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## **Comparison of the efficacy of pharmacological and nonpharmacological treatments in women with primary dysmenorrhea: randomized controlled parallel-group study**

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[ORIGINAL PAPER / GYNECOLOGY]

**Comparison of the efficacy of pharmacological and nonpharmacological treatments in women with primary dysmenorrhea: randomized controlled parallel-group study**

[Short title:] **Treatment approaches in dysmenorrhea**

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**ABSTRACT**

**Objectives:** To compare the effectiveness of pharmacological (PT) and nonpharmacological treatments (NPT) in women with primary dysmenorrhea (PD) and determine the most effective treatment method.

**Material and methods:** We enrolled 85 PD participants with PD who were randomly classified into five groups: pharmacological groups; naproxen sodium (NS) and micronized purified flavanoid fraction (MPFF), nonpharmacological groups; motor imagery focused pelvic floor exercise (MOPEXE) and acupuncture, and no treatment group; control. Initial assessment was conducted in all groups on the first day of the menstrual cycle. After the end of the third menstrual cycle, the specialist physiotherapist and the obstetrician conducted a final evaluation. Intensity and nature of pain were evaluated with the Short-Form McGill Pain Questionnaire (SF-MPQ), and menstrual attitudes and behaviors were evaluated using the Menstruation Attitude Questionnaire (MAQ).

**Results:** In the total pain dimension scores, which are the sum of the affective dimension of pain and sensory dimension scores, the pre–post treatment difference was the highest in the mean of the total pain dimension. The highest was for MOPEXE ( $15.12 \pm 4.44$ ), followed by MPFF ( $7.53 \pm 6.8$ ); acupuncture ( $7.47 \pm 5.28$ ) and NS ( $4.47 \pm 4.91$ ) showed more significant change than the control group ( $p = 0.001$ ). The mean difference in visual analog scale (VAS) scores was highest in MOPEXE ( $4.53 \pm 1.5$ ), followed by acupuncture ( $2.35 \pm 1.66$ ); MPFF ( $1.88 \pm 1.73$ ) and NS ( $1.65 \pm 1.84$ ) scores were more significant than the control group ( $p = 0.001$ ). Regarding total pain intensity, the highest was MOPEXE ( $2.59 \pm 0.94$ ), followed by MPFF ( $1.18 \pm 0.88$ ); acupuncture ( $1.06 \pm 0.83$ ) and NS ( $0.82 \pm 1.01$ ) scores were more significant compared to the control group ( $p = 0.001$ ). There was no significant change in the pre–post difference values in the MAQ subparameters: menstruation as deliberate event, menstruating as bothersome event, menstruation as natural event, anticipation and prediction of the onset of menstruation, and denial of any effects of menstruation; menstruation as a natural event resulted in insignificant changes in parameters ( $p = 0.579$ ,  $p = 0.074$ ,  $p = 0.892$ ,  $p = 0.056$ ,  $p = 0.377$ ).

**Conclusions:** PT and NPT methods in the study were effective in coping with PD-associated pain. MPFF was more effective than the NS group in terms of relieving pain. In terms of pain, MOPEXE and acupuncture groups were as effective as PT. The most effective of these treatment methods was the MOPEXE group created by the researcher.

**Key words:** acupuncture; drug therapy; dysmenorrhea; exercise

## INTRODUCTION

Dysmenorrhea is a menstrual disorder that occurs in women of reproductive age. Dysmenorrhea symptoms can be seen in many ways such as pain in the lower abdomen and back during menstruation, nausea, vomiting, and headache [1]. The two types of dysmenorrhea are as follows: primary dysmenorrhea (PD) and secondary dysmenorrhea. The type of dysmenorrhea is diagnosed by evaluating the medical history and ultrasonography. Dysmenorrhea without an underlying organic problem is called PD. Primary dysmenorrhea etiology includes vasospasm in the myometrium along with an increase in prostaglandin production in the endometrium during the menstrual cycle and uterine hypercontraction with ischemia. Secondary dysmenorrhea is a type of dysmenorrhea that occurs in pathological conditions with anatomical and physiological differences [2].

The incidence of dysmenorrhea in different societies ranges from 16% to 90% [1]. Examination of the treatment options for dysmenorrhea in the literature revealed that nonsteroidal anti-inflammatory drugs (NSAID), one of the pharmacological approaches, was the most commonly used treatment option [3]. There are many different drugs used to treat PD. One of these drugs is micronized purified flavonoid fraction (MPFF) [4], which has rarely been used in treating dysmenorrhea in the literature. Therefore, we compared the effectiveness of naproxen sodium (NS) and MPFF treatment in the present study.

Nonpharmacological PD treatments have been increasingly preferred in recent years because nonpharmacological treatments do not have side effects or which are very rare. In the literature, several nonpharmacological treatments currently exist for PD [5]. These nonpharmacological treatments can be summarized as lifestyle changes (reducing alcohol, smoking, and caffeine consumption; regular sleep; reducing daily salt and animal fat consumption; avoiding very hot and very cold foods and drinks; increasing plant-based nutrition, and so on) [6], vitamin-mineral supplements (zinc, vitamins E and B1, and so on) [7], herbal products (ginger, rose tea, fennel, valerian, honey, and so on) [7], and acupuncture and acupressure, which are traditional, complementary, and physiotherapy treatments (massage, electrotherapy, exercise, kinesio taping, and manipulation techniques) [8].

