ORIGINAL ARTICLE

The impact of a novel herbal Shirazi Thymus Vulgaris on primary dysmenorrhea in comparison to the classical chemical Ibuprofen

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Objective: Primary dysmenorrhea is defined as painful cramps during menstruation with no pelvic pathology. Due to the adverse effects of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are considered as the most common pharmacological treatment for this disorder. The present study was conducted to assess the impact of Shirazi Thymus Vulgaris compared to that of Ibuprofen on primary dysmenorrhea. **Materials and Methods:** A randomized, single-blind clinical trial was conducted amongst 120 female students ofIlam University of Medical Sciences, aged 18-25 years who suffered from primary dysmenorrhea. The participants were randomly divided into two groups; one received the herbal and the other classical treatments. The herbal group received 5 ml of the Shirazi Thymus Vulgaris medication that commercially called BronchoT.D, orally four times a day. The classic group received Ibuprofen orally three times a day. A visual analogue scale (VAS) was used to record pain severity. **Results:** Pain severity was reduced in both herbal and classic groups with no significant differences. Pain duration at the first and second month of treatment was also similar between two groups.**Conclusions:** Shirazi Thymus Vulgaris decreased dysmenorrhea symptoms, which might be attributed to its antispasmodic effects. The herbal Shirazi Thymus Vulgaris can be recommended as an effective medication fortreatment of the primary dysmenorrhea disorder.

Key words: Ibuprofen, primary dysmenorrheal, ShiraziThymus Vulgaris

INTRODUCTION

Primary dysmenorrhea is a gynecological condition characterized by severe uterinepain during menstruation with a prevalence rateranging between 25% and 90%,[1] inthe absence ofpelvicpathology.[2] It is very common during the teenage years after the menarche and less often in women after the age of 20-25 years.The main symptoms are pain, nausea, vomiting, cramps, diarrhea, headache and syncope, which appear to be associated with menstruation with no any organic or pathological cause.[3] Current evidences suggest that molecular compounds called prostaglandins are released during menstruation due to endometrial cells destruction.[4]PGE2 stimulates uterine contractions, cervical narrowing and increases vasopressin release, which leads to ischemia and pain.[5]Symptoms are frequently associated with socioeconomic difficulties such as loosing timeand absence of school or work.[6] Despite the frequency and scores of dysmenorrhea, most women often do not seek medical treatment.[7] The common treatments for dysmenorrhea are non-steroidal anti-inflammatory drugs (NSAIDs) and oral contraceptive pills, both of which work by reducing uterine contractions.[8] Due to the possible side effects of chemical drugs, many consumers are now attempting alternatives traditional or herbal treatments. There is evidences confirming that the nutritional intake and metabolism may play an important role in the cause and treatment of menstrual disorders.[9] Nowadays using of theherbs in treatment of theprimary dysmenorrhea is increasing worldwide. [10]Thyme with broncholytic and secretomotoric effectson beta[11] receptors is an essential element of Shirazi Thymus Vulgaris that has already been used to reducethepain severity of menstrual disorders,[10] probably due to thymol and carvacrol components,[11] and its effects on smooth muscles of the trachea and ileum.[12] Also the effect of Thymus vulgaris on induced spasms in guinea-pig trachea has been investigated.[13] The present clinical trial study aimed to compare the impact of the Shirazi Thymus Vulgaris as an herbal medication and the Ibuprofen as a classic medication in treatment ofprimary dysmenorrhea.

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MATERIALS AND METHODS

A written informed consent form was taken from each participant prior to the enrolment to the study.Sample size was computed using α=5% and absolute error equal to 0.22[10] for correlation between medication and pain with Acceptable Absolute Precision Formula (AAPF). As the medication is licensed under the pharmacological regulations applied by the Iranian Pharmacopeia there is no side effectsis mentioned for this medication at the ordered doses.[10]A P value of 0.05 was considered statistically significant. Data were analyzed using *t*-test Chi-square test, Mann-Whitney U test, and *t*-test. A randomized, single-blind clinical trial (IRCT201105236575N1) was conducted amongst 120 single students aged 18-25 years who suffered from the primary dysmenorrhea at the Ilam University of Medical Sciences.

A check listwas used to collect the demographic data, menstrual history, smoking, diet, exercise and past medical and reproductive histories. The primary outcome was intensity of menstrual pain, which was determined by the visual analogue scale (VAS) to record pain severity (0=no pain, 10=unbearable pain). Participants who were single, suffered from primary dysmenorrheal, accommodated at the campus of Ilam University of Medical Sciences and had no pathological disorders were included in this study.

The eligible participants fulfilled the self-completed questioner and the scale form and were visited physically by a licensed gynecologist before randomization. Randomization was determined on a 1:1 basis using random number tables.

Stratification was done according to the scores of the pain (mild: 1-3; moderate: 4-7; severe: 8-10). The extent of pain was evaluated using the Cox Menstrual Symptom Scale (CMSS), (having no pain ≤ 0, for ≥ 0.5 hours ≤ 1, for 0.5 – 1 hours ≤ 2, for several hours ≤ 3 and several days ≤ 4). Each participant was randomly assigned to the herbal treatment (Shirazi Thymus Vulgaris), or the classic treatment (anti-PG drug Ibuprofen), ending with 60 participants in each group equally.

