

# Comparative evaluation of the efficacy of herbal drugs (fennelin and vitagnus) and mefenamic acid in the treatment of primary dysmenorrhea

Fatemeh Zeraati<sup>1</sup>, Fatemeh Shobeiri<sup>2</sup>, Mansour Nazari<sup>3</sup>, Malihe Araghchian<sup>1</sup>, Reza Bekhradi<sup>4</sup>

## ABSTRACT

**Background:** Different therapeutic methods have been applied for the treatment of dysmenorrhea and the method with the lesser side effects is preferred. The aim of this study was to compare the effects of herbal products (fennelin and vitagnus) and mefenamic acid in the treatment of primary dysmenorrhea.

**Materials and Methods:** This double-blind clinical trial was carried out in 105 students with mild and moderate dysmenorrhea. The students were randomly divided into four groups which received the extracts of fennelin and vitagnus, mefenamic acid, and placebo, respectively. Severity of pain was detected by the Visual Analog Scale (VAS) during one cycle before and two cycles after the intervention. Data were analyzed by SPSS version 16 and ( $P < 0.05$  was considered significant).

**Results:** Demographic characteristics of the students were similar in the four groups. There was no significant difference in the mean of severity of dysmenorrhea during one cycle before the intervention between the four groups, but the difference was significant during two cycles after the intervention. Fennelin had similar effects as vitagnus on dysmenorrhea. Mefenamic acid had less effect than both the drugs ( $P < 0.05$ ).

**Conclusion:** Fennelin and vitagnus had higher effect than mefenamic acid. Use of these products is suggested for dysmenorrhea.

**Key words:** Dysmenorrhea, fennelin, Iran, vitagnus

## INTRODUCTION

Dysmenorrhea occurs in around 50% of women with regular menstruation.<sup>[1,2]</sup> This induces disability in more than 10% of women in their daily activities.<sup>[3]</sup> Prevalence of dysmenorrhea in adolescents is over 85%<sup>[4]</sup> but the prevalence rates have been reported to be as high as 90% in women aged 18-45 years<sup>[5]</sup> The prevalence of dysmenorrhea worldwide is similar to that in the US, with the rates ranging from 15.8 to 89.5% and with higher prevalence rates reported in adolescent populations.<sup>[6-11]</sup>

Nonsteroidal anti-inflammatory drugs (NSAIDs) form the basis of treatment and contraceptive pills are also used in treatment.<sup>[12]</sup> About 10% of patients do not respond to these treatments.

NSAIDs inhibit prostaglandin synthesis, and so, they are important in the treatment of this disease. The effectiveness of these agents has been consistently confirmed, with response rates exceeding 75% in most studies.<sup>[13]</sup>

Since the effective chemical drugs for primary dysmenorrhea, such as mefenamic acid, acetaminophen, ibuprofen, etc., have side effects including dizziness, nausea, diarrhea, digestive disorders, etc., replacing these drugs with herbal ones which have less side effects can be effective. In this case, many researches have been done. According to these studies, those plants with few side effects are easily accepted among people. Two herbal drops known as vitagnus and fennelin are available in the market. Fennelin contains *Foeniculum vulgare* extract. The effects of this plant extract on pain, inflammation, and dysmenorrhea were studied by different researchers.<sup>[14-17]</sup> Vitagnus contains *Vitex agnus* extract and there are different studies about its effects on premenstrual syndrome (PMS).<sup>[18-20]</sup> There is no comparative study about these drugs. Therefore, we decided to compare the effects of these herbal drugs on primary dysmenorrhea.

<sup>1</sup>Department of Pharmacology, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran, <sup>2</sup>Department of Midwifery, Research Center for Child and Maternity Care, Hamadan University of Medical Sciences, Hamadan, Iran, <sup>3</sup>Department of Medical Entomology, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran, <sup>4</sup>Department of Research and Development, The Head of Clinical Research Center of Barij Essence, Tehran, Iran

**Address for correspondence:** Associate Prof. Fatemeh Shobeiri, Research Center for Child and Maternity Care, Hamadan University of Medical Sciences, Hamadan, Iran.  
E-mail: fshobeiri@yahoo.com

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## MATERIALS AND METHODS

This study was a clinical trial carried out on female students of Hamadan Medical School, with primary dysmenorrhea assayed by (Visual Analog Scale (VAS) method. The exclusion criteria were: (1) presence of any systemic disease such as liver, kidney, thyroid, or coagulation disease; (2) hypersensitivity to drug; (3) use of analgesic drugs during the study; and (4) use of oral contraceptive pills (OCP) or intrauterine device (IUD).

### Drugs

One hundred and five study participants were divided into four groups. Group 1 received fennelin, 30 drops every 4 h, 1 day before the start of the cycle until the third day; Group 2 received vitagnus, 40 drops once a day in the morning, 1 day before the start of the cycle until the third day; Group 3 received mefenamic acid capsules 250 mg every 4 h, 1 day before the start of the cycle until the third day; and Group 4 received placebo, 30 drops every 4 h, 1 day before the start of the cycle until the third day. Pain was measured and compared by means of VAS.

Each group was assayed for three cycles, one without any drugs and then two cycles with them.

### Statistical analysis

Statistical analysis was carried out using SPSS version 16. Analysis of variance (ANOVA) was used to compare pain between different groups.