In systematic reviews, acupressure is one of the nonpharmacological treatments. Moreover, studies showing that acupressure therapy is as effective as pharmacological treatments in reducing dysmenorrhea symptoms were noted [9, 10].

Another NPT is exercise. Studies investigating the effects of exercise have shown that regular exercise can reduce pain and other symptoms and improve quality of life [11]. Several exercise types, including yoga, jogging, aerobic exercises, pilates, isometric exercises,

stretching exercises, dance, breathing exercises, relaxation exercises and kegel exercises, have been used to treat PD [8].

In line with this information, there are many PT and NPT modalities applied to individuals with PD.

## **Objectives**

This study aimed to identify the most effective treatment by comparing the efficacy of pharmacological approaches with exercise approaches and acupuncture treatment, which is one of the traditional complementary therapies.

## **MATERIAL AND METHODS**

This study was conducted on women with dysmenorrhea who applied to an obstetrician in Istanbul Medipol University Midwifery Practice Laboratory between February 2020 and January 2021. The study was approved by the Istanbul Medipol University Non-Invasive Clinical Research Ethics Committee with the decision number 10840098-604.01.01.-E.66761 dated December 25, 2019. The study was conducted as a randomized controlled parallel-group study, following the principles of human experimentation set in the Declaration of Helsinki and obtaining the approval of the ethics committee. The participants provided an informed consent form. The clinical trial number for this study is NCT0468785.

We recruited 120 participants to be considered for inclusion by a specialist physician. The study was completed with 85 participants. Figure 1 depicts the flow of participants through the study.

The inclusion criteria of this study were being between 18 and 30 years old, having an active menstrual cycle, and having a positive PD diagnosis using ultrasonographic evaluation by an obstetrician. In this study, the participants were evaluated by an obstetrician using pelvic ultrasonography. In the supine position with full bladder, participants with dysmenorrhea were assessed using pelvic ultrasonography. Obstetrician examination was performed as described in the literature [12].

Study exclusion criteria were hormonal therapy (e.g., patients using progesterone for premenstrual syndrome or dopamine for galactorrhea), psychiatric treatment, intrauterine contraception, use of birth control pills, diagnosed secondary dysmenorrhea, neurological disorders, gastric ulcer, history of gastrointestinal bleeding, history of drug allergy, presence of asthma, presence of disease-causing bleeding disorders, and presence of vascular disease. Moreover, patients with kidney and liver disease were excluded from the study.

Additionally, during the treatment period, participants who received any pharmacological or nonpharmacological treatment other than the treatment type determined in all groups and who were prescribed regular MPFF and NS treatment for any disease other than the menstrual period were excluded from the study.

Participants were randomly divided into five groups (NS, MPFF, acupuncture, MOPEXE [created for the first time by the researcher], and the control).

Participants who met the inclusion criteria for randomization were given enrollment numbers by the physician. The enrollment numbers were randomly selected and grouped by the researchers and groups were recorded.

Following the physician's examination, an initial assessment was conducted in all groups on the first day of the menstrual cycle. The specialist physiotherapist and the obstetrician conducted the final evaluation after the end of the third menstrual cycle.

## **Treatment groups**

### ***Naproxen sodium group***

NS is a pharmacological agent of the NSAID class that has analgesic, antipyretic, and anti-inflammatory effects. It is widely used in dysmenorrhea [13]. NS reduces symptoms of dysmenorrhea by inhibiting cyclooxygenase (COX-1 and COX-2) enzymes and preventing prostaglandin formation [3]. Participants began NS therapy in the first menstrual cycle following the assessment. NS treatment was administered as 550 mg tablets twice a day at most. The treatment was applied only in the menstrual cycle during the 12-week period.

### ***Micronized purified flavanoid fraction group***

MPFF is a U.S. Food and Drug Administration approved medication used in our country. MPFF contains 90% diosmin and 10% hesperidin. MPFF acts on the venous system and reduces venous distension and stasis [14]. MPFF treatment in dysmenorrhea suppresses prostaglandins E<sub>2</sub>, F<sub>2a</sub>, thromboxane A<sub>2</sub>, and prostacyclin; reduces capillary hyperfragility, and increases lymphatic drainage [15]. In the present study, MPFF was used as 90% diosmin and 10% hesperidin in women with PD. Participants began MPFF therapy in the first menstrual cycle following assessment. MPFF treatment was administered in the form of 500 mg tablets twice a day at most. The treatment was applied only in the menstrual cycle during the 12-week period.

### ***Motor imagery focused pelvic floor exercise group***

MOPEXE is an exercise model created by the researcher for the first time, combining Pilates-based exercises with the motor imagery technique accepted in the literature.

The steps to be followed for 60 minutes in the MOPEXE include the following: meditation therapy for five minutes, accelerated progressive relaxation exercises (Bernstein–Borkovec) for 10 min, breathing exercises (diaphragmatic & pursed lip) for five minutes, MOPEXEs for 35 minutes (pelvic stretching, core, and pelvic floor exercises), and meditation therapy for five minutes. MOPEXE consists of Pilates-based exercises. MOPEXE was applied to the participants for 60 minutes twice a week for 12 weeks. The first three sessions were held face-to-face so that the participants could learn the exercises. Subsequent sessions were continued as telerehabilitation. Owing to the COVID-19 pandemic, the participants were followed up with the telerehabilitation method. Telerehabilitation was performed in groups and online via computer or smartphone.

