.8	0.066
Psychosocial	13.5 $\pm$ 12.7	14.1 $\pm$ 13.2	0.587	10.5 $\pm$ 7.8	8.9 $\pm$ 7.1	0.226
Physical	42.5 $\pm$ 24.8	42.2 $\pm$ 26.2	0.898	34.2 $\pm$ 21.5	24.4 $\pm$ 14.1	0.014
Sexual	4.4 $\pm$ 7.5	4.0 $\pm$ 6.6	0.762	4.5 $\pm$ 6.2	3.2 $\pm$ 5.1	0.243
Total	64.9 $\pm$ 40.3	65.5 $\pm$ 42.7	0.873	55.1 $\pm$ 31.2	40.7 $\pm$ 22.4	0.012

MENQOL: menopause-specific quality of life, SD: standard deviation.

^a Dependent sample t-test

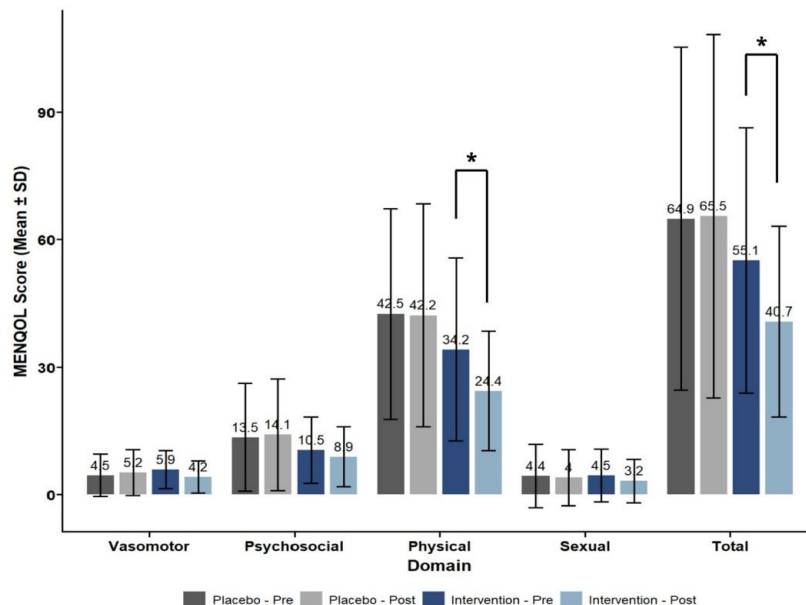


Fig. 2. Average MENQOL scores before and after 4 weeks of intervention.

The subgroup analysis of participants who were 60 years of age or older revealed similar trends to the analysis as a whole. The probiotic group showed a notable increase in how often they had bowel movements, going from an average of 3.0 (IQR 2.0, 3.0) to 5.0 (IQR 3.0, 7.0) times a week ($p = 0.018$); their physical MENQOL scores improved from 39.7 ± 22.7 to 27.4 ± 15.7 ($p = 0.029$), and their

total MENQOL score went down from 62.9 ± 35.6 to 45.5 ± 24.5 ($p = 0.041$); meanwhile, the placebo group had very little change. In addition, stool consistency also improved in the probiotic group, with a reduction in hard stools (from 36% to 9.1%) and an increase in normal stools (from 55% to 82%). However, these changes did not reach statistical significance.

Discussion

The effects of probiotic supplements on constipation and menopausal women's quality of life were examined in this randomized, double-blind, placebo-controlled study. Following a 4-week intervention, the probiotic group's stool frequency increased, and their MENQOL score's physical domain and overall score also improved. Bloating caused one person (4.3%) in the probiotics group to stop taking them.

This study found that in menopausal women with functional constipation, taking probiotic supplements increases the frequency of bowel movements and decreases hard stools. These results were consistent with earlier studies conducted on older adults. In older adults, Ghafar et al reported that supplementation with *Lactobacillus* and *Bifidobacterium* species improved stool form and evacuation within seven days, and Katarina Fehir Šola et al found increased bowel frequency after 12 weeks without adverse effects^(16, 17). In younger adults, Ojetti et al showed that *Lactobacillus reuteri* increased the frequency of bowel movements to 5.28 per week compared to 3.89 per week ($p < 0.05$), although changes in stool form were not significant⁽¹⁸⁾. The efficacy of probiotics did not differ notably between genders or age groups, consistent with previous studies, suggesting that the benefits of probiotics are generally consistent across populations. Furthermore, the current study found that blockage sensation has improved, which has not often been the case in earlier research.

