## Comparison of the Effect of Stretching Exercises and Mefenamic Acid on the Reduction of Pain and Menstruation Characteristics in Primary Dysmenorrhea: A Randomized Clinical Trial

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### ABSTRACT

Objectives: Dysmenorrhea is a common gynecologic disorder. Although non-steroidal anti-inflammatory drugs are commonly used, due to their side effects and lack of response in some individuals, other approaches such as exercise have been considered. This study compared the effect of stretching exercises and mefenamic acid on the reduction of pain and menstruation characteristics in primary dysmenorrhea. *Methods*: In this randomized clinical trial, 122 female students with moderate to severe dysmenorrhea were assessed and were placed in either the exercise or mefenamic acid group. The exercise program was performed for 15 minutes, three times a week and included a five-minute warm up and six belly and pelvic stretching exercises for 10 minutes. The mefenamic acid group received 250 mg capsules every eight hours from the onset of menstruation until pain relief. Both interventions were performed during two consecutive menstrual cycles. Pain intensity was measured using a 10 cm visual analog scale. *Results:* The mean pain intensity was significantly higher in the exercise group only in the first cycle (p = 0.058). In the second cycle, the mean difference in pain reduction in the exercise group was higher than the mefenamic group compared to the start of the study (p = 0.056) and the first cycle (p = 0.007). There was no significant difference in the severity and duration of pain between the groups (p > 0.050). *Conclusions:* Stretching exercises were as effective as mefenamic acid in the treatment of primary dysmenorrhea. Our results suggest that the effect of exercise on relieving menstruation pain increases over time.

ysmenorrhea is defined as difficult menstrual flow<sup>1</sup> and refers to painful cramps during menstruation. These cramps can produce uterine pressure more than 60 mmHg, which results in pain.<sup>1</sup> Pain is usually in the suprapubic area but may radiate to the back of the legs or lower back and may be accompanied by other symptoms such as nausea, diarrhea, and headache.<sup>2</sup> It is a significant health problem in women.<sup>3</sup> Primary dysmenorrhea is common among young women and has been reported in 40–50% of them.<sup>1,4</sup> A systematic review reported that 75% of adolescents experience dysmenorrhea.<sup>5</sup> The prevalence of dysmenorrhea is between 74% to 86.1% in Iran.<sup>6</sup> Dysmenorrhea is one of the most common causes of absenteeism from both school and work resulting in large economic, social, and health costs.<sup>3,7</sup> Furthermore, dysmenorrhea has disruptive effects on quality of life, usual activities,

and individual, family and school adjustment. Patients also need to spend more time performing self-care strategies and looking for medical care to manage the condition.<sup>3,7,8</sup>

There is some evidence that an increase or imbalance in prostaglandins leads to primary dysmenorrhea.<sup>9</sup> Thus, non-steroidal antiinflammatory drugs (NSAIDs) are the first-line treatment option.<sup>10,11</sup> The anti-inflammatory and pain relieving effects of NSAIDs are thought to be due to the inhibition of cyclooxygenase enzyme and reduction in menstrual blood volume.<sup>2,11</sup> They may also have a direct analgesic effect on the central nervous system.<sup>4</sup> In a recent review of 73 randomized controlled trials, the effectiveness of NSAIDs in the treatment of dysmenorrhea was confirmed.<sup>2</sup> Nevertheless, these drugs have some side effects such as gastrointestinal problems and cutaneous adverse drug reactions.<sup>12,13</sup> There is some evidence that long-term use of NSAIDs is associated with a degree of cardiovascular risk.<sup>2,12,14</sup> Therefore, other treatments such as physical activity and mild exercise have been proposed to reduce dysmenorrhea.

