

Comparison of the effects of *Matricaria chamomila* (Chamomile) extract and mefenamic acid on the intensity of premenstrual syndrome

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A B S T R A C T

The study aimed to compare the effects of Chamomile Extract and Mefenamic acid (MA) on the intensity of Premenstrual syndrome (PMS) symptoms.

This study was a clinical randomized double blind trial, carried out with 90 students living in the dorms of Iran. The participants filled the daily forms about the intensity of PMS for two consecutive months. Once the definitive diagnosis of PMS was made, the participants were divided into two groups, each receiving either Chamomile capsule 100 mg or MA 250 mg three times a day. Intensity reduction of emotional symptoms was significantly higher among Chamomile Extract-users (30.1 ± 26.6 and 33.4 ± 25.3 percent) than that among MA-users (11.6 ± 25.7 and 10.7 ± 26.8 percent) after two cycles intervention ($p < 0.001$). Intensity reduction of physical symptoms was not significantly different ($p > 0.05$) among groups. Consumption of Chamomile seems to be more effective than MA in relieving the intensity of PMS associated symptomatic psychological pains.

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1. Introduction

Premenstrual Syndrome (PMS) is one of the common problems during child bearing age [1], experienced among 75% of the women with regular menstruation [2]. The syndrome prevalence has been recently reported to be 83.1% in some studies and 62.4% in some others [3,4]. PMS is usually associated with a periodic manifestation of some physical and behavioral symptoms prior to menses and may affect women's daily routines and work. Afterward, they remain asymptomatic for some time. The most frequent physical symptoms include abdominal bloating, fatigue, breast tenderness, and headache. Behavioral and emotional symptoms include

irritability, anger, depression, increased appetite, and loss of concentration occurring within 7–10 days of menstrual cycle [2,5,6].

There is no definitive etiology for PMS and no established treatment, however, there are some recommended supportive symptom-based treatments, and hormonal therapy to suppress ovulation [2,5]. Some clinical trials have revealed that Mefenamic acid (MA) affects PMS through inhibition of the enzymes involved in prostaglandin synthesis, more significantly than placebos during the week before menstrual period [6]. This medication has vary side effects such as effects on the blood, gastrointestinal tract, kidney and skin. It should be taken 250–500 mg per 6–8 h on daily basis, however, its consumption should not exceed 7 days and should be avoided in case conditions such as hypersensitivity, peptic ulcer and gastrointestinal (GI) bleeding [6–8]. According to World Health Organization (WHO) statistics, 80% of the world population use herbal compounds [9], of which some are proven to be effective in relieving PMS associated symptoms [10].

Some reported studies indicate the efficacy of Chamomile on some conditions related to menstruation such as dysmenorrhea and PMS [11]. It is among the best, effective and widely used traditional medications [12]. FDA has classified Chamomile essential oil as non-risky and safe medicinal item. Chamomiles with

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scientific name, *Matricaria chamomilla*, belong to Compositae family which is a plant native to the Mediterranean region, but now with a wide distribution [13–15]. This medicinal plant has different constituents including Chamazulene with anti-inflammatory, antioxidant effects; Apigenin with anti-inflammatory, analgesic and antineoplastic effect; Flavonoid with anti-inflammatory, anti-anxiety effect and finally Alpha Bisabolol with anti-inflammatory and digestive effect [16].

Given the high prevalence of this syndrome [5], its symptoms and lack of an established definitive treatment for it, and considering the associated harmful adverse effects of synthetic drugs and preference for using medicinal plants including Chamomile with its analgesic, anti-inflammatory, anti-anxiety effect [10,16], and considering also menstrual problems treatment as the responsibility of midwives who play a key role in publicizing the use of herbal medicine [18], the present study seeks to determine the effect of Chamomile essential oil on PMS intensity and compare it with that of MA on the syndrome.

2. Materials and methods

2.1. Design of the study

This prospective, randomized, double blind trial was performed following the approval by the ethics committee of Shahid Beheshti University of Medical Sciences, International Branch, Tehran, Iran, under registration no116/3742 and code IRCT20120125880182N2

recorded by International Center for Registration of Clinical Trials in Iran.

