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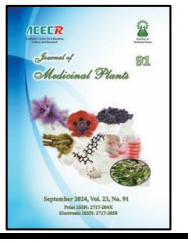

Research Article

The effect of a standardized polyherbal formulation for endometriosis-associated pain: A randomized double-blind placebo-controlled clinical trial

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ABSTRACT

Background: Dysmenorrhea, dyspareunia and endometriosis-associated pain are considered the main complications in young women with endometriosis. Proscur capsule contains several traditional herbal medicines that have shown anti-inflammatory, antioxidant, anti-androgenic, anti-estrogenic, pelvic pain reducing and analgesic effects in previous pre-clinical and clinical studies. **Objective:** This study aimed to investigate the clinical efficacy and safety of a standardized polyherbal formulation (proscur) for endometriosis-associated pain in young women with endometriosis. **Methods:** This study was a single-center, randomized, double-blinded, placebo-controlled, clinical trial. A total of 90 patients aged 20–45 years with endometriosis-associated pain were enrolled. Participants were randomly assigned to the proscur or placebo groups in a ratio of 1:1 and efficacy evaluation was conducted at day 30, 60 and 90. The participants orally administered proscur or placebo two times a day for 12 weeks. The study outcomes were measured based on a change of visual analogue scale (VAS) score and the short form endometriosis health profile questionnaire (EHP-5). **Results:** We observed an increase in pain relief in women who receive proscur. The serum measures of CA-125 declined in those who received proscur. Intervention was well tolerated, and no serious adverse events occurred. **Conclusions:** Our study showed that proscur relieved endometriosis-associated pain and CA-125 level with minimal side-effects after treatment. Therefore, proscur combined with standard medical therapy could provide more clinical benefits for patients with endometriosis-associated pain.

Abbreviations: OCs, oral contraceptives; GnRH, gonadotropin-releasing hormone; NSAIDs, non-steroidal anti-inflammatory drugs; CAM, complementary and alternative medicine; CONSORT, Consolidated Standards of Reporting Trials; VAS, visual analogue scale; EHP-5, endometriosis health profile questionnaire; SD, standard deviation; TNF-α, tumor necrosis factor alpha; VEGF, vascular endothelial growth factor; IL-6, interleukin-6

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1. Introduction

Endometriosis is a chronic and inflammatory gynecological disease characterized by the abnormal presence of endometrial epithelium and stroma outside the uterine cavity [1]. It causes multiple clinical manifestations, including chronic pelvic pain, dysmenorrhea, dyspareunia, nausea, dyschezia, dysuria, fatigue and infertility [1-3]. Among them, endometriosis- associated pain is one of the principal manifestations of endometriosis, which includes dysmenorrhea, dyspareunia, and non-menstrual chronic pelvic pain [4]. More than 170 million women worldwide and up to 10% of reproductive-age women are affected by endometriosis [5]. To diagnose endometriosis, measuring blood biomarker levels such as CA-125 and CA19-9 (important predictors for patients with endometriosis), and imaging methods such as transvaginal ultrasound and MRI are common non-invasive method [6, 7]. Furthermore, visual inspection at laparoscopy and histological confirmation of endometriosis are considered the gold standard tests for definitive diagnosis of disease [8]. Current treatment options include laparoscopic removal of lesions and medical therapies, including hormonal treatments that suppress ovarian hormone production and also pain relief agents [2, 9]. Pharmacological therapy is the first line of treatment, which focusing on the use of oral contraceptives (OCs), gonadotropin-releasing hormone (GnRH) agonists, non-steroidal anti-inflammatory drugs (NSAIDs) and other analgesics [10, 11]. However, medical treatments are often not prescribed long-term due to lack of success, high cost and various side effects, including abnormal uterine bleeding, headache, mood changes, loss of bone marrow density, hot flashes, gastric ulcers, cardiovascular events, and acute kidney injury [2, 12]. Although, laparoscopic ablation or excision of all visible lesions is beneficial in reducing pain and other endometriosis-related symptoms [13], surgery is probably related with peri- and postoperative complications, and the possibility of endometriosis recurrence is high [5, 14]. Nevertheless, endometriosis- associated pain can even continue after medical and/or surgical treatments [15]. Moreover, pain exposes patients to psychological comorbidities such as anxiety and depression and reduced quality of life, including a deterioration of sleep quality and lower activity levels [15, 16]. Given the limitations of standard treatments, there is growing interest in complementary and alternative (CAM) therapies for the management of endometriosis, including adjustment in diet [17], herbal medicines [14, 18], one of the CAM methods [19, 20], and acupuncture intervention [21]. Herbal medicines have a long history of use for various gynecological disorders, including endometriosis [3]. Several preclinical and clinical studies have confirmed the effectiveness of some medicinal plants and their secondary metabolites on endometriosis that they can be used for symptom relief [14].