## RESULTS

A total of 105 female students aged 18-25 years who complained of primary dysmenorrhea were contacted. Demographic characteristics of research groups are presented in Table 1. As specified in the table, the subjects of the study groups were similar in age, number of days of menstruation, age at first menstruation, and dysmenorrhea interval, and the differences were not statistically significant. But the age at menarche was significantly different ( $P < 0.05$ ).

**Table 1: Mean and SD of some demographic characteristics of the studied units**

Characteristic	Drug				P value (ANOVA)
	Placebo (n=25)	Fennelin (n=25)	Vitagnus (n=25)	Mefenamic acid (n=30)	
Age, years	21.60±2.59	21.60±2.59	20.88±1.23	22.20±3.72	0.08
Menarche age, years	13.92±1.15	13.92±1.15	13.44±0.82	13.17±1.23	0.02
Duration of menstrual cycles	6.24±1.66	6.24±1.66	7.04±1.27	6.17±1.41	0.16
Interval of menstrual cycles	27.36±3.63	27.36±3.63	27.28±7.62	27.03±3.81	0.19
Early age of dysmenorrhea	16.16±1.81	16.16±1.81	15.24±1.98	15.50±2.71	0.17

ANOVA: Analysis of variance, SD: Standard deviation

Family history of dysmenorrhea, drug use during menstruation, history of exercise, and disruption in the daily chores were not significantly different.

In this study, pain intensity was evaluated within a cycle (zero cycle) before treatment with oral drops, mefenamic acid, and placebo drops, and the mean pain intensity of the four groups was not significantly different at the end of the cycle; but after the intervention (drugs), this difference was significant ( $P < 0.05$ ) at the end of the first and second cycles [Table 2].

## DISCUSSION

Dysmenorrhea and PMS are the common problems occurring in women during childbearing age. Many studies have been conducted on finding the best treatment for these conditions. Most researches have proved the positive effects of different drugs. Administration of NSAIDs is the most commonly used treatment for dysmenorrhea. NSAIDs decrease the menstrual pain by decreasing intrauterine pressure and lowering prostaglandin F<sub>2</sub> (PGF<sub>2</sub>)-alpha levels in menstrual fluid.<sup>[21-23]</sup> Khodakrami *et al.* examined the effect of combination of three Iranian herbal drugs in the treatment

**Table 2: Mean and SD of severity of dysmenorrhea (menstrual cycle zero, one, and two) in the groups of study according to the type of drug**

Group drug pain severity	M±SD			
	Fennelin	Vitagnus	Mefenamic acid	Placebo
The zero cycle (no drug)	1.9±5.2	1.5±5.8	1.9±5.6	1.4±5.1
The first cycle (with drugs)	2.5±1.3*	4.2±1.3*	4.1±1.8*	0.4±5.0
The second cycle (with drugs)	1.3± 2.2*	1.7±3.2	1.7±3.6*	1.3±4.1
Statistical analysis	F=8.35 P <sup>1</sup> =0.0 P <sup>2</sup> =0.001 P <sup>3</sup> =0.0	F=2.70 P <sup>1</sup> =0.04 P <sup>2</sup> =0.001 P <sup>3</sup> =0.001	F=7.16 P <sup>1</sup> =0.001 P <sup>2</sup> =0.001	F=1.39 P=0.07

\* $P < 0.05$ , P<sup>1</sup>: Comparison between three cycles and placebo; P<sup>2</sup>: Comparison between the first and second cycles; P<sup>3</sup>: Comparison between mefenamic acid and the herbal drug, SD: Standard deviation, M: Mean

of primary dysmenorrhea. The effects of saffron, celery seed, and anise (SCA) extract were compared with those of mefenamic acid and placebo. The authors showed that both SCA and mefenamic acid have adequate analgesic effects on dysmenorrhea. The SCA was found to be more effective than mefenamic acid for severe pain relief in dysmenorrhea.<sup>[24]</sup>

Nazarpoor *et al.* conducted a comparative study between fennelin and mefenamic acid in primary dysmenorrhea. Fennelin showed an effectsimilar to that of mefenamic acid.<sup>[18]</sup> In other studies, similar effects of vitagnus and fennelin were reported primary dysmenorrhea.<sup>[25,26]</sup>

In this study, the pain intensity before treatment with herbal oral drops and mefenamic acid capsules and placebo drops in one cycle (zero cycle) was studied. Average pain intensity in the three groups was not significantly different at the end of the zero cycle; but at the end of the first and second cycles of the intervention (drugs), this difference was significant. The study results showed that both drugs were able to reduce pain during treatment. The effects of the two herbal drugs were the same but higher than that of mefenamic acid. The average pain intensity in both herbal drug groups was reduced not only at the end of the first prescription medication but also at the end of the second month after treatment.

In another study, Shahhosaini *et al.* studied the effect of vitagnus on dysmenorrhea and found that the maximum effect was induced at the end of the third cycle.<sup>[27]</sup> No side effects of the herb were reported in this study.

## CONCLUSION

Treatment with herbal drops vitagnus, fennelin, and mefenamic acid capsule could reduce dysmenorrheal pain, and the effects of vitagnus and fennelin were higher than that of mefenamic acid. Thus, these herbal medicines are safe and effective for use in dysmenorrhea.

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