As motor imagery, the participants were instructed to imagine that they had a ping pong ball in their vagina, and they were asked to squeeze their pelvic floor muscles to keep this imaginary ball in their vagina for 10 seconds. Later, they were asked to relax their pelvic floor muscles for 6 seconds. The intensity of the exercises was increased every 2 weeks and the exercise was performed for both type 1–2 muscle fibers. MOPEXE exercises were uploaded to [www.mopexe.com](http://www.mopexe.com), thereby allowing participants to continue the exercises after the treatment. Photos of exercises performed in the MOPEXE group (pelvic stretching, core, and pelvic floor exercises) are available at [www.mopexe.com](http://www.mopexe.com).

### ***Acupressure group***

Acupressure therapy, which is a noninvasive method applied in Chinese medicine, is a technique performed by applying pressure to the acupoints of the meridians in our body, causing mild pain [16].

In the literature review, CV-6 and CV-4 were acupressure points and LI-4 and SP-6 were bilateral administration [17, 18]. Acupressure was applied to these points for 10 min, twice a day, 10 times (60 s), with 5 s pressure applied to these points and 1 s rest. Acupressure application was taught to the participants by an expert physiotherapist who was trained in acupressure.

Acupressure points were determined by an expert physiotherapist who was trained on this subject. The participants were taught how to apply acupressure on the acupressure points on their own. The first three sessions were held face-to-face. Participants were asked to apply 10 minutes of acupuncture to the determined acupuncture points twice a day, in the morning

and evening, for 12 weeks. Reminder notifications for acupuncture applications were sent by text message during the day. Participants' feedback was recorded. Therefore, the participants were encouraged to do the exercises regularly.

### ***Control group***

In this study, the women included in the control group were asked to stay away from all treatments for 12 weeks. They were informed via daily text messages to refrain from taking any treatment. Feedback was recorded. As a result of this feedback, participants who received pharmacological and nonpharmacological treatment were excluded from the study. After the study ended, the participants were presented with treatment options. Treatment was initiated in selected groups.

### **Outcome measures**

In the present study, changes in dysmenorrhea symptoms between groups and before and after treatment were evaluated using the Short-Form McGill Pain Questionnaire (SF-MPQ) and Menstruation Attitude Questionnaire (MAQ). The demographic characteristics of the participants were recorded.

### **SF-MPQ**

The quality and severity of the pain felt by the participants during menstruation were evaluated with the SF-MAQ. Yakut et al. [19] conducted the Turkish validity and reliability study. It evaluates the sensory dimension of pain and the affective dimension of pain. Affective and sensory dimension scores of pain are measured using a Likert-type scale (0 — no pain, 3 — severe pain). Pain severity was assessed using the visual analog scale (VAS) in the McGill Pain Questionnaire. The total pain dimension subparameter is the sum of the sensory dimension and the affective dimension of the pain. Total pain intensity is measured with a 6-point Likert-type scale (0 — no pain, 5 — unbearable pain). A high score indicates a high level of pain [19].

### **Menstruation Attitude Questionnaire**

MAQ is applied to determine the attitudes and behaviors of the participants during menstruation. Furthermore, Kulakaç et al. [20] conducted the Turkish validity and reliability study. Evaluated subdimensions include menstruation as a deliberate event, menstruating as a bothersome event, menstruation as a natural event, anticipation and prediction of the onset of



menstruation, and denial of any effects of menstruation. The scale is evaluated using a 5-point Likert-type.” A high mean score indicates a “positive” attitude toward menstruation [20].

### Statistical analysis

Data analysis was performed using SPSS (IBM SPSS, Chicago, IL, USA) 22.0 package program. Shapiro–Wilk test was used as a normality test. Between groups comparisons were made using the one-way ANOVA, Brown–Forsythe, or Kruskal–Wallis tests following the normality test results.

Tukey and Tamhane tests were used as post hoc tests. Pre and posttreatment comparisons were made with Paired Samples t-test and Wilcoxon signed rank test. The Chi-square test was used in the analysis of categorical variables. Statistical significance was indicated by  $p < 0.05$  in all analyses.

The sample size was calculated as 85 individuals in G\*Power 3.1.9.4 program for five groups and two time points, with 80% power, 5% type I error, and a minimum 0.20-correlation between variables and 25% effect size. The G\* power analysis of the study was reached.

## RESULTS

A total of 85 women with PD participated in this study. Table 1 shows the demographic characteristics of the participants. Furthermore, there is no significant difference in demographic characteristics across the groups ( $p > 0.05$ ), as shown in Table 1.

**Table 1.** Demographic characteristics of the participants (n = 85)

Variables	NS	MPFF	MO	Ac	C	Total	p-value
	mean ± SD/n (%)	mean ± SD/n (%)	mean ± SD/n (%)	mean ± SD/n (%)	mean ± SD/n (%)	mean ± SD/n (%)	
Age [years]	20.47 ± 1.12	19.82 ± 1.13	19.76 ± 1.14	20.17 ± 0.95	20.91 ± 1.87	20.23 ± 1.39	<b>0.061</b> *
BMI [kg/m <sup>2</sup> ]	22.15 ± 3.68	21.58 ± 2.80	21.91 ± 2.97	22.23 ± 3.75	21.61 ± 3.37	22.09 ± 3.31	<b>0.641</b> *
Age of	10–14	17	15	15	13	14	74

