

The Effects of Chamomile and Flaxseed on Pelvic Pain, Dyspareunia, and Dysmenorrhea in Endometriosis: A Controlled Randomized Clinical Trial

Abstract

Background: Chamomile and flaxseed are traditionally used medicinal plants to treat painful menstruation. Therefore, this study aimed to investigate the effects of chamomile and flaxseed on pelvic pain, dyspareunia, and dysmenorrhea in endometriosis patients. **Materials and Methods:** A controlled randomized clinical trial was conducted on 102 endometriosis patients referred to Reyhane Infertility Center of Qom University of Medical Sciences, Iran, from July 2021 to March 2022. Patients were divided into three groups: chamomile, flaxseed, and placebo, using the block randomization method. Patients used 1000 mg capsules (three times a day) for 8 weeks. A Visual Analog Scale (VAS) was used to measure the severity of pain. Pelvic pain, dyspareunia, and dysmenorrhea were assessed on three occasions. Data were analyzed using the Chi-square, repeated measures ANCOVA, and ANOVA. All statistical analysis was performed using SPSS version 20. **Results:** Before the intervention, there was no significant difference between the three groups regarding dysmenorrhea, pelvic pain, or dyspareunia ($p > 0.05$). The mean score of pelvic pain (on one and two-month follow-ups) in the chamomile and flaxseed groups ($F = 383.07$, $p < 0.001$) was lower than that in the placebo group. The mean score of dyspareunia (on one and two-month follow-ups) in the chamomile and flaxseed groups was significantly lower than that in the placebo group ($F_2 = 479.34$, $p < 0.001$). The mean score of dysmenorrhea on one and two-month follow-ups ($F_2 = 385.67$, $p < 0.001$) in the chamomile and flaxseed groups was lower than that in the placebo group. **Conclusions:** Chamomile and flaxseed may reduce pelvic pain, dyspareunia, and dysmenorrhea associated with endometriosis.

Keywords: Chamomile, dysmenorrhea, dyspareunia, endometrioses, linseed oil, pelvic pain

Introduction

Endometriosis is a chronic inflammatory disease that depends on estrogen.^[1] It is characterized by the presence of endometrial tissue outside the uterine cavity.^[2] The prevalence of endometriosis in women of reproductive age is from 6% to 10%. It is also present in 20%–50% of infertile women and 71%–87% of women with chronic pelvic pain.^[3] The cause of endometriosis is not fully understood. Some theories about its etiology include retrograde menstruation theory, coelomic metaplasia theory, and induction theory. The known risk factors for endometriosis

include younger age at menarche, shorter menstrual cycles, hypermenorrhea, nulliparity, and infertility.^[4] Chronic pains such as dysmenorrhea, dyspareunia, and non-menstrual pelvic pain are the primary symptoms of endometriosis. Some studies

have regarded the pain linked to endometriosis as a debilitating condition that can impact women's quality of life, social relationships, as well as their mental and sexual health.^[5] The potential mechanisms of painful endometriosis include local inflammation of the peritoneum, deep infiltration causing tissue damage, adhesion formation, fibrotic thickening, and the accumulation of menstrual blood in endometriosis implants. These factors contribute to the painful stretching of the implants because of the natural movement of the tissues. The inflammatory nature of this disorder plays an essential role in the symptoms of the disease.^[4] All three main symptoms of endometriosis, namely infertility, pelvic pain, and dysmenorrhea, are related to inflammatory factors and oxidative stress in women with endometriosis.^[6] This relationship can result from the induction effects of oxidative stress, which increase the proliferation of endometriosis cells, contribute

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to pain neural pathways, and elevate inflammatory factors produced by macrophages.^[6]

