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Original article

A clinical comparative study of oral and topical ginger on severity and duration of primary dysmenorrhea

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Abstract

Background and objectives: Primary dysmenorrhea has remained a health problem. This study has compared the effect of oral and topical ginger on severity and duration of primary dysmenorrhea. **Methods**: A single-blind randomized trial was conducted on 70 female students with moderate and severe primary dysmenorrhea. The participants were stratified randomized between two groups of oral and topical ginger. The oral group received 250 mg capsules of ginger powder and the topical group applied five drops of ginger oil topically every 6 hours from two days before through the first three days of menstruation for three cycles. The severity and duration of pain, and the number of mefenamic acid consumption were assessed in each cycle. Before-after changes were evaluated in each group and were compared between two groups. **Results:** The reduction of pain severity was 3(±3.2) in the topical compared to 2.6(±3.4) in the oral group (p<0.001). The reduction of pain duration was 14.5(±20.1) h in the topical compared to 14.5(±19.8) h in the oral group (p<0.001). The reduction of mefenamic consumption was 0.4(±1.6) in the topical (p=0.9) compared to 0.5(±1.3) in the oral group (p=0.006). The reduction in pain severity, duration and mefenamic consumption were similar between two groups (p>0.05). Complications were observed in 54.2% of participants in oral group. **Conclusions:** This study showed that ginger in both oral and topical forms showed similar positive effects on decreasing the severity and duration of pain in primary dysmenorrhea; however, the topical ginger oil was a better choice because it showed no complications.

Keywords: dysmenorrhea, ginger, ginger oil, Iranian Traditional Medicine, topical form

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Introduction

Primary dysmenorrhea is known as painful menstrual cramps without any pelvic pathology [1-4], which is the most common cause of pelvic pain in women [5]. It occurs in 73.2% to 91% of the menstruating females in Iran and worldwide [6,7]. Dysmenorrhea is followed by many social [8] and economic consequences [5]. Also, it affects the women's psychological situation [5] and quality of life [9]. Nowadays, using non-steroidal anti- inflammatory drugs (NSAIDs) such as mefenamic acid is the first-line treatment for primary dysmenorrhea [2,3]; however, the use of NSAIDs has contraindications, complications [2,3,10,11], and in 20-25% cases lack of response to treatment [11]; thus, complementary medicine could help to treat primary dysmenorrhea [12].

Iranian Traditional Medicine (ITM) with a long history of successful management of diseases, can be used for the treatment of primary dysmenorrhea [10]. From Iranian Traditional Medicine point of view, topical application of the oil form of medicines is one of the most effective ways of their administration in primary dysmenorrhea [13,14]. Applying the oil to the lower abdomen is the most acceptable way of usage during menstruation. On the other hand, based on the concepts of ITM, ginger has hot and dry nature and it is effective in the treatment of primary dysmenorrhea because ginger can act as a painkiller and would facilitate the flow of menstrual blood [13,15-17]. Also, multiple clinical studies have shown that oral ginger [12,18-24] or abdominal massage with ginger essential oil [22-24] were effective in the treatment of primary dysmenorrhea. For example, Studies by Rahnama *et al*. in 2010 and 2012 compared ginger capsule with placebo in 78 and 120 students with primary dysmenorrhea, respectively and showed that oral ginger capsule was more effective than placebo [12,18]. In 2012, Rahnama *et al*. found that the effect of 500 mg ginger powder three times a day starting from two days before through the first three days of bleeding on reducing the pain severity was similar to its administration on the first three days of bleeding, but taking ginger capsule from two days before menstrual bleeding was more effective on decreasing the pain duration [12]. On the other hand, in all abdominal aromatherapy massage studies, the main factor of pain relief is unclear whether it is the essential oil itself, the massage, or both. Besides, ginger oil prepared by macerating ginger in sesame seed oil has shown to contain more anti-inflammatory components compared to ginger essential oil [25]. However, all clinical trials have only studied the effect of ginger essential oil and not ginger oil on primary dysmenorrhea [22-24]. Moreover, no study has compared oral and topical forms of ginger; therefore, the aim of this study was to compare the effect of topical versus oral ginger in primary dysmenorrhea.