2.2. Sampling method

Sampling was performed within a six month period from September 2011 to March 2012 (Fig. 1).

2.3. The participants

The study was conducted on 90 students residing in two dorms called Fatemeh and Kowsar, at Kazeroon Islamic Azad University, southern Iran. In doing so, the researcher visited the students in their separate rooms, introduced herself and explained the objectives of the study, and invited them to cooperate in the survey.

631 students were initially selected, out of whom 221 entered into the study. Then, 118 participants were randomly divided into 2 groups of 59 students based on the symptom severity.

Inclusion Criteria: The inclusion criteria were as follows: being single, age within 18–35 years, normal body mass index, regular menstrual cycle (21–35 days), with diagnosed PMS, no physical or psychological ill conditions, not on medication (hormonal, vitamins, herbal, antidepressant, aspirin, or warfarin), no history of allergy to herbal drugs, no sad event occurrence, no surgical operation during the last six months, not being a professional athlete, presence of at least five symptoms based on DSM-IV (Diagnostic and Statistical Manual of Mental Disorders-fourth

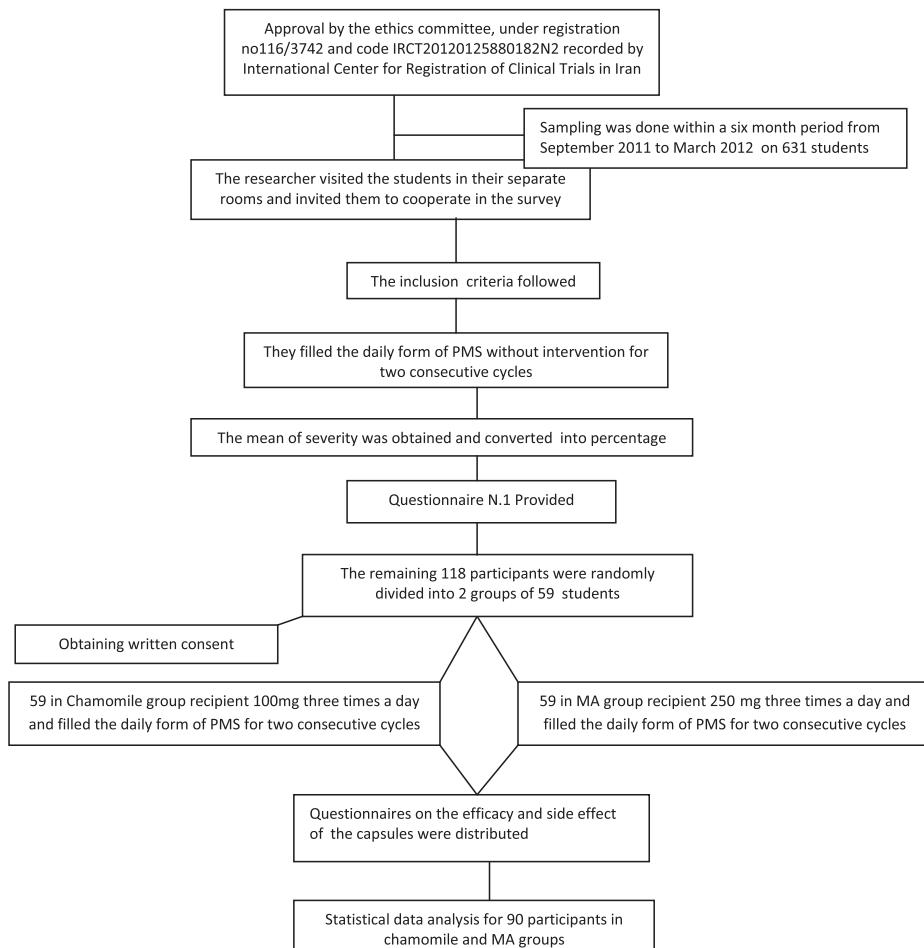


Fig. 1. The process of the study.

edition) for PMS diagnosis with confirmed one symptom out of the first four symptoms including (1. Feeling sad, hopeless or self-deprecating, 2. Feeling tense, anxious, or “on edge”, 3. Marked lability of mood, interspersed with frequent tearfulness, 4. Persistent irritability, anger and increased interpersonal conflicts, 5. Decreased interest in usual activities that may be associated with withdrawal from social relationships), not being depressed based on Beck questionnaire. Those with the above mentioned criteria were entered into the study. An informed written consent was also given by each participant.