The treatment of this disease mainly involves hormone therapy, with surgery being utilized in advanced cases. However, the treatments are associated with various side effects and not entirely effective.^[4,7] Therefore, women with endometriosis often seek additional treatments.^[5] It seems necessary to discover and identify new drugs to manage this disease, and medicinal plants are a valuable source for this purpose.^[7] Treatments should have anti-inflammatory and analgesic effects.^[5] Therefore, studies focus on plant-derived agents as a natural treatment option to achieve high efficiency, avoid side effects, and maintain the chances of a successful pregnancy.^[8] Chamomile is one of the medicinal plants known to relieve pain in traditional medicine sources.^[9] It is an ancient herbal medicine known by the scientific names *Chamomilla Recutita* and *Matricaria chamomilla* worldwide. Aqueous and ethanolic extracts of chamomile flowers have anti-inflammatory, antispasmodic, calming, and anxiety-reducing effects.^[8] Chamomile has antioxidant effects and inhibits the production of prostaglandins.^[9] The use of chamomile reduces abdominal and pelvic pain during menstruation.^[9] In their study, Niazi and Moradi (2021)^[10] showed that the use of chamomile can be considered an effective treatment for primary dysmenorrhea and reducing menstrual bleeding. Najafi *et al.* (2017)^[11] demonstrated that the use of chamomile flower essence following a cesarean section reduced pain and the need for analgesics. The side effects of chamomile are rare and sometimes cause allergic reactions, which are mostly limited.^[9]

The consumption of flaxseed extract can significantly reduce inflammation.^[12] Flaxseed is scientifically known as *Linum usitatissimum*. Phytochemical analysis of flaxseeds revealed that the seeds contain a high concentration of prostanoids, particularly lignans, as well as a small number of phenolic acids, flavonoids, and cyanogenic glycosides. Alpha-linoleic acid, lignans, and flavonoids have anti-inflammatory properties.^[12] Jafarnejhad *et al.* (2016)^[13] showed that flaxseed could reduce the intensity of breast pain. Flaxseed oil is effective in relieving migraines and menstrual pain.^[14] Currently, herbal supplements are considered alternative treatments and more popular because of their natural ingredients and minimal side effects. The effects of herbal medicines remain under investigation and require further research. Studies show that chamomile and flaxseed are effective in reducing pain. However, there is no research comparing their effectiveness in reducing pain associated with endometriosis. Therefore, this study aimed to investigate the effects of chamomile and flaxseed on pelvic pain, dyspareunia, and dysmenorrhea in endometriosis patients.

Materials and Methods

This study was a randomized, placebo-controlled, double-blind clinical trial. The study was registered in the Iranian Registry of Clinical Trials on June 28, 2021 (ID: 97967, IRCT20190625044004N1) to investigate the effects of

chamomile capsules and flaxseed oil on pain related to endometriosis in women. The data were gathered from July 2021 to March 2022. The study population included all women with confirmed endometriosis (verified by surgery or laparoscopy) with grades 1 and 2 who were referred to the Reyhaneh Infertility Center, Qom University of Medical Sciences, Qom, Iran. A convenience sample was recruited from women who met the eligibility criteria. The study inclusion criteria included individuals aged between 20 and 45 years, currently married, without any physical disorders (such as pelvic inflammatory disease, autoimmune, or metabolic diseases), without known mental health issues (as per medical records and patient's health issues (as per and writing Persian, undergoing standard treatment for endometriosis, not diagnosed with other pelvic inflammatory diseases, and not using alcohol, tobacco, or multivitamin supplements. The exclusion criteria included non-use and improper use of drugs (failure to follow the correct instructions for taking medication), sensitivity to chamomile, and flaxseed, and unwillingness to continue treatment. The participants were assured that their information would be kept confidential and that they could leave the study at any stage of the research if they wished. The sample size was calculated based on the mean values and standard deviation of menstrual pain scores in the two groups, which were approximated by the study of Almassinokiani *et al.* (2016).^[15] The sample size was 34 per group ($\alpha = 0.5$, $\beta = 0.1$, $S_1 = 2.5$, $S_2 = 2$, $d = 1.5$).