Experimental

Plant material

Dried *Zingiber officinale* Rosco (ginger) rhizomes were purchased from local market in Tehran, Iran (Aug 2014). A botanist from Traditional Medicine and Materia Medica Research Center (TMRC), Shahid Beheshti University of Medical Sciences, Tehran, Iran, confirmed its scientific identity. A sample was kept for future reference (No. 336 HMS).

Preparation of ginger oil

Dried Ginger rhizomes were crushed and macerated in sesame seed oil (1:5) for seven days. The mixture was subsequently filtered and centrifuged until the yellowish ginger oil was extracted [25]. Dropper containers with proper labels were filled with the final transparent yellowish ginger oil and kept in a refrigerator.

Preparation of ginger capsule

Dried ginger rhizomes were grounded with an ordinary hand mill. The powder was then passed through sieve. The capsules were further filled with 250 mg ginger powder. The weight variation of the capsules was in the acceptable range of United States Pharmacopoeia (USP). Finally,

ginger powder capsules were packed in boxes each containing 20 capsules.

Study design

The study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences: SBMU.REC.1393.550. Furthermore, the trial was registered in the Iranian Registry of Clinical Trials: IRCT2014090219012N1.

This single-blind, stratified randomized controlled clinical trial was conducted on 400 female university students who lived in dormitories of Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Female students who were 18-45 years old with a BMI less than 35, regular menstruation, moderate and severe menstrual pain based on grade 2 and 3 by the verbal multidimensional scoring system (VMS), lack of secondary dysmenorrhea confirmed by history and pelvic sonography, negative history of pelvic or abdominal surgery, no history of stress (divorce of parents, death of first-degree relatives) in the last six months, no history of taking other medications, and negative history of bleeding disorders were included the study. VMS is a scale for assessing the severity of dysmenorrhea with four grades as follows: painless menstruation = 0, menstrual pain with rare use of analgesics or limitation of daily activities = 1, moderate menstrual pain with daily activity impairment and use of analgesics = 2, and severe menstrual pain with significant limitation of daily activities, ineffective use of analgesics, and other symptoms such as headache, tenderness, nausea, vomiting and diarrhea = 3 [12,18,19].

The participants who got pregnant, needed another intervention or had personal request were excluded from the study.

All students in this study gave their informed consent prior to participation in the study.

Intervention

Initially, the demographic questionnaire was completed for each participant by the researcher. In the first cycle, the participants did not take any research drugs and they only took 12 capsules of 250 mg mefenamic acid that they could use every 8 h in case of experiencing pain. The baseline of the pain intensity and duration and the number of mefenamic acid consumption was recorded in the first cycle.

Then in order to increase the accuracy of the study, the participants were classified into two groups of moderate and severe dysmenorrhea based on the severity of pain assessed in the first cycle. Afterwards, the participants in moderate and severe dysmenorrhea groups were divided into two groups of oral and topical ginger, randomly. The participants in oral group started taking a 250 mg ginger capsule every 6 h from two days before through the first three days of menstrual bleeding for three consecutive menstrual cycles. The participants in the topical group applied five drops of ginger oil to their lower abdomen without massage every 6 h from two days before through the first three days of menstrual bleeding for three consecutive menstrual cycles (figure 1). Also, 12 capsules of 250 mg mefenamic acid were given to each participant for each intervention cycle. The participants could take one capsule every 8 hours in case of experiencing pain after 1 h of taking the research drug and were requested to mark the severity of pain in the questionnaire before taking mefenamic acid capsules. The number of used mefenamic acid capsules was recorded in each cycle.

Outcomes

The severity of pain was examined by the VAS during one day before through the first three days of menstrual bleeding in all four cycles. The VAS is a tool widely used to measure the severity of pain [26]. It is a horizontal calibrated ruler from 0-10 cm, with 0 representing “no pain at all” and 10 representing “pain as bad as it could be”. On this scale, 0 to 3 is considered mild, 3 to 7 is considered moderate, and 7 to 10 is considered severe [18]. The duration of pain was assessed by the total hours of experiencing pain during a day before through the first three days of menstrual bleeding in all four cycles.