Even after age stratification, this study showed increases in quality of life, especially in the physical domain of the MENQOL score. These results imply that, in addition to enhancing gastrointestinal function, probiotics may also reduce physical menopausal symptoms like fatigue, joint pain, and muscle stiffness. In a related study, Sawada et al evaluated *Lactobacillus gasseri* CP2305 in 106 Japanese women aged 40–60 over six menstrual cycles and found a 75% reduction in Simplified Menopausal Index (SMI) scores in the probiotic group, compared

to 55% in the placebo group⁽¹⁹⁾. Vasomotor, psychological, and physical symptoms are all included in the SMI, but it does not measure menopause-related quality of life in the same multifaceted way as MENQOL. Therefore, more research is necessary to directly compare how probiotics affect MENQOL and SMI results in order to better understand how they affect menopausal well-being in general.

Increased formation of free radicals and oxidative imbalance are linked to menopausal symptoms, which are mainly caused by a significant drop in estrogen levels⁽¹⁵⁾. Probiotics may help reduce age-related oxidative stress because of their immunomodulatory and antioxidant qualities. Likewise, probiotics can increase the colonization of *Lactobacillus* in the vaginal microbiome, which may lower the risk of genitourinary syndrome of menopause and urinary tract infections, both of which are associated with estrogen deprivation^(20, 21). The physical gains seen in this study could be partially explained by these mechanisms.

Although there is still little data specifically related to menopausal women, the results of this study were in line with earlier studies that have shown the benefits of probiotics in promoting bowel regularity and general well-being. This trial's double-blind, placebo-controlled design, validated outcome measures, and use of the Rome IV criteria for identifying functional constipation are among its strong points. The Rome IV criteria offer a highly detailed, standardized, symptom-based diagnostic framework that guarantees proper participant selection and improves the dependability and comparability of study results. Significant increases in the physical domain and overall quality of life were seen when the MENQOL questionnaire was used, which is noteworthy because these outcomes have rarely been covered in previous probiotic studies with menopausal women.

Although the extent of the improvement was modest, it may hold clinical relevance. The median frequency of bowel movements increased from three

to five times per week, suggesting a practical improvement toward normal bowel regularity. The physical domain of the MENQOL score decreased by 9.8 points (29%) and the total MENQOL score by 14.4 points (26%), both indicating enhanced physical comfort. Previous studies have suggested that a reduction of approximately 10 points in MENQOL may represent a clinically meaningful improvement in the perceived quality of life among menopausal women. Therefore, the present intervention may contribute to better physical well-being⁽²²⁾.

Importantly, the use of quality-of-life assessment tools is well supported in Thai populations. Previous Thai research has demonstrated the value of evaluating health-related quality of life among menopausal women with urogenital symptoms by using the incontinence-specific quality of life (I-QOL) questionnaire⁽²³⁾. This Thai study has primarily focused on urinary incontinence and its impact on the quality of life of menopausal women. The present study extends this concept to menopausal women with functional constipation, supporting the application of validated tools such as MENQOL in Thai menopausal research and reflecting its relevance in local clinical settings.

However, several limitations should be noted. First, the analysis's statistical power might have been reduced by the small sample size. Second, it is possible that the 4-week trial period was not long enough to identify improvements in vasomotor symptoms, constipation-related symptoms, and sexual function; these might need longer treatment durations to show noticeable improvements; therefore, further studies with longer treatment durations are warranted to better evaluate these outcomes. Furthermore, subjective results might have been impacted by an age gap between the two groups; to reduce this potential confounder, future research should use statistical adjustments or age-matched randomization. In addition, enema use, which could potentially affect bowel-related outcomes, was assessed both before and after the intervention to control its confounding effect. The mean frequency

of enema use was comparable between the two groups at baseline and showed no significant change after the intervention, indicating that it was unlikely to have influenced the primary outcomes of bowel movement frequency or stool consistency.

Despite these limitations, subgroup analysis revealed reliable outcomes for persons over 60. To validate these findings and evaluate their wider implications in menopausal care, new studies with larger sample sizes for greater statistical power, longer follow-up periods, and balanced age distribution are necessary. Additionally, prior randomized controlled trials supported the continuous use of probiotics without treatment pauses for menopausal symptoms and constipation⁽⁹⁾.

Conclusion

According to this randomized, double-blind, placebo-controlled study, a 4-week course of an 8-strain probiotic supplement significantly increased the frequency of bowel movements, the overall MENQOL score, and the physical domain of the MENQOL score among menopausal women with functional constipation. These results confirm that probiotics are a non-pharmacological way to treat somatic menopausal symptoms and constipation.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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