	years	(100)	(88.2)	(88.2)	(76.5)	(82.4)	(87.1)	
<b>menarche</b>	15–18	0 (0.0)	2 (11.8)	1 (5.9)	4 (23.5)	3 (17.6)	10	
	years						(11.8)	
	18 years	0 (0.0)	0 (0.0)	1 (5.9)	0 (0.0)	0 (0.0)	1	<b>0.295</b>
	over						(1.1)	
<b>Menstrual period</b>	1–3 days	0 (0.0)	1 (5.9)	0 (0.0)	1 (5.9)	1 (5.9)	3	
							(3.5)	
	4–5 days	5 (29.4)	4 (23.5)	6 (35.3)	6 (35.3)	4 (23.5)	25	
							(29.4)	
	6–7 days	9 (52.9)	9 (52.9)	9 (52.9)	6 (35.3)	8 (47.1)	41	
							(48.2)	
	8–10	3 (17.6)	3 (17.6)	2 (11.8)	4 (23.5)	4 (23.5)	16	<b>0.973</b>
	days						(18.8)	
	< 10	1 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1	
	days						(1.2)	
<b>Menstrual cycle length</b>	10–15	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)	1	
	days						(1.2)	
	16–20	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)	2 (11.8)	3	
	days						(3.5)	
	20–25	3 (17.6)	5 (29.4)	1 (5.9)	5 (29.4)	2 (11.8)	16	
	days						(18.8)	<b>0.270</b>
	26–30	10	10	13	9 (52.9)	9 (52.9)	51	
	days	(58.8)	(58.8)	(76.5)			(60.0)	
	30–40	3 (17.6)	1 (5.9)	0 (0.0)	0 (0.0)	2 (11.8)	6	
	days						(7.1)	
<b>Family history of dysmenorrhea</b>	Irregular	0 (0.0)	1 (5.9)	3 (17.6)	2 (11.8)	1 (5.9)	7	
							(8.2)	
	No	6 (35.3)	8 (47.1)	3 (17.6)	6 (35.3)	3 (17.6)	26	
							(30.6)	
	Yes,	4 (23.5)	5 (29.4)	6 (35.3)	4 (23.5)	4 (23.5)	23	
	mother						(27.1)	
	Yes,	2 (11.8)	1 (5.9)	3 (17.6)	3 (17.6)	4 (23.5)	13	
	sisters						(15.3)	<b>0.782</b>
	Yes,	1 (5.9)	1 (5.9)	1 (5.9)	3 (17.6)	1 (5.9)	7	
	mother's						(8.2)	
relatives								
Yes,	1 (5.9)	1 (5.9)	1 (5.9)	0 (0.0)	0 (0.0)	3		
father's						(3.5)		
relatives								

p\*: One-Way ANOVA; p: Chi-square test.  $p < 0.05$  was considered significant; Ac — acupressure group; BMI — body mass index; C — control group; MO — MOPEXE group; MPFF — micronized purified flavanoid fraction group; n — number of participants; NS — naproxen sodium group; SD — standard deviation

The nondrug coping methods of the participants with dysmenorrhea symptoms are shown in Table 2. There was no significant difference between the groups with nondrug coping methods with dysmenorrhea symptoms 3 months before ( $p = 0.421$ ).

**Table 2.** Nondrug coping methods with dysmenorrhea symptoms 3 months ago (n = 85)

Nondrug coping methods with dysmenorrhea symptoms 3 months before	NS	MPFF	MO	Ac	C	TOTAL	p-value
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Exercise	0 (0.0)	1 (5.9)	1 (5.9)	0 (0.0)	1 (5.9)	3 (3.5)	0.421
Hot application	3 (17.6)	4 (23.5)	4 (23.5)	1 (5.9)	4 (23.5)	16 (18.8)	
Acupressure	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)	1 (5.9)	2 (2.4)	
Lying prone and assuming the fetal position	3 (17.6)	1 (5.9)	1 (5.9)	0 (0.0)	1 (5.9)	6 (7.1)	
Exercise, hot application, herbal tea	1 (5.9)	2 (11.8)	3 (17.6)	2 (11.8)	5 (29.4)	13 (15.3)	
Hot application, herbal tea, lying in prone position, and assuming fetal position	10 (58.8)	8 (47.1)	8 (47.1)	9 (52.9)	4 (23.5)	39 (45.9)	
Acupressure, herbal tea, meditative	0 (0.0)	0 (0.0)	0 (0.0)	2 (11.8)	0 (0.0)	2 (2.4)	

## approaches

All	0 (0.0)	1 (5.9)	0 (0.0)	2 (11.8)	1 (5.9)	4 (4.7)
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p: Chi-square test;  $p < 0.05$  was considered significant; Ac — acupressure group; C — control group; MO — MOPEXE group; MPFF — micronized purified flavanoid fraction group; n — number of participants; NS — naproxen sodium group

When the SF-MPQ scores of the treatment groups were compared before the treatment, there were no significant intergroup differences, except for the total pain intensity ( $p > 0.05$ ). Table 3 lists the pre and posttreatment values of SF-MPQ scores and the differences between the groups.

The difference between the groups in total pain intensity before treatment was between NS and Acupressure groups ( $p < 0.05$ ). Significant changes were observed between the groups and after treatment in all subdimensions including sensory dimension, affective dimension, total pain dimension, VAS, and total pain intensity ( $p < 0.001$ ). The greatest change within a specific group was observed in the MOPEXE group. Relative changes in SF-MPQ are shown in Figure 2.