Two clinical randomized trials showed that stretching exercises were effective in reducing pain intensity in primary dysmenorrhea. They concluded that the effect of regular exercise on dysmenorrhea might be due to the effect of hormonal changes on uterine epithelial tissue or an increase in endorphin levels.<sup>6,7</sup> In a 2010 literature review, the authors concluded that exercise reduces the symptoms associated with dysmenorrhea.<sup>3</sup>

However, data comparing exercise and NSAIDs in the treatment of dysmenorrhea and its outcomes are limited. Additionally, there are some controversies about the effectiveness of exercise on dysmenorrhea, which may be because of different exercise programs. The quality, intensity, and duration of exercise may be associated with different outcomes.<sup>3</sup> Therefore, we sought to compare the effect of stretching exercises and mefenamic acid use on the reduction of pain in primary dysmenorrhea and to compare other outcomes such as menstruation characteristics between the groups.

### **METHODS**

This randomized clinical trial was conducted on the female students of Mazandaran University of Medical Sciences, Iran, over five months in 2014. The study was approved by the university ethics committee. The sample size calculation was 61 for each group (based on the size effect for exercise of  $2.1\pm2.0$  and mefenamic acid of  $3.3\pm1.2$ , a confidence interval of 95% and power of 80%).<sup>2,15</sup> Students living in the university dormitory who had moderate to severe primary dysmenorrhea for more than 50% of menstrual cycles lasting for at least one day and affected their daily activities were included in the study.<sup>3,6,7</sup> The diagnosis of primary dysmenorrhea was made based on having characteristics of pain and ruling out any history of pelvic disorders. The characteristics of pain in primary dysmenorrhea are supra-pubic cramps which appeared in first two years of menarche, begin a few hours or just after the onset of menstruation, and last 48-72 hours.<sup>16</sup> Students were selected from the dormitory since they had similar nutrition (which may have an effect



Eligible students were determined via a convenience sampling using a checklist based on the inclusion and exclusion criteria and were then randomly divided into two interventional groups. All students received an information form and if they agreed to participate, asked to sign a consent form. Demographic and menstrual information such as age, body mass index (BMI), health condition, length and regularity of menstrual cycles, change in bleeding, absence from university, and the need for more analgesics were recorded in a questionnaire. Bleeding change was estimated through the participants' records about consumed pads at baseline and over the course of the study. Ten professors confirmed the validity of the questionnaire. The test-retest reliability was 0.92. Intensity of pain was measured using a 10 cm visual analog scale (VAS). The VAS is an instrument for measuring characteristics with continuous values that cannot easily be directly measured. The pain VAS is usually a horizontal line, 10 cm in length, defined by descriptive words of "no pain" (score of 0) and "very severe pain" (score of 10). Participants were asked to put a mark on the line that they felt represented the most severe pain that experienced during menstruation. The pain score was determined by measuring the distance between the score of 0 and the participants' mark in centimeters using a ruler. Severity of pain was classified as mild (< 4 cm), moderate (4-6 cm), and severe (7-10 cm).

The exercise program included a five-minute warm up in a standing position and then six belly and pelvic stretching exercise for 10 minutes. This program was performed for 15 minutes, three times a week in two menstrual cycles (eight weeks). Exercise was not performed during menstruation.<sup>6,7</sup> Two trained instructors taught the exercise protocol to the students. Students in the mefenamic acid group received 250 mg capsules every eight hours from the onset of menstruation until pain relief also for two cycles.<sup>15</sup> Both interventions were performed during two consecutive cycles. In both groups, the intensity of pain was assessed using the VAS at the end of the first and second menstrual cycles. Follow-up of participants for the assessment of menstruation



Patient characteristics	Mefenamic acid Exercise		<i>p</i> -value	
Age, years (mean±)	21.6±2.0	21.3±2.0	0.414	
BMI, kg/m <sup>2</sup> (mean $\pm$ )	21.8±2.9	22.6±3.6	0.225	
Educational level				
MSc and PhD	16 (72.7)	6 (27.3)	0.032	
BSc	45 (45.0)	55 (55.0)		
University year				
1 <sup>st</sup> and 2 <sup>nd</sup>	23 (48.9)	24 (51.1)	1.000	
3 <sup>rd</sup>	38 (50.7)	37 (49.3)		
Family history of dysmenorrhea				
Yes	40 (54.1)	34 (45.9)	0.095	
No	10 (33.3)	20 (66.7)		
Unknown	11 (61.1)	7 (38.9)		

Table	1: Participants'	demographic	characteristics i	in the mefenamic	c acid and	l exercise grou
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Data given as n (%) unless otherwise indicated. BMI: body mass index; MSc: Master of Science; PhD: Doctor of Philosophy; BSc: Bachelor of Science.

characteristics was also done in this period. Likewise, participants' pain intensity was recorded before taking more analgesics whenever needed for additional relief.