Exclusion Criteria: The exclusion criteria included allergy to drugs, improper use of capsules and developing a significant disease, and taking medications during the study. Based on such criteria, 631 students were initially selected, out of whom 221 entered into the study. The process of the study is presented in Fig. 1.

2.4. Tools for data collection

1. **PMS daily form:** The participants filled the daily form of PMS consisting of 30 items on the symptoms divided into 15 physical ones including breast tenderness, headache, vertigo, bloating, weight gain, swollen extremities, palpitation, arthralgia and myalgia, sweating and chills, change in bowel movement, nausea, acne, recurrent herpes like infection, flushing and hotness, pelvic and abdominal pains and lassitude, fatigue and low energy state and 15 psychological, emotional and behavioral ones consisting of depression, anxiety, tension, emotional and affective instability, anger, irritability, loss of interest in daily routine activities, difficulty in concentration, forgetfulness, unjustified tendency to cry, avoiding socialization and contacts, preference for solitude, feeling of being out of control, change in sleeping pattern, change in appetite or overeating, desire to eat sweets and salt, and tendency to commit suicide. Given the instructions about how to fill out the daily form of PMS symptoms, the participants filled them for two consecutive cycles. The severities of daily symptoms were ranked on a scale ranging from none, mild, moderate to severe and marked by the participants. They were also instructed to mark on the form in case they were on supplementary formulas or medications. The total intensity rates of the symptoms from 7 days prior to menstruation till the first day of it was calculated and divided by the number of emerging days. In doing so, the mean of severity was obtained and converted into percentage. Based on the percentages, the participants were divided into three groups; those with mild symptoms (below 33%), medium group (between 33% and 66%), and severe group (above 66%). At this stage and following the two periods, 103 participants were excluded from the survey due to incorrect filling of the forms, non-confirmed PMS, use of medications or any other unexpected events occurring to them. Then, the remaining 118 participants were randomly divided into 2 groups of 59 students based on the symptom severity and respective demographic data, using Excel software.
2. **The demographic questionnaire:** It consisted of 10 demographic items about their university major, year and semester of education, living place, father's and mother's occupation, average of family income, number of students living in the same room of the dorms, eating at university canteen, and 3 questions related to menstrual age (menarche), PMS emergence time, and length of menstruation period.
3. **The questionnaires on the efficacy and side effect of the capsules:** At the end of each course, questionnaires on the efficacy and side effect of the capsules were distributed among the participants to explore the side effects and to rate their satisfaction.

2.5. Validity and reliability

Content validity was used to assess the validity of the tools. In doing so, the questionnaires were prepared based on the research goal and relevant scientific sources and consultation with ten experts. The required revisions and changes were made to the questionnaire, as suggested by the expert reviewers. To determine the reliability, test-retest method was used and ICC (Intraclass correlation coefficient) was calculated for each item and found to be above 0.75.

2.6. The intervention

Once the definitive diagnosis of PMS was made, the participants were divided into two groups. They were administered to the groups of participants from 21st day till the next onset of menstruation period, three times daily for two cycles.

1. **Chamomile group:** The participants received Chamomile capsule 100 mg three times a day.

MA group: The participants received MA capsule 250 mg three times a day.

Along with the capsules, either Chamomile or MA, PMS daily form was given to each participant to fill for two consecutive days.

2.7. Procedure of the study

Chamomile extract was prepared from the plant purchased from Iran Tehran Zarband company in 2011, in the school of pharmacy lab, Shahid Beheshti University of Medical Sciences, through soaking with ethanol 96%, followed by distillation of the liquid at -40°C with the extraction efficiency of 5%. The obtained extract was then mixed with starch and capsules containing 100 mg of the extract and 150 mg of starch, resembling MA capsules, were prepared. MA capsules 250 mg were purchased from Al-Havi pharmaceutical company (Tehran, Iran) in 2011 and were held together with Chamomile capsules for two weeks in order to become similar in smell. The two types of capsules were put in separate coded packs by the researchers' assistant while researchers and participants were blinded to the type of the ingredients.