Table 4 shows the pre and posttreatment values of MAQ scores and the differences between the groups. In the pretreatment evaluation of the MAQ, a significant difference was observed between the groups before treatment in the subparameters of “Menstruation as a deliberating event,” “Menstruation as a natural event,” and “Denial of any effects of menstruation” ( $p < 0.05$ ). This difference was between the control group and the other groups. There was no significant difference between the groups after the treatment ( $p > 0.05$ ). Figure 3 depicts the changes in MAQ pre and posttreatment and relative changes between groups.

**Table 3.** Results of McGill-Melzack Pain Form (SF-MPQ) subparameters pre-treatment-post-treatment scores and intergroup differences

SF-MPQ	Groups	Pretreatment	Posttreatment	Difference	
		t	nt	X ± SD	p <sub>time</sub>
Sensory dimension of pain	NS	19.59 ± 2.62	16.29 ± 4.38	3.29 ± 3.72	0.002
	MPFF	19.94 ± 3.54	14.12 ± 5.18	5.82 ± 5.21	< 0.001

	MOPEX	18.24 ± 3.67	7.18 ± 1.85	11.06 ±	< 0.001
	E			2.59	
	Acupressure	18.47 ± 2.92	12.76 ± 3.72	5.71 ±	< 0.001
	Control	18.29 ± 4.97	16.43 ± 4.29	1.75 ± 1.6	< 0.001
<b>P<sub>group</sub></b>		<b>0.517</b>	<b>&lt; 0.001</b>	<b>&lt; 0.001*</b>	
	NS	5.59 ± 1.37	4.41 ± 1.84	1.18 ±	0.011**
	MPFF	5.76 ± 1.82	4.06 ± 2.01	1.71 ±	0.001*
Affective dimension of pain	MOPEX	6.18 ± 2.51	2.12 ± 0.93	4.06 ±	< 0.001**
	E			2.16	
	Acupressure	5.47 ± 1.33	3.71 ± 1.83	1.76 ± 1.2	0.001*
	Control	6.59 ± 2.06	6.08 ± 1.93	0.51 ± 0.7	0.009*
<b>P<sub>group</sub></b>		<b>0.410</b>	<b>&lt; 0.001</b>	<b>&lt; 0.001</b>	
	NS	25.18 ± 3.61	20.71 ± 5.8	4.47 ±	0.002
	MPFF	25.71 ± 4.96	18.18 ± 6.87	7.53 ± 6.8	< 0.001
Total pain dimension	MOPEX	24.41 ± 5.62	9.29 ± 2.11	15.12 ±	< 0.001
	E			4.4	
	Acupressure	23.94 ± 3.21	16.47 ± 5.29	7.47 ±	< 0.001
	Control	24.88 ± 6.79	22.51 ± 5.84	2.25 ±	< 0.001
<b>P<sub>group</sub></b>		<b>0.868</b>	<b>&lt; 0.001</b>	<b>&lt; 0.001*</b>	
	NS	7.65 ± 1.41	6 ± 2.03	1.65 ±	0.002*
	MPFF	7.47 ± 2.12	5.59 ± 2.58	1.88 ±	0.002**
Visual Analog Scale (VAS)	MOPEX	7.47 ± 1.23	2.94 ± 1.2	4.53 ± 1.5	< 0.001*
	E			2.35 ±	0.001**
	Acupressure	7.06 ± 1.09	4.71 ± 1.79	2.35 ±	0.001**
	Control	6.29 ± 1.83	5.7 ± 1.5	0.59 ±	0.086**
<b>P<sub>group</sub></b>		<b>0.144*</b>	<b>&lt; 0.001</b>	<b>&lt; 0.001</b>	
Total Pain Intensity	NS	4.35 ± 0.7	3.53 ± 1.07	0.82 ±	0.006**
	MPFF	3.71 ± 0.92	2.53 ± 1.33	1.18 ±	0.001**
				0.88	

	MOPEX	3.82 ± 0.73	1.24 ± 0.44	2.59 ± 0.94	< 0.001**
	E				
	Acupressure	3.24 ± 0.56	2.18 ± 1.01	1.06 ± 0.83	0.002**
	Control	3.82 ± 0.81	3.74 ± 1.01	0.08 ± 0.43	0.336**
<b>p<sub>group</sub></b>		<b>0.002*</b>	<b>&lt; 0.001*</b>	<b>&lt; 0.001</b>	

p<sub>group</sub>: Brown–Forsythe, \*Kruskal–Wallis Test, p<sub>time</sub>: Paired Sample T-Test, \*\*Wilcoxon Signed Rank Test; Ac — acupressure group; C — control group; MO — MOPEXE group; MPFF — micronized purified flavanoid fraction group; n — number of participants; NS — naproxen sodium group; SD — standard deviation; X — mean

**Table 4.** Results of Menstruation Attitude Questionnaire (MAQ) subparameters pre-treatment-post-treatment scores and intergroup differences