In this study, the samples were initially selected using convenience sampling. One hundred two women with confirmed endometriosis (verified by surgery or laparoscopy) who met the eligibility criteria were included in the study, and they also provided written informed consent. In the next step, patients were randomly assigned to one of three groups: chamomile, flaxseed, and placebo. This study used a limited randomization method of block randomization type. The randomization tool was also utilized with random sequence generation software. By using sealed opaque letter envelopes with a random sequence, in this method, each of the random sequences created is recorded on a card, and the cards are placed inside the letter envelopes sequentially. To maintain a random sequence, the outer surface of the envelopes was numbered sequentially. Finally, the lids of the letter envelopes were glued and placed in a box. At the time of sampling, one of the envelopes was opened based on the order in which eligible participants entered the study, revealing the assigned group of that participant. If code A was assigned to the patient, she received drug A. If code B or C was assigned, she received drug B or C. For example, code A was chamomile capsules, code B was flaxseed capsules and code C was a placebo. The coding was conducted by the pharmacist. After the 2-month intervention, the pharmacist displayed the contents of the capsules given to each group. A CONSORT diagram representing the allocation of patients during the 2-month follow-up is presented in Figure 1. A sociodemographic questionnaire and a VAS were used

to collect the data. A researcher-designed questionnaire was used to collect data on sociodemographic variables such as age, duration of disease, education level, occupation, economic status, height, menstrual bleeding, and menstrual history. Patients were asked to record the maximum intensity of pelvic pain, dysmenorrhea, and dyspareunia separately using the Visual Analog Scale (VAS). A form was provided to the research units to assess pain intensity using the VAS, where lines of 100 mm (10 cm) in length were drawn. It was explained to the research units that the zero point on these lines indicates the absence of pain, while 100 indicates very severe pain. Pelvic pain, dyspareunia, and dysmenorrhea were assessed on three occasions: before the intervention, and at one and two-month follow-ups. Patients were asked to rate their pelvic pain, the pain of their last menstruation, and the average pain during intercourse with their sexual partner on separate VAS. All patients received their routine and standard treatment for endometriosis as recommended by their physicians. The drugs, which were completely similar in appearance (shape, size, and color), were unknown to the researcher and the patient and were only known to the pharmacist. Each of the drugs was placed in separate packages coded with letters A, B, and C and provided to the research units. First, to prepare the hydro-alcoholic extract of chamomile and flaxseeds in the laboratory under aseptic conditions, powdered chamomile flowers, and flaxseeds were processed into a hydro-alcoholic extract using an 80% ethanol solvent, followed by a 50% ethanol solvent. The extract was concentrated using a Rotary evaporator device to the maximum extent possible at a temperature of 50°C and reduced pressure. The dried extract was then prepared as a capsule by BoualiSina Qom Herbal Medicine Researchers Company. Patients in all three groups used 1000 mg capsules (three times a day) for 8 weeks. The amounts

used were 9 gm of chamomile, 6 gm of flaxseeds,^[16] and 3 gm of microcrystalline cellulose (placebo). Follow-ups with patients, confirming the use of capsules, addressing study-related inquiries, and preventing sample attrition were conducted weekly using the phone. Every two weeks, the patients visited Reyhaneh's infertility clinic to receive their next capsules. At each visit, they were given a box of used capsules and then received capsules for the next two weeks.

The data was analyzed statistically using Chi-square, ANOVA, and repeated measures ANCOVA with the assistance of SPSS version 20 (IBM Corp, Armonk, NY, USA). Because there was a significant age difference between the two groups, a repeated measures ANOVA was performed with age adjustment.

Ethical consideration

The present study was approved by the Ethics Committee of Qom University of Medical Sciences with the ethics code IR.MUQ.REC.1397.192. At the beginning of the study, the patients were given explanations about the purpose and method of the research. They were also informed about their right to either participate in or withdraw from the study at any time. They were asked to sign a written consent form at the onset of the study and were assured of the confidentiality of their personal information.

Results

The mean (SD) age of the participants was 30 (4.38) years, the mean (SD) age of first menstruation was 12 (0.77) years, and the mean (SD) age of diagnosis was 28 (4.21) years. No statistically significant differences were observed between the study groups regarding education level, job, BMI, income status, menstrual bleeding, menstrual history, and duration of the disease [Table 1]. Furthermore, at the start of the study, the scores for menstrual pain, pelvic pain, and dyspareunia were not significantly different between the three groups [Table 2].

