

Oral fennel (*Foeniculum vulgare*) drop effect on primary dysmenorrhea: Effectiveness of herbal drug

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ABSTRACT

Background: Primary dysmenorrhea refers to the occurrence of painful menstrual cramps of uterus and is considered as a gynecological complaint. The common treatment for this problem is medical therapy such as mefenamic acid [non-steroidal anti-inflammatory drugs (NSAIDs)] and oral contraceptive pills, both of which work by reducing myometrial activity. Fennel contains an antispasmodic and anethol agents and may be helpful for management of primary dysmenorrhea.

Material and Methods: The aim of this study was to evaluate the effects of oral fennel drop for treating primary dysmenorrhea. In this randomized clinical trial study, fennel drop 2% was compared with mefenamic acid for reducing pain of primary dysmenorrhea. Sixty college students suffering from primary dysmenorrhea were randomly assigned to two groups and followed up for two cycles. Statistical analysis was performed using SPSS version 16. $P < 0.05$ was considered to be statistically significant. Parametric and non-parametric tests were adopted.

Results: Comparison of pain intensity in the two groups showed that there was no significant difference in pain relief between the two groups. Comparison of bleeding severity in the study group before and after intervention was demonstrated from the first day to the fifth day (PV on first day, second day, third day, fourth day, and fifth day 0.948, 0.330, 0.508, 0.583, 0.890, respectively).

Conclusion: It seems that fennel can be effective in reducing the severity of dysmenorrhea, but it has an unpleasant taste in view of most of the volunteers.

Key words: Fennel, *Foeniculum vulgare*, herbal drug, primary dysmenorrhea

INTRODUCTION

Primary dysmenorrhea is one of the most common gynecological problems in women.^[1,2] More than 70% of Iranian females experience painful menstruation. Generally, in Iran, 74.5% of the teenage girls suffer from dysmenorrhea. Limitation in social activities has been estimated to be in 50% in this period, and poor school activity was reported in 12.0%.^[3] Between 50% and 80% of females reported some levels of discomfort associated with menstruation and 20% reported severe dysmenorrhea.^[4]

Primary dysmenorrhea is a condition associated with ovulatory cycles.^[1] It is due to myometrium contractions induced by prostaglandins in the second half of menstrual cycle. Many women experience primary dysmenorrhea in about 50% of their menstruation cycle.^[5] It imposes 600 million work-hours absenteeism and \$2 billion of financial loss in the USA. Many suggestions, available for cramps, practically guarantee that all females, troubled by

the symptoms, can find relief with safe and inexpensive treatments and fewer complications. Management of primary dysmenorrhea depends on the severity of the problem and individual woman's response to various treatments.^[6] The common treatment for dysmenorrhea is medical therapy such as non-steroidal anti-inflammatory drugs (NSAIDs) or oral contraceptive pills (OCP).^[5,7-9] These methods are not acceptable for long-term therapy due to their side effects.^[10] Dysmenorrhea lasts often for 8-72 h and is usually associated with the onset of blood flow.^[4] Unfortunately, all NSAIDs have potential gastrointestinal side effects. All women taking NSAIDs should be warned to report dark-colored stools because this may be an indication of gastrointestinal bleeding.^[11] Women with a history of aspirin sensitivity or an allergy should avoid all NSAIDs.^[10,12] *Foeniculum vulgare* contains an antispasmodic and anethol agents.^[13] For centuries, fennel fruits (*F. vulgare*) have been used as traditional herbal medicine in Europe and China.^[14] Fennel seeds were one of the acceptable herbal drugs of primary dysmenorrhea in Iran.^[15,16] *F. vulgare* is helpful in colic and has a slight pain reducing potentiality in dysmenorrhea. Many studies recommended more studies about fennel in primary dysmenorrhea.^[3,8,17,18] With regard to cyclic nature of primary dysmenorrhea, an effective, safe, and suitable method for remedies is obviously necessary. Fennel is an accepted herbal medication for treatment of

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dysmenorrhea in Iranian culture.^[3] In addition, bleeding severity after fennel therapy is controversial. It is important to find a safe and inexpensive way to decrease menstrual pain.^[3,6,18] Present study was performed to determine the efficacy, bleeding severity, and satisfaction with oral fennel as a herbal drug in comparison with mefenamic acid.