The mafenamic acid consumption was evaluated by the total number of used mefenamic acid capsules during a day before through the first three days of menstrual bleeding in all four

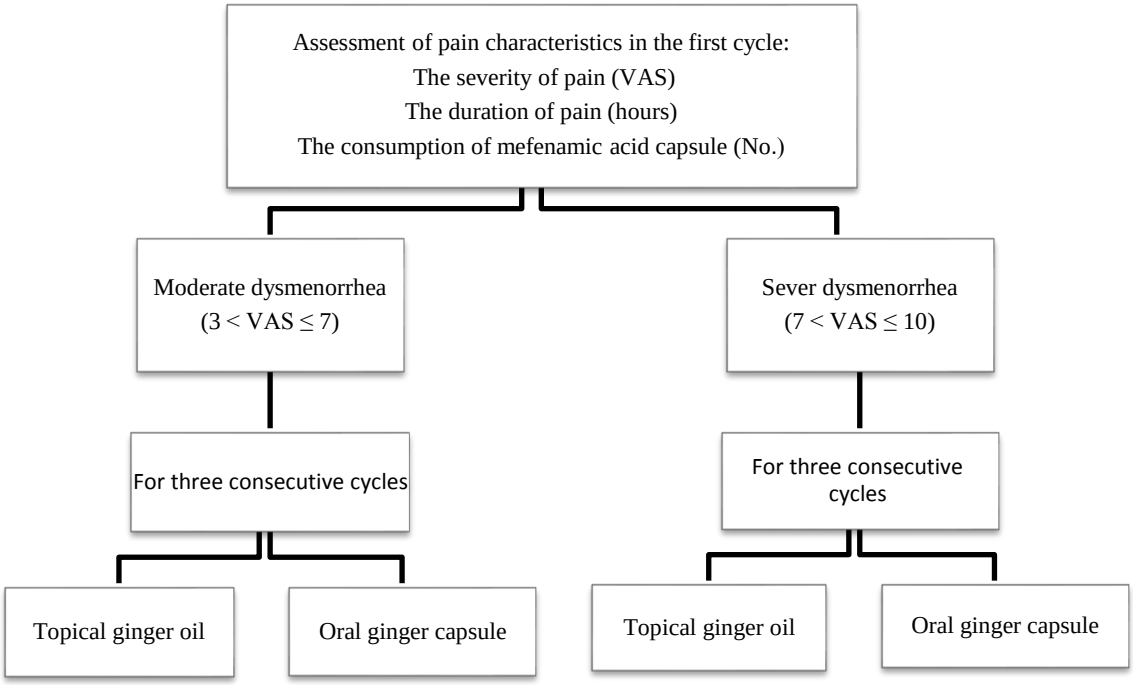

Figure 1. Schematic view of intervention

cycles. The before-after changes in pain severity and duration and mefenamic acid consumption were evaluated in each oral and topical group. Then these results were compared between groups.

Statistical analysis

The sample size was calculated as 35 participants in each oral and topical group, considering the effect size for pain severity = 0.75, type I error = 0.05, power = 80%, and attrition = 20%.

The maximum severity and the total duration of pain and the number of mefenamic acid consumption were assessed in each cycle.

SPSS software version 17 (SPSS, Inc) was used for data analysis. Quantitative data were presented by mean and standard deviation, and qualitative data were presented by number and frequency percentage. Then, the mentioned variables were compared between the two groups using t-test or Mann-Whitney test; moreover, before-after changes of the variables were analyzed in each group via the paired *t*-test or Wilcoxon test. Both intention to treat (with the "last observation carried forward" method for missing data) and per protocol analysis were conducted. *P* values less than 0.05 were considered statistically significant.

Results and Discussion

Initially, 400 female students were assessed for eligibility, of which 90 students participated in the first cycle. After the first cycle, 20 participants were excluded from the study. So, seventy participants were classified into two groups of moderate (n=27) and severe (n=43) dysmenorrhea based on the severity of pain in the first cycle. The participants in each moderate and severe group were randomly divided into two groups of oral and topical. Thirteen and fourteen participants in the moderate dysmenorrhea group and 22 and 21 participants in the severe dysmenorrhea group received oil and capsule, respectively. Thus, there were 35 participants in each oral and topical group and the frequency of moderate and sever pain was statistically similar

in two oral and topical groups (figure 2). Thirty-five participants in the topical group (13 with moderate and 22 with severe dysmenorrhea) and 29 participants in the oral group (13 with moderate and 16 with severe dysmenorrhea) completed the study.