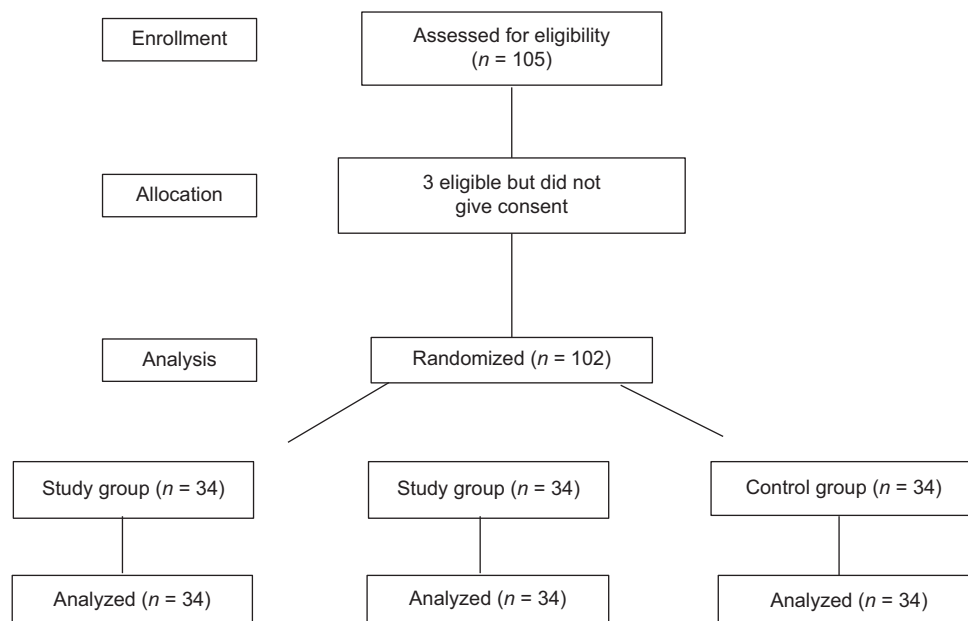


Figure 1: CONSORT diagram showing the sampling and random allocation of study subjects

According to the results of the repeated measures ANOVA analysis, the changes in pelvic pain were different among the three groups.

In addition, a repeated measures ANOVA for between-groups comparison revealed a significant difference in the mean scores of pelvic pain ($F_2 = 383.07, p < 0.001$), dyspareunia ($F_2 = 385.67, p < 0.001$), and dysmenorrhea ($F_2 = 479.34, p < 0.001$) associated with endometriosis at the three measurement time points [Table 3].

According to Tukey's *post hoc* test, there was a significant difference in the mean scores of pelvic pain, dysmenorrhea, and dyspareunia in the pairwise comparisons of treatment groups [Table 4]. The reduction of dysmenorrhea, dyspareunia, and pelvic pain in the chamomile group was greater than in the flaxseed oil [Table 4].

According to the Chi-square test, the requirement for painkillers in the placebo group was significantly higher than in the other groups. Hence, 50% of the placebo group had taken ibuprofen, 21% had taken hyoscine, and 24% had taken it. However, in the chamomile group, none of the participants had used painkillers, while only 11.8% of the flaxseed group had taken ibuprofen ($p < 0.001$).

Discussion

The current study aimed to evaluate the effectiveness of daily chamomile and flaxseed capsules in reducing pelvic pain, dyspareunia, and dysmenorrhea in endometriosis. The results showed that the eight-week use of chamomile and flaxseed capsules could significantly reduce pelvic pain, dyspareunia, and dysmenorrhea. Pelvic pain, dyspareunia, and dysmenorrhea were severe before the intervention. The pain was significantly reduced during the intervention. The reduction of dysmenorrhea, dyspareunia, and pelvic pain in the chamomile group was greater than in the flaxseed oil group. Chamomile reduced the need for pain medication in patients with endometriosis. Pain reduction may indicate a decrease in injury or a reduction in factors that affect pain production mechanisms.^[5]

Limited evidence exists regarding the effect of chamomile and flaxseed capsules on pain caused by endometriosis. This was the first clinical trial to investigate the effects of chamomile and flaxseed extract on pain associated with endometriosis. Chamomile is one of the medicinal plants known to relieve pain in traditional medicine sources.^[17] It may reduce acute and chronic pain.^[18] Some natural healers suggest that drinking chamomile tea can help treat endometriosis.^[19] Chamomile can help reduce primary dysmenorrhea and pelvic pain during

Table 1: Sociodemographic and menstrual history characteristics of study subjects

