

The Effect of *Teucrium Polium* on the pain duration of Dysmenorrhea, The Placebo Controlled Randomized Clinical Trial

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Abstract

Primary dysmenorrhea is a prevalent problem and its effects decrease the quality of life in many women across the world. Due to the side-effects of synthetic drugs, there is an increasing trend toward herbal medicine. The aim of this study was to research the effect of *Teucrium Polium* compared to placebo on the pain duration of Dysmenorrhea. This triple-blind, randomized, clinical trial study was performed on 70 single female students between 20 and 30 years old educating in Shahid Beheshti University (Tehran, Iran) from October 2014 to February 2014. They were allocated randomly into two groups: In *Teucrium Polium* group (n=35) who took 250 mg of *Teucrium Polium* powder q6h for the first 3 days of menstruation for two cycles. The second group (pelacebo) (n=35) received 250 mg starch powder. The pain duration of Dysmenorrhea was determined by visual analog scale (VAS) and questionnaire related to the pain duration. Based on results, there were no differences between two groups for demographic or descriptive variables. Comprising the pain duration showed that the participants in *Teucrium Polium* groups had lower significant pain in the 1st and the 2nd months after the treatment ($P < 0.001$) but in pelacebo group, there was not any significant decrease in the pain duration. No side effects were reported in the *Teucrium Polium* and pelacebo groups. Results showed that *Teucrium Polium* can be effective in decreasing the pain duration in primary dysmenorrhea.

Keywords: *Teucrium Polium*, Pain Duration, Dysmenorrhea, Pelacebo

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Introduction

Dysmenorrhea refers to painful uterine contractions associated with spasmodic pain in the abdomen which occurs during menstrual bleeding [1, 2]. Primary dysmenorrhea is the main cause of work absenteeism and reduced quality of life [1]. The pain is not associated with a pelvic disorder in primary dysmenorrhea. However, it greatly occurs more in the young but may last until the fifth decade of life. Dysmenorrhea is caused by ischemia-associated uterine contractions and increases sensitivity in uterine nerves [3]. It also happens in terms of prostaglandins, vasopressin and leukotrienes in the endometrium [4].

It is reported that the prevalence of primary dysmenorrhea ranges from 16 to 90% in the reproductive ages [5]. Various ways have been recommended to treat the primary dysmenorrhea, such as yoga, massage, transcutaneous electrical nerve stimulation, vitamins, nutritional supplements and herbal medicine.

Prescribed medications include prostaglandin synthesis inhibitors and non-steroidal anti-inflammatory drugs (NSAIDs) to reduce the pain. Non-pharmaceutical treatments are acupuncture and surgery, of which some may have adverse effects or be contraindicated in certain groups of women [2, 5-7]

In recent years, there has been a growing interest in using medicinal plants to prevent and treat of several illnesses across the world, particularly in Iran due to satisfactory successes in treating many diseases and undesirable side effects of chemical drugs[8]. Traditional medicines, like herbal medicine, have been used for treatment of dysmenorrhea across the world, such as Fenugreek, Valeriana offic [9, 10]. *Teucrium Polium* (locally called as kalporeh in Khuzestan Province, Iran) is used traditionally as a remedy in treating headache, convulsion and dysmenorrhea and moreover, its hypoglycemic, hypolipidemic and anti-bacterial effects have been reported in recent studies. Additionally, it is also used traditionally to cure gastrointestinal disorders [11]. The present study was performed to compare the Effect of *Teucrium Polium* and pelacebo in the pain duration of Dysmenorrhea among students. The paper also considered the ongoing studies in the world in the field of traditional medicine and abundance of some plants mentioned as herbs with analgesic and anti-inflammatory effects among Iranian traditional medicines.

Material and Methods

Participants

This was a triple-blind, randomized, placebo controlled trial study, consisted of unmarried students living in a dormitory at Shahid Beheshti University (Tehran, Iran)



from October 2014 to February 2015 with moderate-to-severe dysmenorrhea experiences.

It was estimated that 70 participants were required to reach a statistical significance at 95% confidence interval. Randomly computer-generated numbers were employed to divide participants into two groups for taking *Teucrium Polium* (n=35) or placebo (n=35). Participants, researchers and statistic advisor were kept blinded in allocating treatment. Dysmenorrhea-related variables, including age, age of menarche, age of dysmenorrhea and BMI were the same in two groups. Other variables, such as underlying diseases (Diabetes, Chronic hypertension, Infectious diseases) which may be influenced by *Teucrium Polium* in such people were controlled by excluding those samples from the study. Students with irregular menstrual cycles, endometriosis, history of medication usage, experienced acute stress, and/or vaginal symptoms (burning, irritation, itching, or discharge) were excluded. It was supposed that people with allergy to *Teucrium Polium* or other plants or those who had used herbal drugs during the previous 3 months or had not used it properly should have been excluded. Although a case with allergy to *Teucrium Polium* and placebo was not found.