2.8. Statistics methods for data analysis

Once the questionnaires were collected following each period, the respective data were obtained and analyzed by statistical tests. SPSS version 18 was used along with descriptive statistical techniques such as frequency table, means values, standard deviation to evaluate the efficacy of the treatments and associated side effects on the recipients. Inferential statistical tests such as independent *t*, repeated tests, Bonferroni converted Wilcoxon, Chi-square, Mann Whitney test were used to make intergroup and intragroup comparisons in terms of intensity of PMS and the two groups' corresponding background characteristics. *P* value less than 0.05 was considered significant.

3. Results

Of the 118 participants in the survey, 11 Person from the Chamomile group and 8 from MA group were excluded from the study due to leaving the dorms and avoiding returning the filled forms (Chamomile group), and improper use of capsules, not filling the forms (MA group), in the first stage of treatment. In the second stage, 3 participants from Chamomile group due to improper use of capsules and 6 from MA group due to GI disorder and improper use

of capsules were excluded from the survey. In the end, the data related to 90 participants (45 participants in each group) were evaluated and statistically analyzed (Fig. 2; the study flow chart).

The mean age of participant in Chamomile group was (22.42 ± 2.55) and in MA was (21.71 ± 2.17) year. The BMI indices for the two groups were (22.08 ± 1.78) and (21.78 ± 1.76) Kg.m^2 and duration of the menstrual period were (28.87 ± 1.59) and (28.79 ± 1.5) days, respectively, which were not significantly different. The first menstrual age (menarche) for most participants was 13 years or over, and PMS symptoms emergence was longer than 4 days prior to menstruation. The majority of participants were BA/BS degree students and in third years of university education. The two groups were not significantly different in terms of parents' occupation and education, average family income, number of residents in the dorm room and eating at university canteen (Table 1).

Although the mean values of intensity of general physical and psychological symptoms before menstruation were not significantly different between the two groups of participants (Chamomile and MA recipients, $p > 0.05$), the mean reduction in overall intensity of symptoms after the two courses of treatment was significantly different between the two groups with more efficacy for Chamomile ($p < 0.05$) (Table 2).

As for the reduction of psychological symptoms in the two groups, the results indicated more effectiveness of Chamomile, compared to MA ($p < 0.001$) (Table 3).

The difference between the two groups in terms of relief in physical symptoms was not significant ($p > 0.05$) and both Chamomile and MA acted similarly on physical symptoms in PMS (Table 4).

As for the intragroup mean percent reduction for each of PMS associated physical and psychological symptoms during the treatments, the decline in symptoms was significant in Chamomile group except for palpitation, nausea, emotional instability, trouble in concentrating, change in appetite and tendency for suicide. In MA group, except for bloating, swelling of limbs and extremities, palpitation, sweating, chills, flushing (hotness), change in bowel movement, emotional affective instability, anger and irritability,

unexcused crying, avoiding socialization and contacts, tendency and preference for solitude, change in appetite, and tendency for suicide, the reduction in other symptoms was significant ($p < 0.05$).

As for intergroup comparison, the results indicated that MA was found to be more effective than Chamomile against arthralgia and muscular aches, abdominal and pelvic pains, while Chamomile was significantly more effective than MA against anger and irritability ($p < 0.05$) (Tables 5 and 6).

Regarding the reported side effects of the treatment in Chamomile and MA groups following the two periods of treatment, menstrual bleeding in Chamomile and GI complications in MA group were more severe, but for the other side effects, the two groups did not reveal any significant difference ($p > 0.05$).

4. Discussion

As the results indicate, Chamomile extract was proven to be more effective than MA on reducing the overall intensity of symptoms and particularly psychological symptoms associated with PMS. The mean reduction in the intensity for Chamomile group was higher than that for MA and this was the case with both intergroup and intragroup comparisons. Some reports also lend support to this finding and also the same effect by taking a combination of Chamomile and fennel [12] which might be explained by the anti-anxiety and relieving effect of Chamomile through its ingredients including Flavonoid, Apigenin, Phytoestrogen substances which affect central nervous system [16,18].