Plant-based bioactive compounds such as phenolic compounds (flavonoids and phenolic acids) and some other plant-derived secondary metabolites are effective in endometriosis through different molecular mechanisms of action, including anti-inflammatory, anti-oxidant, anti-proliferative, apoptotic, antiangiogenesis, anti-invasive, immunomodulatory, and estrogen modulating activities [14, 17, 18]. Proscur capsule, a standardized pharmaceutical preparation, containing *Serenoa repens* (W.Bartram) Small (saw palmetto), *Zingiber officinale* Roscoe (ginger), *Camellia sinensis* (L.) Kuntze (green

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tea), *Urtica dioica* L. (nettle), *Rosmarinus officinalis* L. (rosemary) and *Cucurbita muschata* L. (pumpkin). Saw palmetto has anti-androgenic, anti-estrogenic, anti-inflammatory, and antioxidant properties [22]. Several studies have reported ginger, green tea, and rosemary have pelvic pain reducing properties and can reduce dysmenorrhea [23-25]. Furthermore, preclinical studies have shown that nettle, green tea, rosemary, and ginger can reduce the size of endometriosis lesions [26-29]. However, adequate data is not available on the clinical efficacy and safety of proscur for endometriosis-associated pain. Thus, the present study aimed to evaluate the efficacy and safety of proscur capsule on endometriosis-associated pelvic pain in young Iranian women compared to placebo.

2. Materials and Methods

2.1. Study design

This study was a randomized, double-blind, placebo controlled, clinical trial conducted from December 21, 2021 to June 20, 2022, in a tertiary care center. The study protocol was reviewed and approved by the Medical Ethics Committee of Iran University of Medical Sciences [Ethics committee reference number: IR.IUMS.REC.1400.783] and registered in the Iranian Registry of Clinical Trials [IRCT registration number: IRCT20211201053241N1]. The objectives and details of the study were clearly explained to all the included patients and they signed a written informed consent form before participation. For designing and reporting this trial the Consolidated Standards of Reporting Trials (CONSORT) has been used as frameworks of methodology.

2.2. Participants

The study population was mainly enrolled from women with pelvic pain associated with minimal/mild endometriosis. Patients who met these criteria were enrolled in this trial: (1) women aged 20 to 45 years; (2) definitive diagnosis of endometriosis; and (3) moderate to severe endometriosis-associated pain ($4 \leq VAS \leq 10$). Participants with any of the following criteria excluded from the study: (1) Pregnancy intention within three months; (2) breast feeding; (3) need for endometriosis surgery; and (4) unwillingness to take herbal medicine. Moreover, the main withdrawal criteria were as follows: (1) Usage of any hormonal agents and/or other alternative and complementary medications that might interact with the intervention during the study; (2) medication compliance less than 80 %; (3) occurrence of pregnancy; and (4) intolerable adverse events.

2.3. Randomization and blinding

The subjects who met the eligibility criteria randomly were divided into two groups using a random form. Randomization was done by block method and in a 1:1 constant allocation ratio using the "Random allocation software". The random list was prepared by a statistician, then sealed envelopes were used for allocation concealment. The type of intervention (A/B) was written inside sealed envelopes and the number of patients was written on the envelope. The envelopes were given to the person doing the sampling. Therefore, the patients and the person who is evaluated the symptoms and outcomes were blinded of the type of intervention.

2.4. Interventions

The patients in intervention group (n = 45) received one proscur capsule twice a day every morning and night with plenty of water for 12 weeks. The control group (n = 45) received placebo capsule based on the same regimen and

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duration (two times a day for 12 weeks). Both groups were allowed to use oral mefenamic acid (MFA) 250 mg capsule if they could not tolerate the pain during the study period. The number of MFA capsules consumed on average in the last month was recorded at the beginning of the study and on the 30th, 60th and 90th days of the study. Demographic characteristics, including age, marital status, occupation, menarche onset, endometriosis onset, level of CA-125, intensity of period pain, dyspareunia, and pelvic pain, and amount of painkiller consumption to control pain were recorded at the beginning of the study.