Attrition was 6 participants (17%) in the oral group due to its complications or patient compliance issues (1 with moderate and 5 with severe dysmenorrhea), while there were no drop-outs in the topical group (figure 2).

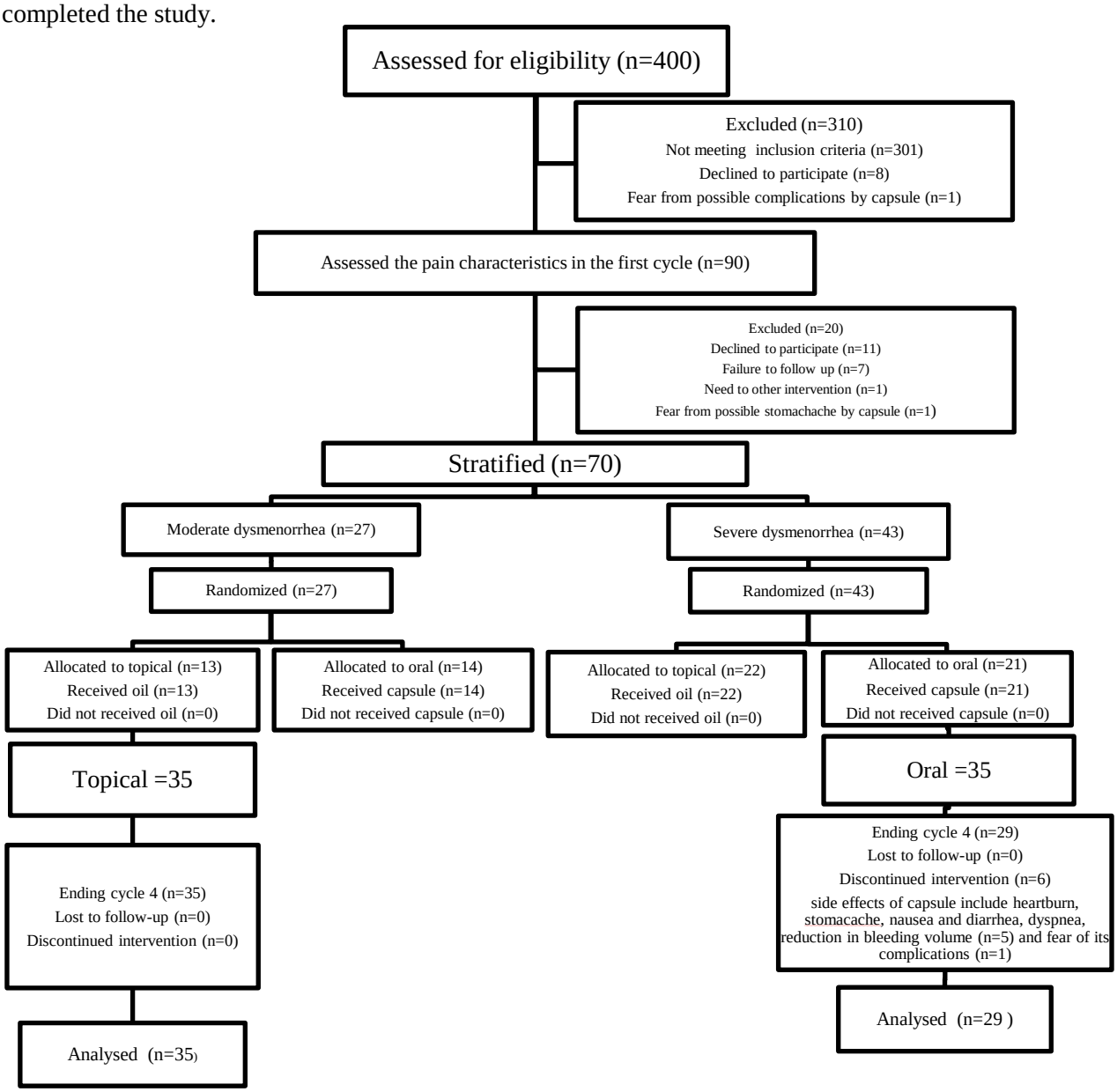

Figure 2. Distribution of participants

According to table 1, the demographic and baseline characteristics did not differ statistically between the two groups (p>0.05). According to table 2, a significant reduction was seen in the severity of pain in each oral (2.6 ± 3.4) and topical group (3 ± 3.2) (p<0.001). This reduction in pain severity was statistically similar between oral and topical groups (p>0.05).