Our findings are consistent with those of previous studies in which Chamomile was found to be effective against anxiety and anger [11,19], though in some studies no significant difference was observed between anxiety scores the participants who received Chamomile and those receiving placebos, the intragroup difference in the reduction of intensity was significant. It also reduces anxiety and generalized anxiety disorder were seen in patients taking the drug [11,19,20]. In the present study, in addition to intragroup reduction of anxiety due to Chamomile consumption, in both groups Chamomile served as the more effective agent against the

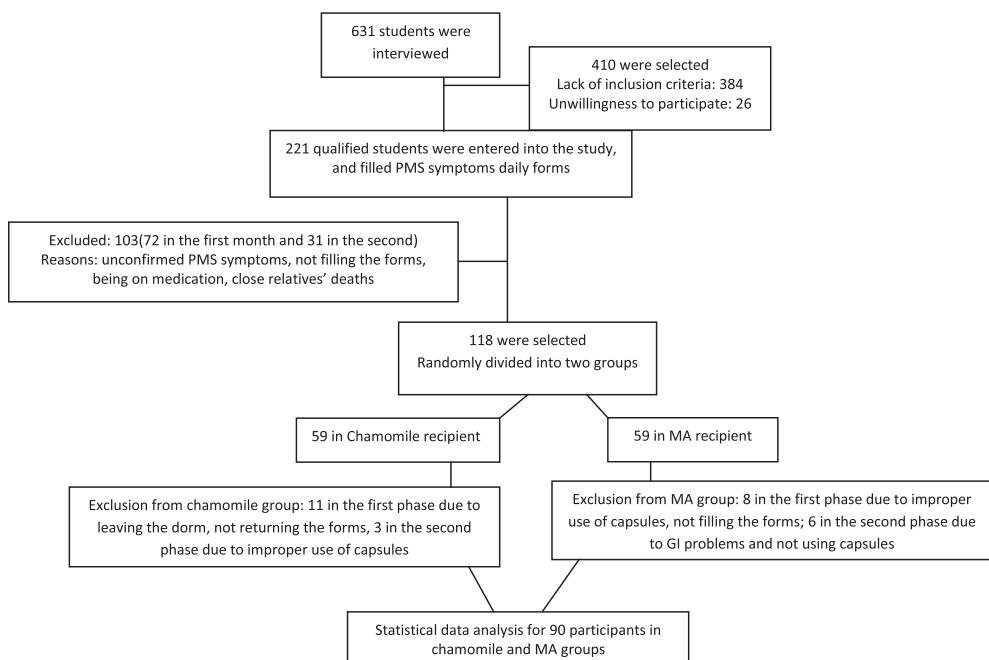


Fig. 2. The consort flow chart.

Table 1

Comparison of absolute and relative frequencies of chamomile and MA groups in terms of demographic and menstrual related variables.

Variable group	Chamomile	Mefenamic acid	Independent T-test results
	<u>n = 45</u>	<u>n = 45</u>	
	Mean ± SD	Mean ± SD	
Age (year)	22.42 ± 2.55	21.71 ± 2.17	p = 0.15
BMI (kg.M ²)	22.08 ± 1.78	21.78 ± 1.76	p = 0.41
Menstrual period length (day)	28.87 ± 1.59	28.79 ± 1.54	p = 0.63
Menarche age (year)	13.22 ± 1.29	13.36 ± 1.43	p = 0.64
Onset of symptoms (day)	4.96 ± 2.05	4.62 ± 1.94	p = 0.43
Variables	n (percent)	n (percent)	Test results
Semester	- Higher than 4th semester 18(40)	23(51.1)	p = 0.12
	- Lower than 4th semester 27(60)	22(48.9)	Mann–Whitney
Degree	- Associate 1(2.2)	0	p = 0.99
	- Bachelor 42(93.3)	44(97.8)	Mann–Whitney
Father's occupation	- Doctorate degree 2(4.4)	1(2.2)	p = 0.93
	- Unemployed 1(2.2)	1(2.2)	Chi-square
	- Laborer, farmer 7(15.6)	5(11.1)	
	- Low position staff 7(15.6)	11(24.4)	
	- Senior staff 1(2.2)	1(2.2)	
	- Own business 22(48.9)	21(46.7)	
	- Retiree 7(15.6)	6(13.3)	
Mother's occupation	- Housewife 43(95.6)	43(95.6)	p = 1
	- With occupation 2(4.4)	2(4.4)	Chi-square
Father's education	- Illiterate, literate 6(13.3)	2(4.4)	p = 0.35
	- Junior school degree 9(20)	9(20)	Mann–Whitney
	- High school degree 16(35.6)	18(40)	
	- University degree 14(31.1)	16(35.6)	
Mother's education	- Illiterate, literate 8(17.8)	4(8.9)	p = 0.83
	- Junior school degree 16(35.6)	22(48.9)	Mann–Whitney
	- High school degree 18(40)	15(33.3)	
	- University degree 3(6.7)	4(8.9)	
Family average income	- Ten million rls or above 30(66.7)	31(68.9)	P = 0.82
	- Less than ten million rls 15(33.3)	14(31.1)	Mann–Whitney
Number of students in the dorm room	- Less than 6 11(24.4)	13(28.9)	p = 0.63
	- More than 6 34(75.6)	32(71.1)	Mann–Whitney
Using university canteen	- Yes 9(20)	10(22.2)	p = 0.79
	- No 36(80)	35(77.8)	Chi-square