2.5. Preparation of the proscur and the placebo capsules

Proscur capsule was the product of Goldaru Herbal Pharmaceutical Company, Isfahan, IRAN. Each capsule contains *Serenoa repens* (W.Bartram) Small (saw palmetto) extract with *Zingiber officinale* Roscoe (ginger) extract, *Camellia sinensis* (L.) Kuntze (green tea), *Urtica dioica* L., *Rosmarinus officinalis* L. (rosemary) and *Cucurbita muschata* L. (pumpkin) seed oil. (The ingredients of each proscur capsule are as follows: saw palmetto: 160 mg, green tea: 50 mg, pumpkin seed oil: 48 mg, ginger: 40 mg, stinging nettle (ethanolic extract): 25 mg, stinging nettle (aqueous extract): 25 mg, rosemary: 5 mg and selenium 25 mcg). The proscur and placebo capsules were identical in shape, size, color, taste, and smell (placebo capsules contained starch). Both of them were prepared in the same place. Participants consecutively received treatment packages.

2.6. Sample size calculation

The sample size was calculated using two-mean comparison formula. When an α value of 0.05 with power 80 % and a 20 % dropout rate were considered and the effect size of 0.65 was assumed for dysmenorrhea, the sample size of each group was determined to be 45.

2.7. Study outcomes

The principal objective of this study was to determine the effect of proscur capsule on dysmenorrhea in patients with endometriosis. Pain intensity was measured using visual analogue scale (VAS) at the beginning of the study and on the 30th, 60th and 90th days of the study. The VAS is one of the most common, feasible, valid and reliable scales to measure the intensity or frequency of pain. It is a line that starts from zero and ends with the number 10, the amount of pain that a patient feels ranges across a continuum from none (0) to an extreme amount (10) of pain [30-32].

The short form endometriosis health profile questionnaire (EHP-5) was used to investigate the effect of endometriosis on the quality of life of the study participants. The EHP-5 consists of two parts. The first part contains 5 questions about the effect of endometriosis on walking, mood, self-image and social support and the second part contains 6 questions about the effect of endometriosis on doing personal work, child care, sexual intimacy, concern about infertility. Both parts include never, rarely, sometimes, often, and always answers that assess the severity of the problem in the previous 4 weeks (5 items, ranges 0-4). The patient must answer the 5 questions in the first part and the questions related to her condition (regarding marriage and having children) in the second part. Finally, the total score of 5 questions of the first part (core questionnaire) and 6 questions of the second part (modular questionnaire) is prepared a total score (range 0–100, from best to worst possible health status). This questionnaire was designed by Jones et al. [33-35] and its Persian version was validated by Goshtasebi et al. [36]. At the

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end of each month, the intensity of pain and the amount of painkiller consumption were recorded, and at the end of the third month, the EHP-5 questionnaire was completed again.

2.8. Adherence/patient safety

To check medication compliance, patients were asked to mark the medication consumption in a sheet at each appointment and provide it to the project manager at the end of each month to assess how the patient took each of her medications. Patients were asked to hand over all their empty medication cans. During the study, all patients were observed weekly for any adverse events.

2.9. Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences software (version 23, BM Corp., Armonk, N.Y., USA). Mean and standard deviation were used to describe quantitative data, and frequency percentage was used to describe qualitative data. After assessing the distribution of quantitative variables by Kolmogorov-Smirnov test, the Mann-Whitney U test was used to compare the intensity of pain and the amount of pain reduction between two groups. The qualitative data were compared with Chi-square or Fisher-exact test (where assumptions of Chi-square test did not exist) between groups. The changes in the pain intensity in each group during the study was evaluated with the Friedman test (a non-parametric equivalent for repeated measures ANOVA). P value was considered 0.05 to compare the percentage of pain reduction between two groups.

3. Results

Among a total of 145 patients with endometriosis-associated pain were investigated for eligibility, 90 patients were included in the study and 45 people were randomly assigned to each group. In the intervention group, three patients were excluded from the study due to heart burn and in the placebo group, two patients were excluded because of abdominal pain. Finally, 85 patients completed the study and were included in the analysis (43 patients in proscur group and 42 patients in the placebo group). A CONSORT flow diagram of the study is presented in Figure 1. Baseline demographic properties and general characteristics of the patients are demonstrated in Table 1.