There was a significant reduction in the duration of pain in both oral (14.5 ± 19.8) and topical groups (14.5 ± 20.1) (p<0.001). The reduction of pain duration was statistically similar between the two groups (p>0.05) (table 2).

Table 1. Demographic and baseline characteristics of participants

Variables	Topical Mean (SD)	Oral Mean (SD)	*p* value
Age (years)	23.1 (4)	22.9 (3.8)	0.8
BMI (kg/m^2)	21.6 (2.9)	22.8 (3.1)	0.1
Age of menarche (years)	13.1 (1.4)	13.3 (1)	0.4
Age at start of dysmenorrhea (years)	15.2 (2.4)	15.9 (2.8)	0.2
Duration of menstrual bleeding (days)	6.4 (1.5)	6.3 (1.1)	0.6
Interval of cycles (days)	28.4 (2.6)	28.7 (1.8)	0.6
Duration of exercise (minutes/week)	165.2 (110.1)	187.2 (74.5)	0.5

Although a significant reduction in mefenamic acid consumption was observed only in the oral group (0.5 ± 1.3) (p=0.006), but there was no significant difference in mefenamic acid consumption between oral and topical groups at the end of the study (p>0.05) (table 2).

In the moderate dysmenorrhea group, there was a significant reduction in the severity of pain in the topical group as compared with the oral group (p=0.04) (table 3).

In the severe dysmenorrhea group, the severity of pain did not differ statistically between the two groups (p=0.2) (table 3). According to table 3, there was no significant difference in the duration of pain between the oral and topical groups in moderate and severe dysmenorrhea (p=0.6).

According to table 3, there was no significant difference in mefenamic acid consumption between the oral and topical groups in moderate and severe dysmenorrhea (p=0.4).

There were no side effects, fear of oil complications, and drop-out in the topical group. Therefore, topical ginger oil was well-tolerated by the participants. In the oral group, three students withdrew from the study due to fear of complications; two of them left the study before starting the intervention.

Side effects were reported in 19 participants (54.2%) in the oral group, including headache (n=1, 2.8%), stomachache (n=7, 20%), heartburn (n=2, 5.7%), nausea (n=2, 5.7%), belching (n=2, 5.7%), diarrhea (n=4, 11.4%), itching (n=1, 2.8%), dyspnea (n=1, 2.8%), and reduced bleeding volume (n=1, 2.8%).

Table 2. Comparison of pain characteristics between the oral and topical groups without classification of moderate and severe dysmenorrhea.

Pain characteristics	Groups	Pre intervention		Post intervention					
				Intention to treat analysis		Per protocol analysis		Before-after changes	
		Mean (SD)	*p* value	Mean (SD)	*p* value	Mean (SD)	*p* value	Mean (SD)	*p* value
Severity of pain (VAS)	Topical	7.5 (2.2)	0.9	4.6 (3.1)	0.3	4.7 (3)	0.7	3 (3.2)	<0.001
	Oral	7.6 (2.4)		3.8 (3.2)		4.9 (2.8)		2.6 (3.4)	<0.001
Duration of pain (hours)	Topical	24 (18.1)	0.6	9.5 (10.1)	0.7	9.5(10.1)	0.7	14.5(20.1)	<0.001
	Oral	22.2(19.9)		8.7(11.5)		8.5 (11.9)		14.5(19.8)	<0.001
Mefenamic acid consumption (No.)	Topical	1.2 (1.6)	0.7	0.6 (1)	0.7	0.6 (1)	0.8	0.4 (1.6)	0.9
	Oral	1.1 (1)		0.6 (0.9)		0.7 (0.9)		0.5 (1.3)	0.006

Table 3. Comparison of pain characteristics between the oral and topical groups in moderate and severe dysmenorrhea with classification of moderate and severe dysmenorrhea.