MATERIALS AND METHODS

In the present randomized parallel-group clinical trial, we compared fennel drop 2% and mefenamic acid (cap 250 mg) in the management of primary dysmenorrhea. The subjects were 60 female students from Roghaye female student dormitory of Shahid Sadoughi University of Medical Sciences. The study was approved by ethical committee of Shahid Sadoughi University of Medical Sciences. In addition, it was registered in Iranian Registration of Clinical trials (IRCT; Irct ID: IRCT201107096826N2). Informed consent was obtained from each subject. Primary dysmenorrhea is clarified as periodic, spasmodic pain in the absence of certain pelvic pathology in menstrual cycle. It usually begins in teenage years after the establishment of ovulation cycles. It is caused by myometrial activity ensuing in uterine ischemia. All students were visited by a gynecologist, and she confirmed the existence of primary dysmenorrhea with history taking and sonography, if necessary. Every 18-25-year-old student who suffered from primary dysmenorrhea with moderate to severe intensity was randomly assigned to each of the two study groups by use of a random number table. The questionnaire and checklist were delivered to the subjects through a face-to-face interview. Holistic checklist inquiring the onset of the pain before bleeding, any history of gynecological disorders, pain relief with NSAIDs, and any history of pelvic disorder was used to diagnose primary dysmenorrhea. Diagnosis of primary dysmenorrhea was based on a history with negative pelvic evaluation findings.^[6]

Medication was started at the beginning of the pain. The study group received 25 drops of Fennelin 2% every 6 h.^[18] Each 1 ml drop contains 15.5 mg Antole (Barijessence Herbal Drug Company, Kashan, Iran). If pain was not reduced until 2 h, the subject received mefenamic acid cap 250 mg every 6 h, if necessary.^[19] Control group received mefenamic acid cap 250 mg every 6 h, if necessary.

Inclusion criteria were 18-25 years of age, living in a dormitory, nonsmoker, no systemic disease, not taking OCP and other hormonal and herbal drugs prior to and during menstrual cycle, a regular menstruation condition, and suffering from moderate to severe primary dysmenorrhea.

Exclusion criteria were intolerance to fennel drop, no desire to take any of the treatments, and taking other NSAID (Non anti inflammatory drugs) through study.

Menstrual pain intensity was measured by Visual Analog Scale (VAS),^[14] by use of a horizontal 10-cm line with the statements “no pain at all” on the extreme left-hand end and “the worst possible pain” or “unbearable” on the extreme right-hand end. VAS is scored by measuring the distance from the end of the scale indicating absence of pain (or no distress or no pain relief) to the place marked by the patient.^[16] Students were followed up for two menstruation cycles. A checklist including VAS, number of pad consumptions, and the amount of drug usage from the day before and the first day until the fourth day of menstruation, and satisfaction with fennel drop was given to all the students to fill. For ethical considerations, the subjects in study group could take mefenamic acid cap if their pain was not reduced with fennel drop. Adequate drug was taken by participants of each group (fennel drop 2% and mefenamic acid cap 250 mg in study group and mefenamic acid cap 250 mg in control group). Study group was compared with the control group and by themselves before and after the new intervention.

Primary outcome was pain relief in study and control groups and also in the study group before and after invention. Time point was before menstruation and the first day until the fourth day of menstruation. Secondary outcome was menstruation bleeding in study and control groups and also in the study group before and after invention. The time point was the first day to the fifth day of menstruation, and method of measurement was pad count. Mean number of mefenamic cap 250 mg usage was compared in study and control groups. In addition, satisfaction with the drugs was asked for in the two groups at the end of the questionnaire.