According to the Iranian pharmacopoeia, product of bronco-TD, each 100 ml containing 25 mgZatariaMultiflora, Oil Thymol and Carvacrol was alternatively used in the herbal treatment for standardization. Therefore, the first herbal group received 5 ml of the Shirazi Thymus Vulgaris which, commercially named BronchoT.D[10] and is one of the formulateddrug used by the Iranian pharmacopeia and according to the results of other studies,[10] orally four times daily until the pain score reached less than 3 (mild score). The classic group received Ibuprofen; three tablets (400mg) orally three times a day.The participants were permitted to take another drug that they usually took for their pain relief, in addition to the allocated treatment in case of continued pain. However, at the end of the trial, these participants were excluded in data analysis. Changes in the scores and the pain duration of clinical trial participants were compared at the first and second months in both groups.

Statistical comparisons were determined using the Mann-Whitney U test, unpaired *t*-test, and within-group comparisons were analyzed by paired t test or Wilcox on matched pairs rank sum test for paired data as appropriate. SPSS software Package 16 was used to analyze the data of this project.

This study was undertaken with the approval of the Ethical Committee of the Ilam University of Medical Sciences. The participation in the study was voluntary and the participants were free to withdraw from the study whenever they wished.An informed consent was obtained from all participants before the enrolment to the study.

RESULTS

There was no significant differences between the two groups in terms of characteristics studied at randomization. The symptoms reported during menstruation were as follows: all the participants showed uterus cramps among which those with low back pain were (44.1%), fatigue (22.6%), nausea (12.9%), headache (11.8%), diarrhea (7.5%) and vomiting (1.1%), respectively. All subjects evaluated for tow cycles. About 3 hours after intervention at the first day of menstruation the mean of pain severity amongst the herbal group was decreased from 7.48±0.69 to 5.37±1.59 while among the classical group it was lowered from 7.15±0.78 to 5.31±0.95, respectively using the given dose (explained at method section).

There was no statistically significant decrease in pain score and pain duration in the women who received classic treatment compared to those in herbal group.

The comparison of pain duration between two groups in the first month of intervention. In the second day of intervention, 32.3% of participants in the herbal group and 24.8% in the classic group had mild score of pain and therefore did not ask for more interventions. However, only 1.1% of participants in both groups had a severe pain score. There was no significant difference in pain score between groups at the second month of intervention (P<0.54). Pain duration at second month of treatment was similar between groups (P<0.62).

DISCUSSION

Researches have already identified the over-production of uterine prostaglandins such as prostaglandins F2α and E2 as

a contributing factor to primary dysmenorrhoea. These trials confirmsthat NSAIDs inhibit the cyclooxygenase enzymes leading to inhibit the production of prostaglandins.[14] In the present study, both herbal and classic treatments had equivalently reduced the severity and the duration of primary dysmenorrhea. The effects of Zatariamultiflord as an herbal treatment can be attributed to the reduction of PG synthesis by its acting as an antispasmodic and anti-PG. Marjoribanks *et al*.[2004] in a review study, evaluated 63 individuals in a randomized controlled trial in women with primary dysmenorrhea and found that NSAIDs were more effective than placebo for pain relief (OR 7.91; 95% CI 5.65–11.09), although overall adverse effects were also significantly more common among customers (OR 1.52; 95% CI 1.09–2.12),.[15] A recent research has evaluated the effects of Zatariamultiflora essential oil on primary dysmenorrhea in which participants were randomly divided into three groups: The first group received placebo, the second group received the essence of Zatariamultiflora 1% and the third group received the essence of Zatariamultiflora 2%.All participants evaluated for 3 cycles. Results showed that mean dysmenorrhea severity was decreased from 7.8±1.6 to 7.4 ±1.8 in placebo group, from 7.3±1.5 to 3.1±1.5 in Zatariamultiflora essential oil 1% group and from 7.5±1.7 to 2.6±1.4 in Zatariamultiflora essential oil 2% group, respectively. A significant difference was reported between two treated groups compared to the placebo group.[10]

In another randomized, double-blind trial; the effect of an Iranian herbal drug on the treatment of primary dysmenorrhea has been examined. The participants were randomly divided into three groups: herbal drug (a combination of Saffron, Celery seed, and Anise), Mefenamic acid, and placebo groups. After an intervention, pain scores was reduced significantly and pain duration scores was also decreased in the herbal group (P<0.001) as well as Mefenamic acid group (P<0.01) compared to the placebo group.[5] In another clinical trial which evaluated the effects of Valerian Officinal, the pain severity of dysmenorrhea was significantly reduced (P<0.001)after the intervention.[16]

CONCLUSION

These results suggest that Zatariamultiflord as an herbal treatment represents an effective treatment for primary dysmenorrhea. Further clinical trials are recommended to look at the possible side effects.

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