n, number; rls, rials; p, p value P < 0.05 (significant).

PMS associated intensity of symptoms which is justifiable by the properties attributed to Chamomile [16].

Results of the present study showed no significant difference in suicide attempts after Chamomile use while a significant decrease in suicide attempts by those using Chamomile has been reported in previous studies [19]. It might be due to potentially low incidence of such a condition in our study population [21].

In agreement with previous reports, Chamomile extract and MA could relieve physical symptoms of the PMS [11,22], yet there was no significant difference in this respect between two groups of study. Consistent with present study, reduction in intensity of each physical symptom [11] and relief of dysmenorrheal pain were shown following Chamomile consumption [23,24]. Also, it is demonstrated that Chamomile and MA could relieve breast tenderness, headache, abdominal and pelvic pains, arthralgia, and myalgia. The efficacy of topical Chamomile compound on eczema,

itching, and herpes like skin conditions, facial acne and pimples [25,26]. Similar to the present study, another study showed the effectiveness of Chamomile tea on palpitation, and remarkable increase in brachial blood pressure, with no hemodynamic changes detected [27]. Another report supported the relieving property of Chamomile in milk feeding children colic, which is similar to the present results indicating its positive effect on bloating and change in bowel movement [28]. Consumption of Climex (Composition of Angelica and Chamomile Tea) in menopause women can help relieve hotness and flushing [29]. Although at the present study, Chamomile could not help to nausea relief in PMS, but it relieves pregnancy related nausea in a previous study [30].

The causes of PMS have not been known well, but it seems that prostaglandins are mainly the mediators which are responsible for the emergence of the PMS associated symptoms [5,6]. Taking into account the findings of present study, it can be suggested that

Table 2

Comparison of mean percent of PMS overall symptom intensity.

Treatment phase	Chamomile	Mefenamic acid	Independent T-test
	<u>n = 45</u>	<u>n = 45</u>	Results (p)
Prior to treatment	48.4 ± 15.6	43.9 ± 13.7	0.15
After first phase of treatment	23.3 ± 17.9	29 ± 14.3	0.09
After second phase of treatment	20.4 ± 17.8	27.6 ± 15.9	0.04

n, number P, P value P < 0.05 (significant).

Table 3

Comparison of mean percent of PMS psychological symptom intensity.

Treatment phase	Chamomile	Mefenamic acid	Independent T-test
	<u>n = 45</u>	<u>n = 45</u>	Results (p)
Prior to treatment	50.1 ± 22.8	44.7 ± 15.8	0.2
After first phase of treatment	19.9 ± 19.4	33 ± 18.6	0.001
After second phase of treatment	16.6 ± 18.1	34 ± 21.4	<0.001

n, number P, P value P < 0.05 (significant).

Table 4

Comparison of mean percent of PMS physical symptom intensity.