Statistical analysis was performed using Statistical Analysis Software (SAS) version 16. A $P < 0.05$ was considered statistically significant. Parametric and non-parametric tests such as Friedman, Wilcoxon, and Mann-Whitney were adopted. Mean differences of continuous parametric data were analyzed with the use of Student's *t*-test and paired *t*-test.

RESULTS

Twenty-nine students in the study group and 30 students in the control group were followed up. One student discontinued the trial due to malodor and bad taste of fennel drop. The mean age in study and control groups was 21.07 ± 1.8 and 21.17 ± 1.6 , respectively. Menstruation cycle interval was 29.69 ± 4.14 and 28.8 ± 2.16 in the study and control groups, respectively, with no significant difference ($P = 0.84$). Duration of menstruation was 6.30 ± 1.2 and 6.5 ± 1.2 in the study and control groups, respectively, with no significant difference ($P = 0.96$). Twenty-three students (88.5%) in the study group and

25 (86.2%) in the control group were single. Comparisons of pain intensity in the two groups have been presented in Table 1. There were no significant differences in pain relief between the two groups ($PV = 0.85$).

Mann-Whitney analysis test was used to compare bleeding severity in the two groups. Comparison of bleeding severity in the two groups has been displayed in Table 2. According to the results of the analysis, there was no significant difference in bleeding severity in the study and control groups ($PV = 0.948$, $PV = 0.330$, $PV = 0.506$, $PV = 0.583$, and $PV = 0.890$ on first day, second day, third day, fourth day, and fifth day, respectively).

Comparison of pain intensity in the study group before and after intervention has been shown in Table 3. There was no significant difference in pain relief between two cycles ($PV = 0.948$, $PV = 0.330$, $PV = 0.508$, $PV = 0.583$, and $PV = 0.890$ on first day, second day, third day, fourth day, and fifth day, respectively). Comparison of bleeding severity in the study group before and after intervention has been demonstrated in Table 4. Wilcoxon signed test was used to compare bleeding severity in menstruation cycle, and although there was no significant difference between two menstruation cycles until the fourth day ($PV = 0.196$, $PV = 0.432$, $PV = 1.000$, and $PV = 1.000$ on first day, second day, third day, and fourth day, respectively), it was significant in the fifth day ($PV = 0.001$). Only one case had severe menstruation after taking fennel drop. Mean number of analgesic caps consumed was one and five in the study and control groups, respectively, and only four subjects in the study group took mefenamic acid cap 250 mg. Number of mefenamic acid caps 250 mg was significantly lower in the study group compared to the control group ($P < 0.05$).

Mean analgesic consumption in the study group before intervention was six and after intervention was one. After intervention, it was significantly lower ($P < 0.001$); just four subjects took mefenamic acid cap 250 mg during herbal medication.

Malodor and bad taste were reported as complications in the study group. Twenty students (70%) in the study group avoided trying this protocol because fennel essence had a bad taste and mefenamic was more comfortable to use.

DISCUSSION

It is important to find a safe and inexpensive way to decrease menstrual pain. Xiu-ying in a trial reported that acupuncture, compared to Chinese herbs, reduced menstrual symptom.^[20] Many researchers showed fish oil could reduce pain.^[21] In a systematic review, they reported herbal remedies can be used for dysmenorrhea,^[22] and

Table 1: Comparison of pain intensity in the two groups

Groups menses day	Test		Witness		PV
	Mean pain	SD	Mean pain	SD	
Before bleeding	2.6	3.9	2	2	0.421
First day	8.7	2.4	9.4	1.9	0.225
Second day	6.3	3.3	5.8	3.7	0.606
Third day	2.7	3.2	3.6	3.6	0.331
Fourth day	1.7	2.9	1.3	1.3	0.577

Table 2: Comparison of bleeding severity in the two groups

Menses day	Test		Witness		PV
	Mean	SD	Mean	SD	
First day	2.13	0.83	2.03	0.77	0.948
Second day	2.5	0.5	2.3	0.66	0.330
Third day	2.3	0.6	2.2	0.71	0.506
Fourth day	1.5	0.73	1.66	0.71	0.583
Fifth day	0.51	0.61	0.5	1.32	0.890