MAQ	Groups	Pretreatment	Posttreatment	Difference	
		X ± SD	X ± SD	X ± SD	p <sub>time</sub>
Menstruation as a deliberating event	NS	19.35 ± 1.73	19.76 ± 2.7	-0.41 ± 2.81	0.554
	MPFF	19.71 ± 2.42	19.82 ± 2.01	-0.12 ± 3.06	0.876
	MOPEX	19.47 ± 1.23	20.29 ± 2.23	-0.82 ± 2.65	0.219
	E				
	Acupressure	19.47 ± 2.21	19.88 ± 2.2	-0.41 ± 3.26	0.610
	Control	21.65 ± 1.73	21.86 ± 1.8	0.14 ± 1.64	0.604
<b>p<sub>group</sub></b>		<b>0.003</b>	<b>0.036</b>	<b>0.579</b>	
Menstruating as a bothersome event	NS	15.71 ± 2.78	15.12 ± 2.45	0.59 ± 1.58	0.145
	MPFF	15.18 ± 2.07	15.29 ± 2.08	-0.12 ± 1.36	0.727
	MOPEX	15 ± 2.32	15.71 ± 2.59	-0.71 ± 1.1	0.018
	E				
	Acupressure	15.12 ± 1.62	15.88 ± 2.57	-0.76 ± 1.68	0.079
	Control	14.59 ± 2.72	15.1 ± 3.16	0.43 ± 2.05	0.310

<b>P<sub>group</sub></b>		<b>0.736</b>	<b>0.866</b>	<b>0.074*</b>
Menstruation as a natural event	NS	11.94 ± 1.56	12.65 ± 2.15	-0.24 ± 0.157 1.86
	MPFF	13.29 ± 2.39	13.12 ± 1.87	-0.71 ± 0.719** 1.96
	MOPEX	13.18 ± 1.78	13.41 ± 2.35	0.43 ± 0.608 2.05
	Acupressure	14.06 ± 1.52	14.35 ± 1.87	0.18 ± 0.569 1.7
	Control	19.76 ± 2.25	20.27 ± 2.04	-0.29 ± 0.289 2.08
<b>P<sub>group</sub></b>		<b>&lt; 0.001*</b>	<b>&lt; 0.001</b>	<b>0.892*</b>
Anticipation and prediction of the onset of menstruation	NS	27 ± 2.37	27.29 ± 3.12	-0.29 ± 0.477** 1.83
	MPFF	25.76 ± 2.41	25.88 ± 2.87	-0.12 ± 0.850* 2.52
	MOPEX	26.71 ± 2.23	25.24 ± 2.99	1.47 ± 0.018* 2.29
	Acupressure	26.47 ± 2	26.41 ± 1.91	0.06 ± 0.768** 1.39
	Control	27.82 ± 3.57	27.36 ± 4.08	-0.36 ± 0.338** 1.89
<b>P<sub>group</sub></b>		<b>0.354*</b>	<b>0.070*</b>	<b>0.056*</b>
Denial of effects of menstruation	NS	19 ± 1.84	18.88 ± 1.93	0.12 ± 0.800** 2.57
	MPFF	19.53 ± 1.59	18.76 ± 1.86	0.76 ± 0.171** 2.11
	MOPEX	19.76 ± 1.82	19.12 ± 1.8	0.65 ± 0.081** 2.5
	Acupressure	20.12 ± 1.05	20.24 ± 1.03	-0.12 ± 0.707* 1.27
	Control	13 ± 3.95	13.84 ± 3.94	0.69 ± 0.039* 1.62
<b>P<sub>group</sub></b>		<b>&lt; 0.001*</b>	<b>&lt; 0.001*</b>	<b>0.377*</b>

p<sub>group</sub>: One-Way Analysis of Variance, \*Kruskal–Wallis Test, p<sub>time</sub>: Paired Samples T-Test, \*\*Wilcoxon Signed Rank Test; Ac — acupressure group; C — control group; MO — MOPEXE group; MPFF — micronized purified flavanoid fraction group; n — number of participants; NS — naproxen sodium group; SD — standard deviation; X — mean

## DISCUSSION

There are different treatments for PD [9]. However, the number of studies examining the superiority of the treatments used in the treatment of dysmenorrhea is insufficient [5]. Therefore, the present study compared the effectiveness of different treatments used in dysmenorrhea. In the present study, while the change in SF-MPQ scores was significant in all PT and NPT groups, no significant change was found in the MAQ scores in which menstrual attitudes and behaviors were evaluated.

PD is a gynecological problem that commonly occurs between the ages of 17–24 years [1]. In terms of body mass, PD is also seen in women with normal body mass index [1]. The present study is consistent with the literature.

In the literature, NSAIDs are the first treatment option in PD [3, 13]. Many studies investigating the effects of NSAID showed improved symptoms of dysmenorrhea [13]. In a study, the pain change of acetaminophen and NS within 12 hours in PD was investigated. Pain changes were evaluated using “Total Pain” Relief and Sum of Pain Intensity Difference. As a result of the evaluations, NS was found to be more effective than acetaminophen [21]. Ortiz et al. [22], the effect of naproxen-paracetamol-pamabrom versus pyrilamine-paracetamol-pamabrom treatment on pain change was compared, and it was observed that both treatments reduced PD symptoms according to VAS, but had no superiority over each other. Similar to these studies, the intensity and nature of pain were evaluated with the SF-MPQ in the present study. In this study, the change in SF-MPQ scores was significant in all groups.

Another pharmacological agent used in our study was MPFF. Mukherjee et al. [4], the efficacy of MPFF in women with abnormal uterine bleeding was investigated during three menstrual cycles. In the study, pain change was evaluated using the VAS. MPFF treatment was shown to be effective in reducing pain for treating dysmenorrhea.