Variable	Classification	Chamomile Group n (%)	Flaxseed oil Group n (%)	Placebo Group n (%)	df	p
Education	Less than Under diploma	7 (20.59)	10 (29.41)	8 (23.53)	2	0.690
	University education	27 (79.41)	24 (70.59)	26 (76.47)		
Job	housewife	18 (52.94)	23 (67.65)	20 (58.82)	2	0.461
	Employed	16 (47.06)	11 (32.35)	14 (41.18)		
BMI*	Normal	19 (55.88)	19 (55.88)	23 (67.65)	2	0.521
	Overweight	15 (44.12)	15 (44.12)	11 (32.35)		
Income status	Low	13 (38.24)	11 (32.35)	6 (17.65)	4	0.104
	medium	14 (41.18)	17 (50.00)	25 (73.53)		
	Good	7 (20.59)	6 (17.65)	3 (8.82)		
Duration of disease	5 Year	5 (14.71)	8 (23.53)	8 (23.53)	4	0.528
	6 Year	0 (0.00)	1 (2.94)	0 (0.00)		
	7 Year	29 (85.29)	25 (73.53)	26 (76.47)		
Menstrual bleeding	Low	7 (20.59)	6 (17.65)	4 (11.76)	4	0.162
	medium	19 (55.88)	24 (70.59)	28 (82.35)		
	Much	8 (23.53)	4 (11.76)	2 (5.88)		
History of menstruation	Regular	34 (100.00)	31 (91.18)	29 (85.29)	2	0.076
	Irregular	0 (0.00)	3 (8.82)	5 (14.71)		

*Body Mass Index

Table 2: Baseline characteristics of the participants in three groups of the study

Variable	Chamomile Group Mean (SD)*	Flaxseed oil Group Mean (SD)*	Placebo Group Mean (SD)*	F	df	p**
Age,	31.56 (4.48)	31.14 (4.24)	28.38 (3.81)	5.78	2	0.004
Age of monarch	12.05 (0.85)	11.85 (0.65)	11.67 (0.76)	2014	2	0.123
BMI***	24.60 (2.42)	24.50 (1.64)	24.34 (1.48)	0.16	2	0.849
Pelvic pain, Baseline	9.23 (0.81)	8.91 (0.86)	8.85 (0.60)	2.41	2	0.095
Dysmenorrhea, Baseline	9.47 (0.74)	9.11 (0.91)	9.29 (0.83)	1.52	2	0.224
Dyspareunia, Baseline	9.32 (0.80)	9.26 (0.82)	9.05 (0.77)	1.02	2	0.365

*SD=Standard deviation, **ANOVA test. ***Body Mass Index

Table 3: Comparison of mean and standard deviation score of the pelvic pain, dysmenorrhea and dyspareunia in between the of chamomile, flaxseed and placebo

Variable	Time period	Mean Mean (SD)*			Repeated measures ANOVA**		
		Chamomile Group	Flaxseed oil Group	Placebo Group	F	df	p
Pelvic pain	Control cycle	9.23 (0.82)	8.91 (0.86)	8.85 (0.60)	383.07	2	<0.001
	First cycle	2.06 (1.01)	4.79 (1.07)	9.00 (0.82)			
	Second cycle	1.00 (1.02)	3.71 (1.17)	8.85 (0.93)			
Dysmenorrhea	Control cycle	9.47 (0.74)	9.11 (0.91)	9.29 (0.83)	385.67	2	<0.001
	First cycle	2.32 (0.88)	4.65 (0.95)	8.76 (0.74)			
	Second cycle	1.53 (0.96)	3.5 (0.99)	8.59 (0.74)			
Dyspareunia	Control cycle	9.32 (0.80)	9.26 (0.82)	9.05 (0.77)	479.34	2	<0.001
	First cycle	1.88 (1.32)	4.09 (0.79)	8.79 (0.73)			
	Second cycle	0.91 (1.03)	3.09 (0.97)	8.59 (0.82)			

*SD=Standard deviation, **Repeated measures ANCOVA adjusted for age

Table 4: Pairwise comparisons of pelvic pain, dysmenorrhea and dyspareunia between the groups