Pain characteristics	Group	Sever dysmenorrhea				Moderate dysmenorrhea			
		Pre intervention	*p* value	Post intervention	*p* value	Pre intervention	*p* value	Post intervention	*p* value
		Mean (SD)		Mean (SD)		Mean (SD)		Mean (SD)	
Severity of pain (VAS)	Topical	8.9 (0.9)	0.5	5.4 (3.2)	0.2	5.9 (1.3)	0.4	3.5 (2.4)	0.04
	Oral	8.7 (1.9)		4.3 (2.9)		6.1 (1.2)		5.7 (2.4)	
Duration of pain (hours)	Topical	23.9 (17.8)	0.7	7.7 (7)	0.6	24.2 (19.5)	0.9	12.5 (13.6)	0.6
	Oral	20.5 (12.3)		7 (7.8)		24.8 (28.2)		11.4 (15.5)	
Mefenamic acid consumption(No.)	Topical	1.5 (1.5)	0.6	0.8 (1.1)	0.4	0.7 (1.6)	0.2	0.4 (0.7)	0.4
	Oral	1.2 (1)		0.6 (1)		1 (1)		0.6 (0.7)	

Thus, oral ginger capsule was not well tolerated by the participants in contrast to topical ginger oil.

This was the first comparative study of the effect of two dosage forms on primary dysmenorrhea. Also, this study investigated the effect of the topical application of the oil form without massage on primary dysmenorrhea for the first time.

The results of the present study showed that ginger in both oral and topical forms had similar positive effects on decreasing the pain severity and duration of primary dysmenorrhea. The side effects of oral ginger were observed in more than half of the participants. Moreover, some participants left the study due to the fear of the complications of the capsule, while there were no side effects in the topical ginger oil group. Topical ginger oil was tolerated better than oral ginger by the participants.

Our results provided more evidence for the ITM perspective. According to the ITM, topical application of the oil form of medicines is one of the most effective ways of their application in primary dysmenorrhea [13,14]. Thus, uncomplicated positive effects of topical ginger oil are in line ITM. On the other hand, palliative effect and facilitating the flow of menstrual blood of ginger in ITM perspective [13,15-17] could explain the effect of ginger on primary dysmenorrhea.

As for oral ginger, the results of this study are in accordance with all prior studies, indicating that oral ginger is effective on primary dysmenorrhea [27]. For instance, Kashefi *et al*. [20], Jenabi [21], Rahnama *et al*. [12,18], Ozgoli *et al*. [19], Dawood-Abadi *et al*. [28] and Shirvani *et al* [29] reported that oral ginger reduced the severity of dysmenorrhea. Studies by Rahnama *et al*. in 2010 and 2012 compared ginger capsule with placebo in 78 and 120 students with primary dysmenorrhea, respectively and showed oral ginger capsule was more effective than placebo [12,18]. In 2012, Rahnama *et al*. found that the effect of 500 mg ginger powder three times a day starting from two days before through the first three days of bleeding on reducing the pain severity was similar to its administration on the first three days of bleeding, but taking ginger capsule from two days before menstrual bleeding was more effective on decreasing the pain duration [12].

As for ginger oil, no study has evaluated the effect of the topical application of ginger macerated oil on primary dysmenorrhea. All previous studies have explained the effect of ginger essential oil in combination with massage on primary dysmenorrhea. For example, Rizk reported that aromatherapy abdominal massage with ginger essential oil reduced pain severity without any changes on pain duration [22], while our findings showed that topical application of ginger oil decreased both severity and duration of pain. Hur *et al.* [24] and kim *et al.* [23] stated that aromatherapy abdominal massage with an essential oil containing ginger and other plants reduced pain severity. However, the main factor for pain relief in Rizk [22], Hur *et al.* [24] and kim *et al.* studies [23] was unclear to be massage, essential oil, or both. Also, in the studies conducted by Hur *et al.* [24] and kim *et al.* [23], the main essential oil that caused pain relief was unclear. On the other hand, aromatherapy abdominal massage in the study by Kim *et al*.

showed 3.8% adverse effects while there were no side effects in the present study [28]. This difference may be due to different methods of oil preparation or consumption.