Descriptive statistics (mean, standard deviation (SD), frequency, mean difference), Student's *t*-test and chi-square test were used for data analysis.

### RESULTS

One-hundred and twenty-two participants were equally divided into two groups: the mefenamic acid group (n = 61) and the exercise group (n = 61). Demographic characteristics of participants in the mefenamic acid and exercise groups were compared using the Student's *t*-test and chi-squared test and are shown in Table 1.

The mean pain intensity in the exercise group was significantly higher than the mefenamic acid group in the first cycle after intervention [Tables 2 and 3]. Pain intensity was significantly different between the groups in the second cycle as the mean difference between baseline and first cycle was higher in the exercise group compared to the mefenamic acid group [Table 4 and Figure 1]. Chi-square analysis showed that the severity of dysmenorrhea and pain duration had no significant difference between the groups during the study [Table 2, 3, and 4].

Length of menstruation in the first and second cycle was longer in the exercise group, but bleeding changes were not significantly different between groups [Table 5]. Despite the fact that the participants who took additional analgesic drugs in the exercise **Table 2:** Comparison of pain between themefenamic acid and exercise group at baseline.

Pain	Mefenamic acid	Exercise	p-value
Pain intensity, cm	55.0±20.4 (49.82–60.24)	60.3±14.5 (56.55-63.96)	0.104
Pain duration, days	$1.7 \pm 0.9$ (1.43-1.90)	$1.8 \pm 0.7$ (1.60-1.96)	0.444
Severity of dysmenorrhea, n (%)			0.849
Moderate	41 (51.3)	39 (48.8)	
Severe	20 (47.6)	22 (52.4)	

Data given as mean  $\pm$  SD and (95% confidence interval for mean) unless otherwise stated.

# **Table 3:** Comparison of pain between themefenamic acid and exercise group in the first cycle.

Pain	Mefenamic acid	Exercise	p-value
Pain intensity, cm	39.0±17.8 (34.46-43.56)	45.4±19.2 (40.50-50.34)	0.058
Pain duration, days	$1.4 \pm 0.6$ (1.2-1.6)	$1.6 \pm 0.8$ (1.38-1.79)	0.131
Pain reduction between baseline and the second cycle, mean (SE)	16.0 (2.2)	14.8 (2.5)	0.724
Severity of dysme	enorrhea, n (%)		0.475
Mild	22 (52.4)	20 (47.6)	
Moderate	35 (51.5)	33 (48.5)	
Severe	4 (33.3)	8 (66.7)	

Data given as mean ± SD and (95% confidence interval for mean) unless otherwise stated. SE: standard error.

Pain	Mefenamic acid	Exercise	<i>p</i> -value
Pain intensity, cm	33.8±17.7 (29.21-38.29)	31.6±16.03 (27.46-35.68)	0.477
Pain duration, days	$1.6 \pm 0.7$ (1.44 - 1.80)	$1.5 \pm 0.7$ (1.29-1.69)	0.378
Pain reduction between the first and the second cycle, mean (SE)	5.3 (2.24)	13.9 (2.1)	0.007
Pain reduction between baseline and the second cycle, mean (SE)	21.3 (2.91)	28.7 (2.5)	0.056
Severity of dysr	nenorrhea, n (%)		0.357
Mild	33 (45.8)	39 (54.2)	
Moderate	28 (56.0)	22 (44.0)	

**Table 4:** Comparison of pain between the mefenamicacid and exercise group in the second cycle.

Data given as mean ± SD and (95% confidence interval for mean) unless otherwise stated. SE: standard error.

group were more than the mefenamic acid group, the difference was not statistically significant in the first (61.0% and 39.0%, respectively) or second cycles (64.0% and 36.0%, respectively). Students in the exercise group had more absences (63.0%) than the mefenamic acid group (37.0%) at baseline (p = 0.055), but absences were the same in the two groups after the first and second cycles (50.0% in both groups).