Similar to the present study, treatment continued for three menstrual cycles. Pain change was evaluated with SF-MPQ. MPFF treatment was found to be an effective pharmacological treatment in reducing pain from dysmenorrhea symptoms. Although MPFF treatment is effective on dysmenorrhea, it is rarely used in the literature. More detailed evaluations are needed in the future to disseminate the use of MPFF treatment.

In recent years, many alternative treatment and exercise approaches, which are preferred in the treatment of dysmenorrhea owing to mild or nonexistent side effects, have been discussed in the literature [9, 10]. In some studies, the effects of alternative therapies and exercise approaches were found to be similar to the effects of NSAID therapy [23, 24].



Motahari-Tabari et al. [23], the effects of stretching exercises and mefenamic acid treatment were compared. Pain changes and intensity were evaluated using the VAS. The study lasted two menstrual cycles. Based on the results of this study, it was found that stretching exercises were as effective as mefenamic acid in coping with pain.

In another study [24], the effects of ginger tablets and mefenamic acid treatment on pain in dysmenorrhea were compared. The study lasted two menstrual cycles. Pain changes and pain intensity were evaluated using the VAS. The effect of ginger is similar to ibuprofen and mefenamic acid as determined on the basis of the results of the current study.

The assessments of the current study are similar to the literature. Moreover, the treatment in the current study lasted three menstrual cycles. The study strength is that the treatment duration was longer than in other studies.

When the studies on acupressure treatment, which is one of the nonpharmacological approaches, are examined, it is seen that different acupuncture points are investigated in the literature. Yu et al. [17], it was noted that the most commonly used acupuncture points in the treatment of dysmenorrhea were SP-6, SP-8 CV-3, CV-4, CV-6, and BL-32. Blödt et al. [25] also evaluated the effect of the self-acupressure application on LR-3, LI-4, and SP-6 points on PD symptoms using the Numeric Rating Scale. Self-acupressure is effective in reducing pain from dysmenorrhea symptoms. The study was conducted over the phone during six menstrual cycles and reported that the acupressure effectiveness would be demonstrated with at least three menstrual cycles.

In the current study, similar to the literature, self-acupressure was applied to CV-6, CV-4, LI-4, and SP-6 points during three menstrual cycles. Moreover, the pain was evaluated with the MPQ in the current study. Furthermore, acupressure points similar to the literature were used. In this respect, the current study is similar to the literature.

There are many recent studies investigating the effects of exercise types on dysmenorrhea [11]. In parallel with this information, the MOPEXE exercise model, which includes many different exercise types, was created by the researcher. In the MOPEXE, the exercises were performed in line with the motor imagery technique. Guillot et al. [26] and Fusco et al. [27] showed that the performance was higher in the dynamic imagery group in which movement and motor imagery techniques were performed simultaneously. Moawed et al. [28], on pelvic floor exercises, it was observed that pelvic floor strength increased more in the motor imagery group. Additionally, it was stated that motor imagery approaches added to conventional training would increase the effectiveness of treatment. When the literature is examined, for this purpose MOPEXE can be seen as an approach for motor imagery exercises

to make the patient aware of the pelvic floor muscles and to understand the pelvic floor movement.

Systematic reviews stated that acupressure and different exercise types are as effective as pharmacological approaches in reducing PD symptoms [8, 30, 31]. Armour et al. [31] showed that the exercise duration in PD when applied for 45–60 min, thrice a week for 8–12 weeks, reduced pain. Another review stated that effective exercises for pain severity and duration in dysmenorrhea should be performed for 8 weeks and should include stretching exercises [11].

In this study, in parallel with systematic reviews, MOPEXE exercises, including different exercise types, were performed for 12 weeks (twice a week for 60 min). Pain changes were also evaluated with the SF-MPQ in parallel with the reviews.

Although studies in which self-acupressure applications reduce pain severity were noted when systematic reviews examining the effect of acupressure treatment in PD are examined, the effect could not be fully determined due to low-quality studies in the literature. In systematic reviews, pain assessment of acupressure therapy was evaluated using the MPQ and VAS in parallel with the current study [32, 33].

In this study, in parallel with the literature, self-acupressure therapy was as effective as pharmacological agents in reducing dysmenorrhea symptoms when applied twice a day for 12 weeks.

The limitation of this study is that it does not measure pelvic floor muscle strength although MOPEXE focuses on the pelvic floor and it has some participants because it was conducted during the COVID-19 pandemic.

## **CONCLUSIONS**

In this study comparing PT and NPT groups in women with PD, it was observed that pain associated with dysmenorrhea decreased in all groups. There was no significant change in menstrual attitude in all groups. MPFF treatment was more effective in reducing pain than NS treatment. Acupressure treatment was also as effective as the drug groups in reducing pain. The change in pain scores was higher in the treatment groups than in the control group. There was no significant change in menstrual attitude scores between the treatment groups and the control group. The greatest change in nature and intensity of pain among all treatment groups was in the MOPEXE group. There is a need for future studies in which pharmacological and nonpharmacological treatments are used together.

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## **Authorship contributions:**

Initial conception: GE, NA, EA; design: GE, NA; data collection or processing: GE, NA; analysis or interpretation of data: GE, NA, EA; literature search: GE, NA; writing and revision of paper: GE, NA, EA.

## **Conflict of interest**

The authors declare that they have no conflict of interest.