Previous investigations have shown the most compelling theory in dysmenorrheal mechanism is an increase in prostaglandin synthesis in the uterine [19,20]. On the other hand, Grzanna *et al.* stated that ginger was a dual suppressor of prostaglandin and leukotriene biosynthesis through inhibition of cyclooxygenase-1,2 and 5-lipoxygenase, respectively. Therefore, ginger and NSAIDs were similar in suppressing prostaglandins but different in suppressing leukotriene. Thus, ginger could have the same therapeutic effects with fewer complications than NSAIDs [30], which has also been observed in the previous studies [19, 29, 31]. For example, Ozgoli *et al.* divided 150 students with primary dysmenorrhea into three groups receiving 250 mg ginger, 250 mg mefenamic acid, and 400 mg ibuprofen [19] and Shirvani *et al.* divided 122 students with primary dysmenorrhea into two groups of 250 mg ginger and mefenamic acid [29]. Both of them showed that ginger had the same effect as NSAIDs on reducing dysmenorrheal pain [19,29].

The results of this study showed topical ginger macerated oil and oral ginger capsule had similar positive effects on reducing the severity and duration of primary dysmenorrhea. Since ginger oil in addition to pain relief was safe and well tolerated, topical ginger oil could be a better choice than oral ginger in the treatment of primary dysmenorrhea. On the other hand, the superiority of topical oil is in line with ITM that suggests topical oil is the best form of medication in pain relief of primary dysmenorrhea.

It is recommended to conduct further studies with larger sample sizes to determine more differences between topical and oral ginger in primary dysmenorrhea. Other studies are also warranted to evaluate the efficacy of ginger macerated oil in other menstrual symptoms.

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Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the content of the paper.

References

[1] Grandi G, Ferrari S, Xholli A, Cannoletta M, Palma F, Romani C, Volpe A, Cagnacci A. Prevalence of menstrual pain in young women: what is dysmenorrhea? *J pain Res*. 2012; 5(1): 169-174.

[2] Lefebvre G, Pinsonneault O, Antao V, Black A, Burnett M, Feldman K, Lea R, Robert M. Primary dysmenorrhea consensus guideline. *J Obstet Gynaecol Can*. 2005; 27(12): 1117-1146.

[3] Berek JS, Novak E. *Berek and Novak's Gynecology*. 15th ed. Philadelphia: Lippincott Williams & Wilkins, 2012.

[4] Harel Z. Dysmenorrhea in adolescents and young adults: an update on pharmacological treatments and management strategies. *Expert Opin Pharmacother*. 2012; 13(15): 2157-2170.

[5] Dmitrovic R, Kunselman AR, Legro RS. Continuous compared with cyclic oral contraceptives for the treatment of primary dysmenorrhea: a randomized controlled trial. *Obstet Gynecol*. 2012; 119(6): 1143-1150.

[6] Sultan C, Gaspari L, Paris F. Adolescent dysmenorrhea. *Endocr Dev*. 2012; 22: 171-180.

[7] Panahandeh Z, Pakzad Z, Ashouri R. Survey the prevalence, knowledge and practice of Guilan university students about

dysmenorrhea. *J Guilan Uni Med Sci*. 2008; 17(66): 87-94.

[8] Patel V, Tanksale V, Sahasrabhojanee M, Gupte S, Nevrekar P. The burden and determinants of dysmenorrhoea: a population-based survey of 2262 women in Goa, India. *Int J Obstet Gynecol*. 2006; 113(4): 453-463.

[9] Kor N, Jouybari L, Sanagoo A. The health believes and home remedies of the Turkmen people for dysmenorrhea. *Jentashapir J Health Res*. 2012; 2(4): 157-164.

[10] Zaidi SA, Khatoon K, Aslam K. Role of herbal medicine in ussuruttams (dysmenorrhoea). *J Acad Indus Res*. 2012; 1(3): 113-117.

[11] Marjoribanks J, Proctor M, Farquhar C, Derks RS. Nonsteroidal anti-inflammatory drugs for dysmenorrhoea. *Cochrane Database Syst Rev*. 2010; Article ID CD001751.

[12] Rahnama P, Montazeri A, Fallah Huseini H, Kianbakht S, Naseri M. Effect of *Zingiber officinale* R. rhizomes (ginger) on pain relief in primary dysmenorrhea: a placebo randomized trial. *BMC Complement Altern Med*. 2012; 12(1): 92-100.