Table 3: Comparison of pain intensity in the test group before and after intervention

Menses day	Mean pain		Mean pain		PV
	Before	SD	After	SD	
First day	3.12	0.83	2.03	0.77	0.948
Second day	2.50	0.50	2.30	0.66	0.330
Third day	2.30	0.60	2.200	0.71	0.508
Fourth day	1.50	0.73	1.66	0.71	0.583
Fifth day	0.51	0.61	0.50	1.32	0.890

Table 4: Comparison of bleeding severity in the test group before and after intervention

Menses day	Reduced bleeding		Increased bleeding		Without change		PV
	No.	%	No.	%	No.	%	
First day	13	45	9	31	7	24	0.196
Second day	4	14	7	24	18	62	0.432
Third day	6	20	7	24	16	56	1.000
Fourth day	8	27	7	24	14	49	1.000
Fifth day	20	69	0	0	9	31	0.001

another study showed *F. vulgare* plant is an antispasmodic and can relieve menstruation pain.^[14,16,23]

Ostad in his investigation showed a decline in frequency of contractions induced by prostaglandin E2 (PGE2).^[11] Jahromi confirmed that fennel drop can be used as an efficient and safe herbal remedy to reduce pain in dysmenorrhea.^[19] Modaresnejad in her research found no significant statistical difference in pain between fennel and anti-inflammatory drugs on primary dysmenorrhea.^[8] Khorshidi also reported both

mefenamic acid caps and herbal drug were pain relievers in menstrual cycle.^[3] Jahromi, Modaresnejad, and Khorshidi corroborated this part of our study. Khodakrami showed both mefenamic acid and herbal drugs effectively relieved dysmenorrhea pain. She suggested more clinical trials are needed to investigate the efficacy of fennel.^[17] For ethical considerations, the study group could also take mefenamic acid cap 250 mg if their pain did not reduce with fennel drop. Fortunately, only four cases in the study group took mefenamic acid cap 250 mg together with herbal medication.

The second aim was to investigate the effect on severity of menstruation bleeding in each group. Torkzahrani in her investigation showed that there was no significant difference in bleeding severity in fennel users.^[6] She showed the essence of fennel could be used as a safe and effective herbal drug for primary dysmenorrhea. Namvar Jahromi reported a case who had severe bleeding after using fennel.^[18] Khorshidi's results confirmed that the total amount of bleeding in treatment groups significantly increased.^[3] In our study, only on the fifth day of menstruation, the severity of menstruation bleeding significantly increased in the study and control groups ($PV = 0.001$) and only one case had severe menstruation after taking fennel drop. Also, a comparison of bleeding severity in the study group before and after intervention showed that 45% of the subjects who had taken fennel had severe bleeding in their cycle, which is probably due to the effect of muscular relaxation of fennel.

Khorshidi reported no noticeable side effect in the two groups except for one subject with nausea due to mefenamic acid. Conversely in our study, many volunteers complained of some side effects such as nausea due to malodor and bad taste of fennel drop.^[3] Jahromi reported no complications in therapeutic dose of mefenamic acid cap, while five subjects left the study due to the odor of fennel.^[18] Although the researcher did not observe noticeable side effects in the two groups, 70% of the subjects in the study group did like to try this protocol once more. Although the fennel drop can be used for primary dysmenorrhea, its new generation in the form of tablets or capsules seems more suitable for use, compared to oral drop.

CONCLUSION

The present study showed that the efficacy of fennel drop 2% in pain relief in primary dysmenorrhea is comparable to the efficacy of common NSAIDs such as mefenamic acid cap. Investigators recommend that another product of fennel such as tab, cap, or fennel oil might be more acceptable than the essence. One subject had severe menstruation after

taking fennel drop. We suggest conducting more studies on the side effects of herbal medications such as fennel as well as menstruation pattern.

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