Procedures

Teucrium Polium (from one geographical region) was purchased from Barijesans Pharmaceuticals (Kashan, Iran). After the identification and the verification of *Teucrium Polium* samples in Pharmacogenosy Laboratory at the Faculty of Pharmacology of Shahid Beheshti University of Medical Sciences, the samples were ground down. *Teucrium Polium* powder was placed into capsules (250 mg) by an automated machine. The safety dose, based on the PDR (Herbal Medicine) book [12], was 250 mg for *Teucrium polium* and according to this comprehensive book, (There is in safety dose of this plant, effective content of chemical materials) The herbal capsules were belt according to standards of herbal medicine book, step by step, from first stage (obtaining of extract to safety amount and packaging).

Also the toxicity dose of plant on kidney and liver [13, 14] is caused by permanent usage therefore it does not happen to alternative use of the plant (3 days monthly in dysmenorrhea) [15]. Chemical composition of the plant included: cedrol, guaiol, lindool, beta pinene [11]. The placebo capsules included of potato starch. The capsules were the same in shape, color, and packaging. *Teucrium Polium* and placebo capsules were taken four times a day [For the first 3 days of menstruation]. The intervention continued for two consecutive menstrual cycles. The subjects were allowed to take NSAIDs such as ibuprofen and Acetaminophen, if required. However, they were asked to take these medications ≥ 1 hour after taking the given capsules by researcher and write down pain severity before consuming the sedative and they were excluded from the study.

Content and test-retest methods were employed to assess the validity and reliability before the intervention and during each treatment cycle, ($r = 0.85$) of the questionnaire. The following demographic data was collected: age, body mass index (BMI), educational level, occupation of the

parents, exercise program, and stressful factors in the past 6 months. A self-reported checklist was used for collecting data on the number of sedative drugs taken for dysmenorrhea and pain severity.

During the first three days of menstruation, the pain severity and pain duration was scored in each sample three times a day on a 10 cm visual analog scale (VAS) when samples felt the most pain in 8–13, 13–18, and 18–24 hrs. (Per 8 hour) and was classified as “mild” (score of 1–3), “moderate” (4–7), or “severe” (8–10) [6].

VAS validity has been established in many studies, in which it has a wide range of applications and is considered as one of the most useful and reliable measures for pain [6, 9, 16]. The imprint codes were recorded on a separate sheet for the capsules, drug intervention performed in the second and third menstruations.

Statistical analyses

SPSS ver20 (SPSS, Chicago, IL, USA) was used to analyze statistically. Descriptive data is presented as frequencies, mean values and standard deviations and t-test which are used for comparison of age, age of menarche and other variables between the two groups. The Repeated Measure test was employed to compare pain duration of dysmenorrhea among three menstrual cycles. The Mann-Whitney test was used for comparison of satisfaction in both groups. $P < 0.05$ was considered significant.

Ethical considerations

The study protocol was approved by the Research and Ethics Committee of International Branch, Shahid Beheshti University of Medical Sciences and registered in the Iranian Registry of Clinical Trials (Number IRCT2014120917501N1). Students were aware of the purpose and methods of the study and provided with written consent forms for participation.

Results

Pain duration at baseline had no significant differences between the groups. In the *Teucrium polium* group, pain duration reduced from 4.3 (7.0) (Day) at baseline to 1.4 (8.0) in the second cycle (Table 2), and it decreased from 3.9 (0.1) to 3.0 (0.8) in the placebo group (Table 3). Pain duration differed in each intervention cycle in the *Teucrium polium* groups compared with placebo group (Table 4). There was difference in pain duration between two groups (Figure 1). No side effect was reported in both groups of *Teucrium Polium* and placebo.

Table 1. Demographic characteristics of the participants.

| variation | T. polium** | Placebo** | P*(Independent t-test) |
|--------------------------------------|-------------|-----------|------------------------|
| Age (year) | 21(1.91) | 22 (1.1) | 0.136 |
| BMI(Kg/m2) | 20(2.87) | 20(1.3) | 0.861 |
| Age at menarche(year) | 13(1.39) | 13 (1.07) | 0.277 |
| Duration between menstrual (day) | 26(3.15) | 25 (2. 0) | 0.541 |
| Duration of menstrual(day) | 6(1.12) | 6(1.0 2) | 0.530 |
| Age at onset of dysmenorrheal (year) | 15(2.30) | 15 (2.41) | 0.418 |
| Duration of dysmenorrhea | 2(1.02) | 2(0. 01) | 0.744 |

**Mean values and standard deviations

Table 2. Comparison of the mean values and the standard deviations of Pain duration before and after the treatment in *Teucrium polium* group.

| Pain duration | mean ±SD (T. Polium) (day) |
|---------------------------------------|----------------------------|
| First cycle | 4.3 (0.7) |
| Second cycle | 1.9 (0.8) |
| Third cycle | 1.4 (0.8) |
| Test consequent (Independent Samples) | P=0.001 |

Table 3. Comparison of the mean values and the standard deviations of Pain duration before and after the treatment in placebo group.