Groups	Pelvic pain		Dysmenorrhea		Dyspareunia	
	Mean Difference	p*	Mean Difference	p*	Mean Difference	p*
Chamomile vs Placebo	4.80	<0.001	4.44	<0.001	4.77	<0.001
Flaxseed oil vs Placebo	3.09	<0.001	3.12	<0.001	3.33	<0.001
Chamomile vs flaxseed oil	-1.70	<0.001	-1.31	<0.001	-1.44	<0.001

*Adjustment for multiple comparisons: Tukey HSD (Honestly Significant Difference)

menstruation.^[4] It can reduce the symptoms of premenstrual syndrome.^[20] Chamomile aromatherapy is effective in reducing pain after a cesarean section.^[21] In their study, Aradmehr *et al.* (2017),^[22] demonstrated that chamomile cream effectively reduced episiotomy pain in women. It could relieve migraine pain.^[23] Chamomile was a well-tolerated, safe, and effective treatment for women with mild to moderate mastalgia.^[24] The previous studies and the current study demonstrated the effect of chamomile on pain. However, the results of some studies are significant due to variations in sample sizes, the type and location of pain, different dosages of chamomile, the frequency of consumption, and the duration of use. The analgesic properties of chamomile may be attributed to the following reasons: (1) the effects of Chamazulene and apigenin on activated macrophages lead to the inhibition of propagation and synthesis of nitric oxide, (2) chamomile flavonoids with potent inhibitory effects against prostaglandin E2 in macrophages can act as a selective inhibitor of cyclooxygenase -2, and (3) chamomile polyphenols can reduce pain by inhibiting anti-inflammatory biomarkers in THP1 macrophages, which have anti-inflammatory effects.^[21] Chamomile was found to be relatively safe and well-tolerated by most patients. Side effects reported with chamomile treatment were assessed as rare and mild.^[18]

Flaxseed is another medicinal plant used in traditional medicine to reduce pain.^[25] The effects of this oil in reducing the pain of migraines and menstruation have been reported.^[14] A study by Mirghafourvand and *et al.* (2015)^[26] on 159 women with cyclic mastalgia showed that the consumption of 25 gm of flaxseed and 3.2 to 4.8 mg of vitamin E tablets for two menstrual cycles was effective in reducing cyclic mastalgia. Jafarnezhad *et al.* (2016)^[13] carried out a study on 90 patients

with cyclic mastalgia. They found that daily intake of flaxseed (30 mg), evening primrose oil (two capsules of 1000 mg), and vitamin E (1 capsule of 400 Units) for two menstrual cycles resulted in a reduction in the severity of breast pain. The reduction level was similar in all three groups; however, flaxseeds and evening primrose oil influenced the severity of breast pain after one cycle of consumption. Flaxseed oil is recommended to mothers as a suitable remedy for cesarean wound healing.^[27] Flaxseed; may be used as a helpful adjuvant therapy for patients with rheumatoid arthritis.^[28] It contains compounds, such as omega-3 fatty acids, lignans, and flavonoids, which have anti-inflammatory properties.^[25] Flaxseeds are very beneficial for the body's health. The side effects of flaxseed are mild, uncommon, and reversible.^[26]

Because of the substances found in chamomile and flax seeds, as well as the fewer side effects of herbal medicines compared to chemical ones and considering that most women prefer to use complementary medicine, these plants can be safely used to relieve pain related to endometriosis. The strengths of this study included the simultaneous use of two herbal medicines for treating pelvic pain, and dyspareunia associated with endometriosis. Additionally, this study was the first to demonstrate the effectiveness of chamomile and flaxseed in reducing endometriosis pain. The results of this study can complement those of previous studies and serve as a foundation for future research. The research methodology and results of this study can serve as fundamental information for future research.

The limitations of this study included the short duration, lack of assessment of the sustainability of the effect after discontinuation, and absence of control over painkiller consumption in the samples.

Conclusion

The results of the present study showed that chamomile and flaxseed were effective in relieving pelvic pain, dyspareunia, and dysmenorrhea associated with endometriosis. Further, clinical studies should be conducted on the long-lasting effects, sustainability of the impact after discontinuation, risks, and side effects of this drug prescription method, as well as the appropriate dose of the drugs to use routinely in clinical practice for the treatment of endometriosis.

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Conflicts of interest

Nothing to declare.

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