Treatment phase	Chamomile	Mefenamic acid	Independent T-test
	n = 45	n = 45	Results (p)
Prior to treatment	46.8 ± 19.9	43.1 ± 22.6	0.41
After first phase of treatment	26.8 ± 20.3	25 ± 19	0.67
After second phase of treatment	24.2 ± 21.9	21.3 ± 17	0.48

n, number P, P value P < 0.05 (significant).

Chamomile with anti-inflammatory and relieving effects coming from Chamazulene and alpha bisabolol [16] and MA with its anti-prostaglandin, relieving effect, can be both effective against the physical symptoms in PMS [6,8].

In our study, the treatment cycle with Chamomile was only 7 days, while in other studies on other medicinal herbs the treatment cycles were longer. For example Vitex agnus was used through whole of cycle (from the beginning of one menstrual period to the other) [31] and a Ginkgo Biloba and Evening primrose were used for two weeks [17,32] for relieving of PMS symptoms. Furthermore, Chamomile is a common, well known and accessible herbal medicine in Iran [12], so it could be used easier than other herbs to relieve PMS symptoms. In fact, the results showed Chamomile is more effective than MA on PMS psychological symptoms. It may be due to presence of Flavonoid, a CNS stimulating molecule, and Apigenin and Luteolinin, which are antianxiety and relieving because of their binding with Benzodiazepine receptors. Besides, anti-prostaglandin effect of MA [16] makes it more effective than Chamomile on some physical symptoms and so the obtained results in the present study seem to be reasonable.

The results showed an increasing menstrual bleeding as the side effects of treatment with Chamomile. It is also indicated in traditional medicine [33] which could be attributed to a type of Coumarin in its compounds [16]. GI complications as the side effect of MA use in our study were also observed in previous studies [7,8]. In previous studies, no increased menstrual bleeding following Chamomile consumption was reported [23]; however, in a study in 2006, cautious use of Chamomile by women on anticoagulant medicine was suggested [34]. Therefore, it is advisable to use Chamomile to relieve PMS associated symptoms. However, in cases of anemia or anticoagulant medication, Chamomile should be used with caution and after consultation with physicians. Also, further prospective studies need to be conducted on this issue to strengthen its documentation.

The strength of the study lies in prospective, large sample size (90 subjects), double blind, randomized study of effects of two medicines on subsets of symptoms.

The present study, as observed in some other similar ones, suffers from some limitations of which the noted one is data collection through self-report, which was alleviated by frequent contacts of the researchers with the participants during the study procedures. Besides, statistical comparison for each symptom at a time was performed and a significant difference was seen between the two groups of participants, but the number of participants was not considered when making such a comparison.

This clinical trial was better to be placebo controlled, because although statistically significant improvement in mean scores of symptoms occurred with Chamomile, but intensity reduction of overall symptoms was significant in mefenamic acid group too. But, we had no placebo group because of some signs and symptoms may occur in some samples and may cause ethical problems.

Table 5

Comparison of mean percent for each physical PMS symptom intensity.

Medication (treatment)	Physical symptom	Prior to treatment	After first phase of treatment	After second phase of treatment	Repeated test	
					Intra g	Inter g
Chamomile	Breast tendered	30.19	19.71	16.4	<0.001	0.26
MA		25.38	13.31	11.6	<0.001	
Chamomile	Headache	26.58	13.28	1.08	<0.001	0.1
MA		28.09	1.76	0.11	<0.001	
Chamomile	Vertigo	15.25	6.88	5.16	<0.001	0.15
MA		19.45	11.57	9.58	0.004	
Chamomile	Bloating	23.64	17.23	13.54	0.019	0.72
MA		18.09	15	16.74	0.53	
Chamomile	Weight gain and swelling	21.43	11.07	10.57	0.02	0.058
MA		9.98	5.66	5.66	0.055	
Chamomile	Palpitation	10.71	8.13	7.4	0.135	0.96
MA		12.44	7.62	6.65	0.24	
Chamomile	Arthralgia and malaise	31.42	18.45	17.46	<0.001	0.02
MA		29.44	7.12	4.67	<0.001	
Chamomile	Sweating and chills	7.5	3.94	3.94	0.03	0.81
MA		5.77	3.93	3.93	0.27	
Chamomile	Flushing (hotness)	16.5	10.3	9.6	0.012	0.28
MA		8.7	8.6	7.6	0.72	
Chamomile	Change in bowel movement	15.14	7.37	4.92	0.001	0.13
MA		17.96	13.55	13.29	0.17	
Chamomile	Nausea	10.9	8.3	7.8	0.22	0.69
MA		11.1	5.9	6.1	0.01	
Chamomile	Facial acne	24.52	13.05	12.06	<0.001	0.14
MA		30.3	19.93	17.7	0.001	
Chamomile	Herpes	5.4	0	0.4	0.001	0.08
MA		7.2	2.9	2.9	0.03	
Chamomile	Abdominal pelvic pain	35.3	20.9	21.6	0.005	<0.001
MA		20.5	8.8	5.6	<0.001	
Chamomile	Fatigue and listless	35.3	19.2	18.2	<0.001	0.22
MA		27.2	15.7	13.5	<0.001	