The severity of dysmenorrhea, pelvic pain, dyspareunia and painkiller consumption in two groups at different times of the study are shown in Table 2.

At the end of the study, the percentage of reduction in the severity of dysmenorrhea, dyspareunia, pelvic pain and painkiller consumption in the intervention group was more than the placebo group. The amount of painkiller consumption showed a significant decrease in the intervention group after 3 months, while there was no significant change in the control group.

During the study, the level of CA-125 in the proscur group changed from 151.16 ± 79.7 to 52.6 ± 35.52 ($P < 0.001$) and in the control group, it went from 109 ± 47.35 to 97.31 ± 42.64 ($P < 0.001$). Although the amount of this antigen showed a significant decrease in both groups after 3 months, the percentage of decrease was 62.56 ± 17.3 % in the proscur group and 6.7 ± 7.69 % in the control group. However, the CA-125 in the proscur group decreased significantly more than the control group ($P < 0.001$).

The results of the EHP-5 questionnaire before and after the intervention in two groups are shown in Table 3.

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There is a significant difference between the two groups in terms of the EHP-5 scores after the intervention. In the intervention group, 11 people complained of the capsule being stuck in the esophagus and a burning sensation that got better with eating, and 4 people complained of stomachache. Abdominal pain was also reported in 2 patients in the placebo group.