[13] Ibn Nafis A. "*Al-Shamel fi al-sanaat al-tebbiat"*. Tehran: Research Institute for Islamic and Complementary Medicine, 2008.

[14] Chashti M. "*Exir-e aazam"*. Tehran: Research Institute for Islamic and Complementary Medicine, 2007.

[15] Aghili Khorasani M. "*Makhzan al-advie"*. Tehran: Research Institute for Islamic and Complementary Medicine, 2008.

[16] Sultana A, Lamatunoor S, Begum M, Qhuddsia Q. Management of Usr-i-Tamth (menstrual pain) in Unani (Greco-Islamic) Medicine. *J Evid-Based Complement Altern Med*. 2015; Article ID 2156587215623637.

[17] Moemen Tonekaboni M. "*Tohfat ol-moemenin*". Tehran: Shahid Beheshti University of Medical Sciences, 2007.

[18] Rahnama P, Fallah Huseini H, Mohammadi H, Modares M, Khajavi Shojaee K, Askari M, Mozayani P. The effects of *Zingiber officinal* R. on primary dysmenorrhea. *J Med Plants*. 2010; 4(36): 81-86.

[19] Ozgoli G, Goli M, Moattar F. Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in women with primary dysmenorrhea. *J Altern Complement Med*. 2009; 15(2): 129-132.

[20] Kashefi F, Khajehei M, Cher MT, Alavinia M, Asili J. Comparison of the effect of ginger and zinc sulfate on primary dysmenorrhea: a placebo-controlled randomized trial. *Pain Manag Nursing*. 2014; 15(4): 826-833.

[21] Jenabi E. The effect of ginger for relieving of primary dysmenorrhoea. *J Pak Med Assoc*. 2013; 63(1): 8-10.

[22] Rizk SA. Effect of aromatherapy abdominal massage using peppermint versus ginger oils on primary dysmenorrhea among adolescent girls. *J Am Sci*. 2013; 9(11): 497-505.

[23] Kim YJ, Lee MS, Yang YS, Hur M-H. Self-aromatherapy massage of the abdomen for the reduction of menstrual pain and anxiety during menstruation in nurses: A placebo-controlled clinical trial. *Eur J Integr Med*. 2011; 3(3): 165-168.

[24] Hur MH, Lee MS, Seong KY, Lee MK. Aromatherapy massage on the abdomen for alleviating menstrual pain in high school girls: a preliminary controlled clinical study. *Evid-Based Complement Altern Med*. 2012; Article ID 742421.

[25] Shirooye P, Mokaberinejad R, Ara L, Hamzeloo-Moghadam M. Volatile constituents of ginger oil prepared according to Iranian Traditional Medicine and conventional methods: a comparative study. *Afr J Tradit Complement Alternat Med*. 2016; 13(6): 68-73.

[26] Reed MD, Van Nostran W. Assessing pain intensity with the visual analog scale: a plea for uniformity. *J Clin Pharmacol*. 2014; 54(3): 241-244.

[27] Daily JW, Zhang X, Kim DS, Park S. Efficacy of ginger for alleviating the

symptoms of primary dysmenorrhea: a systematic review and meta-analysis of randomized clinical trials. *Pain Med*. 2015; 16(12): 2243-2255.

[28] Dawodabadi-Farahani M, Vakilian K, Seiedzade-Aghdam N. Comparison the effect of ginger and valerian on primary dysmenorrhe: triple blind randomized clinical trial. *Complement Med J*. 2013; 3(2): 66-75.

[29] Shirvani MA, Motahari-Tabari N, Alipour A. The effect of mefenamic acid and ginger on pain relief in primary dysmenorrhea: a randomized clinical trial. *Arch Gynecol Obstet*. 2015; 291(6): 1277-1281.

[30] Grzanna R, Lindmark L, Frondoza CG. Ginger-an herbal medicinal product with broad anti-inflammatory actions. *J Med Food*. 2005; 8(2): 125-132.

[31] Yu A. Complementary and alternative treatments for primary dysmenorrhea in adolescents. *Nurse practitioner*. 2014; 39(11): 1-12.