n, number P, P value P < 0.05 (significant) MA, Mefenamic Acid, intra g, intragroup, inter g, intergroup.

Table 6

Comparison of mean percent for each psychological PMS symptom intensity.

Medication (treatment)	Psychological symptoms	Prior to treatment	After first phase of treatment	After second phase of treatment	Repeated test	
					Intra g	Inter g
Chamomile	Depression	34.5	10.5	7.8	<0.001	0.07
MA		3.5	4.1	3.9	0.002	
Chamomile	Anxiety	11.07	13.55	11.07	<0.001	0.83
MA		22.2	14.5	14.7	<0.007	
Chamomile	Emotional instability	22.5	11	8.6	0.14	0.11
MA		23.3	19.9	18.73	0.17	
Chamomile	Anger and aggression	29.67	14.7	15.2	0.001	<0.01
MA		32	27.8	28.3	0.21	
Chamomile	No interest in daily routines	28.2	12.7	10.8	<0.001	0.56
MA		26.5	17.7	16.7	0.001	
Chamomile	Troubles with concentration	21.6	13.8	12.5	0.129	0.06
MA		28.1	16.2	16.7	<0.001	
Chamomile	Forgetfulness and attention deficit	12.5	3.4	2.9	<0.001	0.14
MA		18.3	9.8	7.8	0.003	
Chamomile	Unexcused crying	12.3	6.8	4.9	<0.001	0.07
MA		14	11.5	12.3	0.36	
Chamomile	Avoiding socialization	15.2	5.1	4.6	<0.001	0.78
MA		11.1	7.1	9.3	0.13	
Chamomile	Tendency for solitude	17.2	11.8	8.3	<0.001	0.24
MA		18.8	16.2	16.7	0.37	
Chamomile	Out of control feeling	10.3	4.9	4.1	0.009	0.43
MA		14	6.4	6.6	0.006	
Chamomile	Change in sleep pattern	28.9	14.7	11.8	<0.001	0.28
MA		30.1	20.9	18.4	<0.001	
Chamomile	Change in appetite	20.4	13.8	14.2	0.06	0.43
MA		16.7	11.1	11.3	0.15	
Chamomile	Tendency for taking salt or sweet	14	6.9	6.9	0.002	0.87
MA		12.4	6.8	9.8	0.047	
Chamomile	Tendency for suicide attempt	0.49	0.7	0.7	0.92	0.14
MA		4	0.7	1.4	0.055	

n, number P, P value P < 0.05 (significant), MA, Mefenamic Acid, intra g, intragroup, inter g, intergroup.

5. Conclusion

As demonstrated in the study, Chamomile treatment seems to alleviate general physical and psychological PMS associated symptoms, and more effective than MA against psychological and behavioral ones. Chamomile acts similar to MA in relieving physical symptoms. The treatment course for both agents was one week in this study with the respective results emerging; therefore, it is suggested not to use such medications throughout the whole menstrual period. One of the most important conclusion drawn from our study is that clinical trials on PMS treatment are preferred to be placebo controlled, because although statistically significant improvement in symptom occurred with Chamomile, but intensity reduction of overall symptoms was significant in mefenamic acid group too.

Conflict of interest

No competing financial interests exist.

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