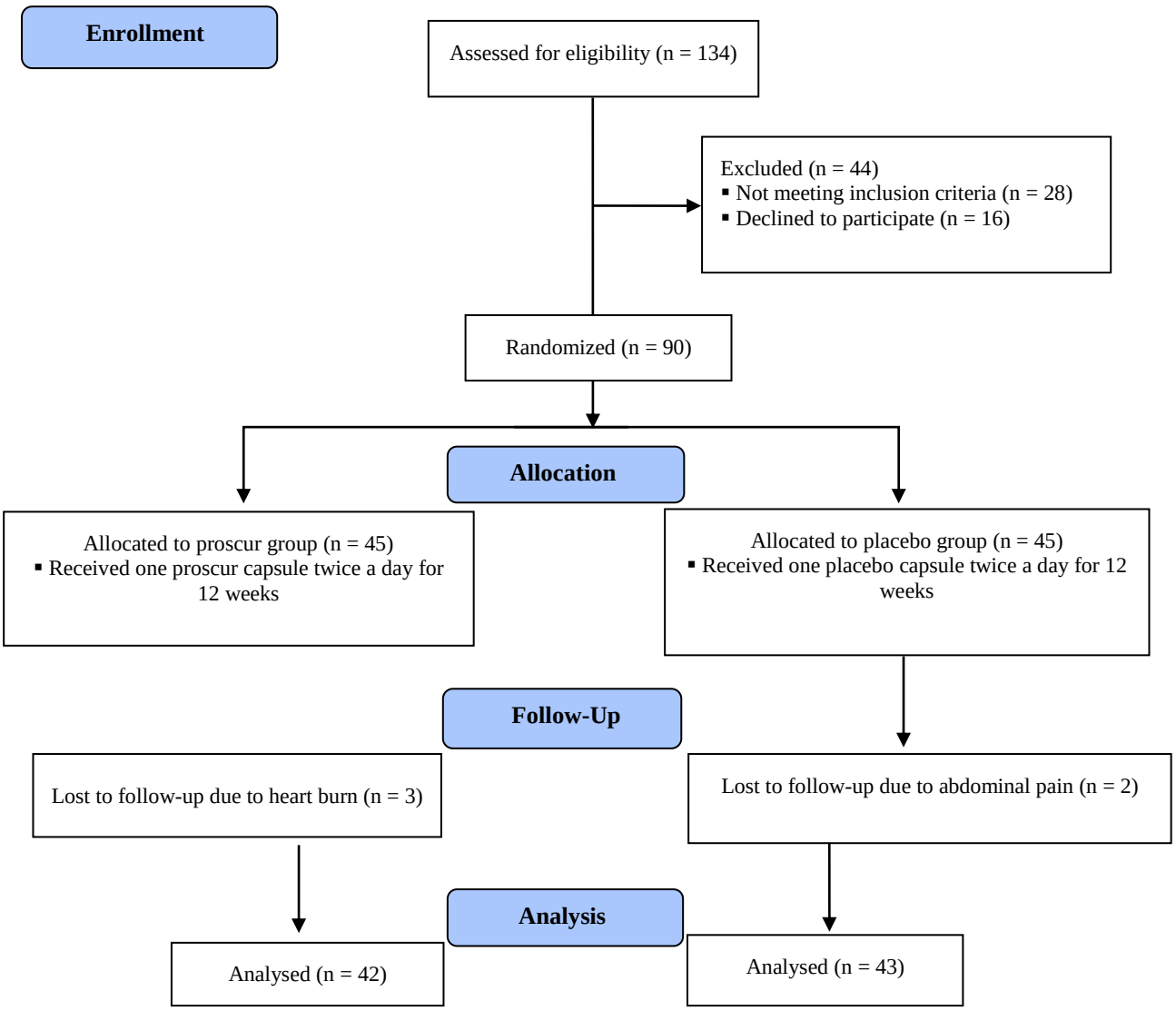

Fig. 1. The CONSORT flow diagram of the study

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Table 1. Basement characteristics of the participants

		Proscur (n = 43)	Placebo (n = 42)	p value
Age (year)		32.69 ± 7.68	31.78 ± 7.72	0.587
Marital status	**Single**	21 (48.8 %)	22 (51.2 %)	1
	Married	22 (51.2%)	20 (48.8 %)	
Age of menarche (year)		12.22 ± 0.86	11.97 ± 0.81	0.24
Age at onset of endometriosis (year)		21.4 ± 3.17	21.5 ± 3.54	0.989

Note: Values are presented as mean ± SD or percent.
Abbreviations: SD, standard deviation.

Table 2. Primary and secondary outcomes before and after interventions in each group

	Group	Baseline	30th day	60th day	90th day	P value[a]	Changes from baseline to 90th day	P value[b]
Severity of dysmenorrhea	Proscur	7.09 ± 1.1	4.45 ± 1.44	2.72 ± 0.98	1.5 ± 0.59	< 0.001	78.77 ± 8.12	< 0.001
	Placebo	6.56 ± 0.7	6.02 ± 0.74	6.17 ± 0.71	6.24 ± 0.61	0.014	2.51 ± 8.15	
Severity of dyspareunia	Proscur	5.92 ± 1.89	3.13 ± 1.57	2 ± 1.04	1.43 ± 0.72	< 0.001	78.84 ± 9.67	< 0.001
	Placebo	6.56 ± 0.72	6.05 ± 0.53	5.88 ± 0.96	6.05 ± 0.53	0.096	4.44 ± 11.6	
Severity of pelvic pain	Proscur	6.73 ± 1.12	4.02 ± 1.27	2.27 ± 0.81	1.45 ± 0.59	< 0.001	78.13 ± 9.31	< 0.001
	Placebo	6.47 ± 0.7	6.14 ± 0.73	6.12 ± 0.73	6.15 ± 0.5	0.021	3.3 ± 8.49	
Amount of painkiller used (number)	Proscur	4.24 ± 1.34	2.48 ± 0.89	1.81 ± 0.62	1.37 ± 0.56	< 0.001	65.6 ± 18.05	< 0.001
	Placebo	4.7 ± 0.99	4.34 ± 0.88	4.47 ± 0.94	4.52 ± 0.99	0.209	-0.14 ± 8.19	

Note: Values presented as mean ± SD or percent.
Abbreviations: SD, standard deviation.
[a] Friedman test
[b] Mann–Whitney U test was used to compare the mean difference of variables between the two groups (non-normally distributed).

Table3. EHP-5 scores before and after interventions in each group

	Group	Baseline	p value*	90th day after intervention	p value*
Score of EHP-5 core questionnaire	Proscur	52.31 ± 11.57	0.57	27.75 ± 15.52	< 0.001
	Placebo	52.37 ± 8.62		50 ± 6.62	
Score of EHP-5 modular questionnaire	Proscur	47.07 ± 18.53	1	24.5 ± 16.86	< 0.001
	Placebo	45.12 ± 12.53		44.24 ± 12.06	
EHP-5 total score	Proscur	99.39 ± 26.2	0.837	52.25 ± 31.13	< 0.001
	Placebo	97.5 ± 15.93		93.93 ± 14.67	

Note: Values are presented as mean ± SD or percent.
Abbreviations: EHP-5, endometriosis health profile questionnaire.
*Mann Whitney U test