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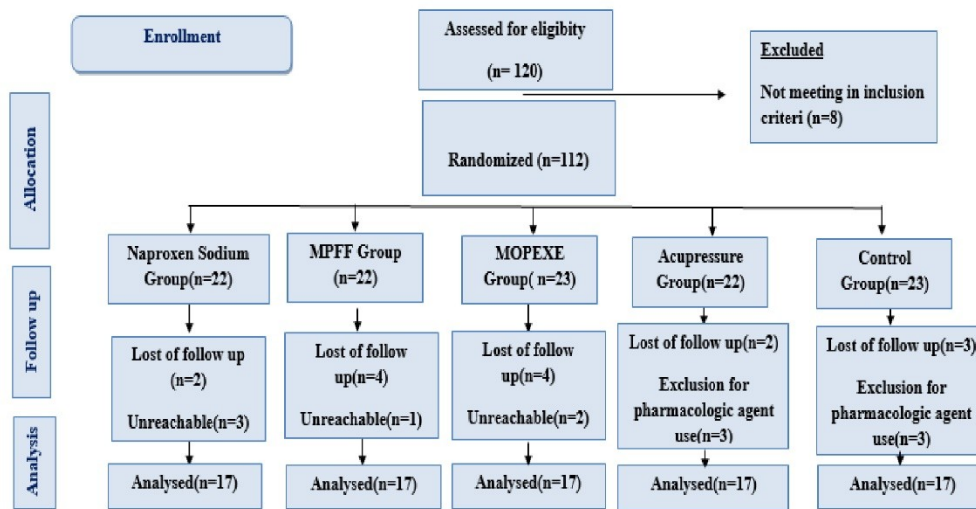
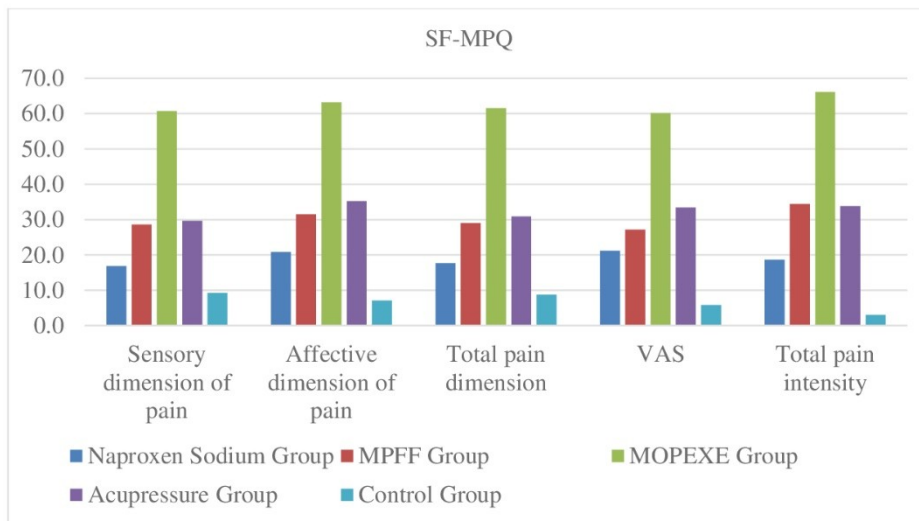


Figure 1. CONSORT Flow Diagram

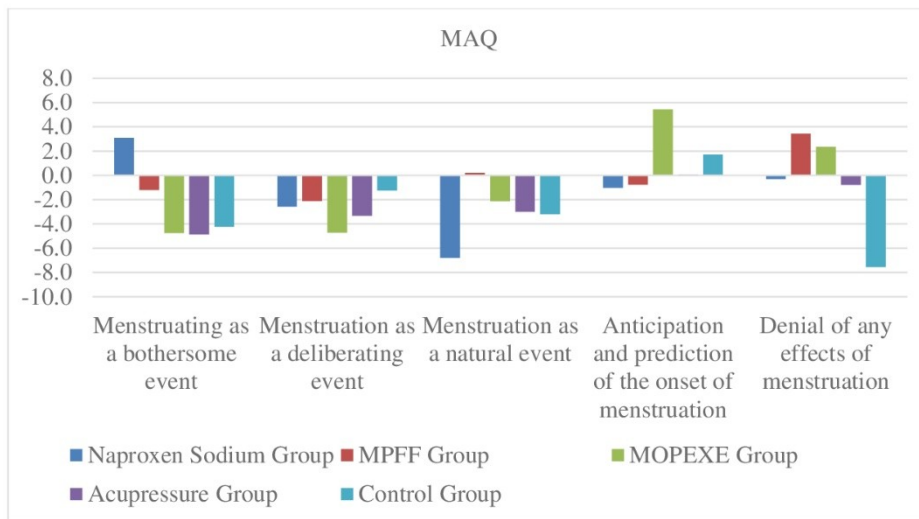
Figure 1. Consort flowchart



**Figure 2.** Relative percentage change of SF-MPQ sub-parameters on *pre*-treatment, *post*-treatment and between groups (n=85)

**Figure 2.** Relative percentage change of SF-MPQ subparameters on pretreatment, posttreatment, and between groups (n = 85)





**Figure 3.** Relative percentage change of MAQ sub-parameters on *pre*-treatment, *post*-treatment and between groups (n=85)

**Figure 3.** Relative percentage change of MAQ subparameters on pretreatment, posttreatment, and between groups (n = 85)