## DISCUSSION

Today, non-medical approaches concentrate on treating dysmenorrhea. Exercise and physical activity have been suggested as alternative methods to treat



**Figure 1:** Change in pain intensity in the mefenamic acid and exercise group over the study period.

dysmenorrhea and its symptoms.<sup>3,18</sup> In the existing research, the impact of exercise was compared to using mefenamic acid as a common treatment for dysmenorrhea. Our results indicated that although pain decreased in the first month after starting the intervention in both groups, the mean pain in the exercise group was significantly more than the mefenamic acid group. In the second month, the decline in the intensity of pain in both groups continued and the mean pain in the exercise group was lower than the mefenamic acid group. The mean difference of reduced pain in the first cycle was not significant between the groups, but pain in the second cycle significantly decreased in the exercise group compared to the first cycle and baseline levels. At baseline, only moderate and severe dysmenorrhea were observed in the groups, and after one menstrual cycle, some cases of mild dysmenorrhea appeared and

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Table 5: Menstruation c	haracteristics in th	he metenamic	acid and	l exercise groups.

Menstruation characteristics	Mefenamic acid			Exercise		
	Baseline	First cycle	Second cycle	Baseline	First cycle	Second cycle
Menstrual intervals, days	28.4±2.8	28.0±4.0	28.0±2.7*	29.2±3.4	29.0±4.3	29.2±2.9*
Length of menstruation, days	6.6±1.2	5.9±1.3**	6.2±1.2	6.8±1.3	6.5±1.1**	6.1±1.2
Bleeding, n (%)						
Increase		3 (4.9)	5 (8.2)		6 (9.8)	9 (14.8)
Decrease		20 (32.8)	21 (34.4)		16 (26.2)	21 (34.4)
No change		38 (62.3)	35 (57.4)		39 (63.9)	31 (50.8)

Data given as mean  $\pm$  SD unless otherwise indicated. \*p = 0.030, \*\*p = 0.012.



severe dysmenorrhea cases declined in both groups. After two cycles, no severe dysmenorrhea case was reported in both groups.

According to our results, at first, exercise is effective in reducing the pain of dysmenorrhea similar to mefenamic acid and the effect of exercise on relieving pain increases over time. Thus, it is possible that if exercise was continued on a regular basis, the pain intensity difference in the exercise group would become significant compared to the mefenamic acid group. Abbaspour et al,<sup>7</sup> observed that exercise decreased the intensity of dysmenorrhea and sedative use after three and four cycles in highschool students. Shahr-jerdy et al,<sup>6</sup> using the same exercise protocol reported the reduction of pain intensity and sedative use after eight weeks. Another study reported that after 12 weeks of water exercise, the duration and intensity of pain dropped.<sup>19</sup> When comparing the impact of using a warm water bottle and exercise, researchers reported that pain intensity decreased significantly in the third month after the intervention.<sup>20</sup> Based on these findings, it seems that the effect of exercise on dysmenorrhea appears over time.

Other studies reported improved dysmenorrhea following long-term exercise, and in those who performed regular exercise compared to those who occasionally did. In a study of athletes, the authors concluded that exercising before menarche was accompanied with higher reductions in the prevalence of dysmenorrhea, and vigorous exercise was associated with a decrease in intensity.<sup>21</sup> In other research, women with no primary dysmenorrhea performed more than one hour of physical exercise daily compared with women who had primary dysmenorrhea.<sup>22</sup> A three-year survey found that the prevalence of dysmenorrhea was 39% in the exercise group and 61% in the control group.<sup>23</sup> Ganon et al,<sup>24</sup> also reported that the duration of exercise had a significant correlation with reduced premenstrual symptoms.