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4. Discussion

As far as we know, the present study is the first clinical trial that evaluated the effects of proscur capsule on the endometriosis-associated pelvic pain in young women. The findings of our study demonstrated that consumption of formula proscur consisting of saw palmetto, green tea, pumpkin seed oil, ginger, nettle and, rosemary could significantly relieve endometriosis-associated pain and CA-125 level, when used for 12 weeks. The pathogenesis of endometriosis is not precisely known [17], however, the interaction between hormonal, immune, inflammatory and proangiogenic processes are involved in the development of endometriosis [37]. Although clinical trials are lacking, there are preclinical studies showing the potential effectiveness of the bioactive compounds in proscur in the management of endometriosis through various molecular mechanisms, including anti-inflammatory, antioxidant, anti-androgenic, anti-estrogenic, and pelvic pain-reducing activities. Saw palmetto extract has anti-androgenic, anti-estrogenic, anti-inflammatory and prolactin inhibiting effects [22, 38]. Green tea has shown anti-inflammatory, antioxidant and pain-relieving properties [39-41]. Moreover, it has anti-angiogenic, anti-proliferation, anti-metastasis, and apoptosis induction properties. Administration of green tea has been shown to inhibit the growth of endometriosis in preclinical study [27]. In a study on the experimental mouse model of endometriosis, treatment with green tea catechin displayed anti-angiogenic effects and was able to significantly prevent the development of endometriosis [42]. Major bioactive component of green tea called epigallocatechin-3-gallate (EGCG) has anti-angiogenic and anti-oxidation activity, which can reduce the size and weight of endometriosis lesions. Moreover, it was able to prevent the growth of lesions by increasing apoptosis and inhibiting the function of microvessels in experimental endometriosis lesions [43]. A cross-sectional study found that green tea consumption was associated with a lower prevalence of dysmenorrhea in women of reproductive age. Furthermore, green tea consumption was more significant in reducing moderate to severe dysmenorrhea than mild dysmenorrhea. However, the exact amount and duration of green tea consumption were not stated in this study [24]. According to currently available evidence, nettle-derived phytochemicals have been shown to possess anti-inflammatory, antioxidant and immunomodulatory activities [44] . Treatment with nettle in the rat model of endometriosis was able to significantly reduce the size of the lesion and the number of adhesions. Also, the levels of angiogenesis mediators (tumor necrosis factor alpha (TNF-α), vascular endothelial growth factor (VEGF), and interleukin-6 (IL-6)) decreased due to the presence of flavonoids in this plant [45]. Phytocompounds in rosemary, responsible for anti-inflammatory, antioxidant, antiproliferative, and antitumor activities [46]. Administration of carnosic acid and rosmarinic acid of rosemary could significantly reduce the size of endometriosis lesions in mice compared to the control group. Both compounds were able to considerably suppress cell proliferation [28] .

A comparison of rosemary and MFA capsules on menstrual bleeding and primary dysmenorrhea in a clinical trial on 82 female students with moderate dysmenorrhea showed rosemary has pain relief properties and can reduce dysmenorrhea the same as MFA capsules [25]. Pumpkin have anti-inflammatory and antioxidant activities. Pumpkin seeds

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contain a notable amount of omega 3 [47]. Omega-3 treatment in a rat model was able to significantly reduce the size and tissue parameters of experimentally induced endometriotic implants [48]. The results of a meta-analysis showed that omega-3 consumption is effective in reducing the severity of dysmenorrhea [49]. Ginger root has anti-inflammatory and antispasmodic activities and is used for dysmenorrhea caused by endometriosis [17]. The application of ginger extract in a rat model caused reduction and atrophy of the endometriotic implants [29]. A crossover clinical trial study of 168 single female students with menstrual pain reported that the use of ginger for two consecutive cycles was as effective as a painkiller (Novafen) in relieving dysmenorrhea [23]. According to the findings of a systematic review of clinical trials, ginger was effective in treating primary dysmenorrhea, and its use was as effective as NSAIDs without any side effects [50]. This study has several limitations. Due to the limited evidence available on the clinical outcome of any of the plant alone in similar conditions, it was not possible to compare the findings obtained in the present study with other clinical studies. Furthermore, to assess the long-term effects of the intervention, patients had no follow-up after the study ended.