| Pain duration | mean ±SD (placebo) (day) |
|---------------------------------------|--------------------------|
| First cycle | 3.9 (0.1) |
| Second cycle | 3.1 (0.1) |
| Third cycle | 3.0 (0.8) |
| Test consequent (Independent Samples) | P=0.36 |

Table 4. Comparison of the mean values and the standard deviations of Pain duration before and after the treatment in both groups.

| Pain duration | mean ±SD (day) |
|------------------------------------|---------------------------|
| First cycle | Teucrium polium 4.3 (7.0) |
| | placebo 3.9 (0.1) |
| Second cycle | Teucrium polium 1.9 (8.0) |
| | placebo 3.1 (0.1) |
| Third cycle | Teucrium polium 1.4 (8.0) |
| | placebo 3.0 (0.8) |
| Test consequent (Repeated Measure) | P=0.001 |

Discussion

This was the first report of a study on the effects of *Teucrium Polium* and on the alleviation of pain in primary dysmenorrhea.

Females with dysmenorrhea suffer from excessive production of endometrial prostaglandins[1]. It is seen that *Teucrium polium* (locally called 'kalpooreh') possesses therapeutic effects against diabetes, fungal infections, with analgesic and anti-inflammatory properties. It is also used traditionally as a remedy in treating headache, dysmenorrhea, convulsion and gastrointestinal disorders moreover its hypoglycemic, hypo lipid emic and antibacterial effects are reported in recent studies [11]. In our research, *Teucrium polium* is used for the first time to decrease the pain duration of dysmenorrhea in human.

Teucrium polium has an inflammatory action and it as herbs with analgesic and anti-inflammatory herb can remove contraction of smooth muscle. The chemical composition of the plant included: cedrol, guaïol, lindool, beta pinene and flavons and flavonoids [15]. This content can in condition of contraction of smooth muscle and inflammation remove all of painful condition.

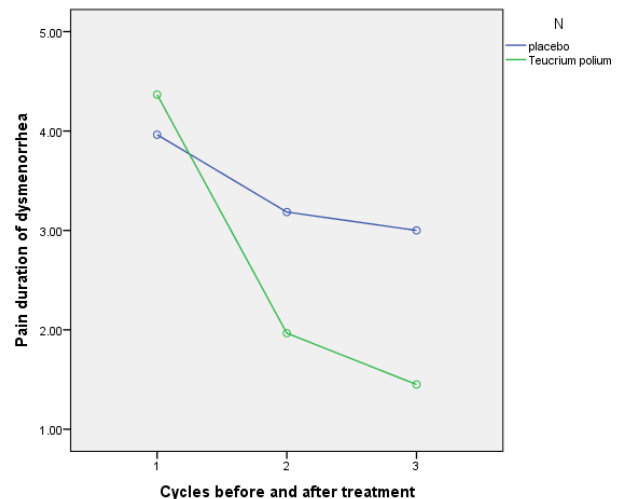


Figure 1. The difference of Pain duration of dysmenorrhea between both groups.

Garib naseri et al.,’s study indicated that *Teucrium polium* has an antispasmodic effect on virgin rat uterus [15]. In another study, Garib naseri et al., also recognized the anti-spasmodic effect of *Teucrium polium* on gastrointestinal system [11]. Allahtavakoli et al.,’s study stated that hydro-alcoholic extract of *Teucrium polium* had reductive effect on castor oil-induced diarrhea in male rat [17]. Antispasmodic effects of *Teucrium polium* were confirmed in animal models [11, 15, 17]. Phytochemical studies have showed that flavons and flavonoids are two major components in *Teucrium polium* extracts and causes the antispasmodic effects in *Teucrium polium* [11]. Study of Shahraki et al., demonstrated that *Teucrium polium* had analgesic effects similar to morphine [18] which may justify its effectiveness in reduction of pain duration in dysmenorrhea.

Our findings indicated that *Teucrium polium* significantly reduces pain duration of primary dysmenorrhea. Satarzade et al., observed positive effect of *Achillea millefolium* on duration of pain and menstrual bleeding, as our study [19]. In research of Younesy et al., significant effects of Fenugreek Seed on the severity and systemic symptoms of dysmenorrhea, observed [9]. Mirabe et al.,'s study indicated that Valeriana Officinalis had positive effects on the reduction of Dysmenorrhea as our study [10]. All of these studies demonstrate that natural remedies are effectiveness medicine, also without important side effects [20].

The effectiveness of *Teucrium polium* on pain duration of dysmenorrhea and its harmlessness have been observed in this study. *Teucrium polium* has effective power, in decreasing pain duration in subjects with primary dysmenorrhea. Further researches regarding the effects of *Teucrium polium* on other symptoms associated with primary dysmenorrhea, the efficacy and safety amount of this plant are needed.

Conclusion

The current study indicated that *Teucrium polium* decreases the pain duration of primary dysmenorrhea. Adverse effects were not reported for *Teucrium polium*, therefore, the herb can be administered safely to manage the condition.

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