In addition to duration, the type and intensity of exercise can affect the results. Some investigators found that moderate physical activity was effective in decreasing physical symptoms associated with menstruation (e.g., pain) while others observed vigorous exercise to be effective. <sup>18,25,26</sup> Yet, several other researchers found a poor correlation or no relationship between physical activity and dysmenorrhea.<sup>18,27–31</sup> A previous study in a group of women who performed vigorous exercise reported a 30% increase in dysmenorrhea cases.<sup>32</sup> A Cochran review suggested that the different results seen can be due to the use of various exercise protocols or studies with methodological weaknesses.<sup>3</sup> Additionally, the difference in dysmenorrhea type may influence the results.

The exercise analgesic effect is thought to be applied through nonspecific mechanisms.<sup>6</sup> Dysmenorrhea has a dose-response association with stress.<sup>6,23,33,34</sup> Stress accelerates uterine contractions and menstrual pain.<sup>34,35</sup> As a result, by decreasing stress and psychological pressures, and enhancing mood, exercise may decrease pain.<sup>8,32,36</sup> Moreover, exercise can cause the release of endorphins, which are pain-relieving factors.<sup>8,26,37</sup> Another potential mechanism is the improvement of pelvic blood circulation and local metabolism during exercise.<sup>8,21</sup> Consequently, exercise may prevent prostaglandin accumulation, which results in uterine contraction, ischemia, and pain.<sup>38</sup> Some believe that stretching exercises can be effective in removing abdominal spasms that stimulate nerve routes.<sup>4,18,39</sup>

In this study, pain duration in the second cycle in the exercise group was less than the mefenamic acid group, though the difference was not significant. Several other researchers reported the effect of exercise on reducing the duration of pain.<sup>6,7,37,40</sup> This influence may be due to the faster transfer of prostaglandins following physical exercise.<sup>40</sup> The effect of mefenamic acid on decreasing the length of menstruation was significantly higher than exercise in the first cycle. A larger number of students in this group reported reduced bleeding compared to the exercise group. In the second cycle, the difference in menstrual duration between the two groups was not significant, and a similar number in both groups reported reduced bleeding. Abbaspour et al<sup>7</sup> also reported reduction in bleeding duration in the fourth cycle. In another study, by the eighth week of isometric exercise, despite a decrease in the intensity and duration of pain, there was no change in bleeding volume.<sup>37</sup> However, by conducting a combination of stretching and resistance exercises for 90 minutes, three times weekly for eight weeks, another study reported reduced bleeding, and pain and duration.<sup>40</sup> Therefore, the effect of exercise on duration and bleeding volume may be increased with prolonged exercise protocols or exercise type change. It seems that this effect is the result of hormonal changes.<sup>40</sup> The

prolonged menstrual intervals in the exercise group compared to the mefenamic acid group may be related to these hormonal changes. Only one study reported the effect of exercise on the length of menstrual cycle, which was not significantly different to the control group. More studies are necessary to understand this variable.<sup>6</sup>

The number of students who needed to take analgesic drugs declined in the exercise group, which was consistent with other studies.<sup>6,7,40</sup> Because the reduction of pain intensity increased over time in the exercise group, a decrease in taking medication is reasonable. In addition, following the reduction of pain, a decline in university absence was seen.

The limitation of our study was that the exercise protocol was only performed for a short time, and did not allow us to observe the effect of long-term exercise on dysmenorrhea. Furthermore, the results were not compared with a control group, blinding was not performed, and bleeding volume, stress level and weight changes were not assessed.

### CONCLUSION

Regular exercise can be useful as an easy, accessible, and inexpensive approach to improve dysmenorrhea; however, the quality, intensity, and duration of exercise can influence the results. Consequently, comparative and blind studies in this field are recommended to distinguish the physical and psychological effects of exercise on dysmenorrhea.

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