5. Conclusion

The results of the present study provide evidence of the efficacy of the proscur mixture (saw palmetto, green tea, pumpkin seed oil, ginger, nettle, and rosemary) as a supplement in the management of patients with endometriosis. The findings of this study show that short-term use of proscur capsule and conventional medicine can improve pelvic pain in patients with endometriosis. In addition, this product declined the serum measures of CA-125. More randomized controlled trials with larger sample sizes and longer follow-up periods are still necessary to confirm the findings of the present study.

Author contributions

EA: Project administration, conceptualization and visualization. FHD: Methodology, statistical analysis, review and editing original draft. AHJ: Supervision, review and editing original draft. AF: Provision of study materials/patients and carried out experiments. MD: Writing, review and editing original draft. All authors read and approved the final version of the manuscript.

Conflicts of interest

The authors do not have any conflict of interest to declare.

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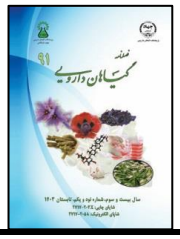

مقاله تحقیقاتی

اثر یک فرمول استاندارد شده چند گیاهی برای درد مرتبط با اندومتریوز: یک کارآزمایی بالینی تصادفی دوسوکور کنترل شده با دارونما

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چکیده

مقدمه: دیسمنوره، دیسپارونی و درد ناشی از آندومتریوز از عوارض اصلی در زنان جوان مبتلا به اندومتریوز محسوب می‌شوند. کپسول پروسکور حاوی چندین داروی گیاهی سنتی است که در مطالعات پیش بالینی و بالینی اثرات ضد التهابی، آنتی‌اکسیدانی، ضد آندروژنی، ضد استروژنی، کاهش‌دهنده درد لگنی و ضد درد را نشان داده‌اند. **هدف:** این مطالعه با هدف بررسی کارایی بالینی و ایمنی یک فرمول استاندارد چند گیاهی (پرئسکور) برای دردهای مرتبط با اندومتریوز در زنان جوان مبتلا به اندومتریوز انجام شد. **روش بررسی:** این مطالعه یک کارآزمایی بالینی تصادفی، دوسوکور، تک مرکزی و کنترل شده با دارونما بود. در مجموع ۹۰ بیمار ۲۰ تا ۴۵ ساله با درد مرتبط با اندومتریوز وارد مطالعه شدند. شرکت‌کنندگان به‌طور تصادفی به گروه‌های پروسکور یا دارونما به نسبت ۱:۱ تقسیم شدند و ارزیابی اثربخشی در روزهای ۳۰، ۶۰ و ۹۰ انجام شد. شرکت‌کنندگان به‌مدت ۱۲ هفته دو بار در روز پروسکور یا دارونما را به صورت خوراکی دریافت کردند. نتایج مطالعه بر اساس نمره تغییر مقیاس آنالوگ بصری (VAS) و فرم کوتاه پرسشنامه پروفایل سلامت اندومتریوز (EHP-5) اندازه‌گیری شد. **نتایج:** ما شاهد افزایش تسکین درد در زنانی بودیم که پروسکور دریافت کردند. اندازه سطوح سرمی CA-125 در کسانی که پروسکور دریافت کردند کاهش یافت. مداخله به خوبی تحمل شد و هیچ عارضه جانبی جدی رخ نداد. **نتیجه‌گیری:** مطالعه ما نشان داد که پروسکور درد ناشی از اندومتریوز و سطح CA-125 را با حداقل عوارض جانبی پس از درمان تسکین می‌دهد. بنابراین، پروسکور همراه با درمان دارویی استاندارد می‌تواند مزایای بالینی بیشتری را برای بیماران مبتلا به درد مرتبط با اندومتریوز فراهم کند.

مخففها: OCs، داروهای ضد بارداری خوراکی؛ GnRH، هورمون آزاد کننده گنادوتروپین؛ NSAID ها، داروهای ضد التهابی غیر استروئیدی؛ CAM، طب مکمل و جایگزین؛ CONSORT، استانداردهای تلفیقی گزارش کارآزمایی‌ها؛ VAS، مقیاس آنالوگ بصری؛ EHP-5، پرسشنامه مشخصات سلامت اندومتریوز؛ SD، انحراف استاندارد؛ TNF-α، فاکتور نکروز تومور آلفا؛ VEGF، فاکتور رشد اندوتلیال عروقی؛ IL-6، اینترلوکین-۶

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