

Comparison of the Effects of *Matricaria chamomila* (Chamomile) Extract and Mefenamic Acid on the Intensity of Mastalgia Associated With Premenstrual Syndrome

Farangis Sharifi¹; Masoumeh Simbar^{2,*}; Faraz Mojab³; Hamid Alavi Majd⁴

¹Department of Midwifery, Kazerun Branch of Islamic Azad University, Kazerun, IR Iran

²Department of Midwifery and Reproductive Health, International Branch, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

³Department of Pharmacognosy, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

⁴Department of Biostatistics, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Masoumeh Simbar, Department of Midwifery and Reproductive Health, International Branch, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran. Tel: +98-7212243930-40, E-mail: f_sharifi44@yahoo.com

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Background: Mastalgia (breast pain) is a symptom that usually affects 70% of women at any given point during their life time.

Objectives: This study aimed to compare the effects of chamomile extract and mefenamic acid (MA) on the intensity of Mastalgia associated with premenstrual syndrome (MAPMS).

Patients and Methods: This study was a randomized double blind clinical trial carried out on 90 students living in dormitories at Kazerun Islamic Azad University, Kazerun, Iran from September 2011 to March 2012. The participants filled in the daily forms for two consecutive months. Once the definitive diagnosis of MAPMS was made, the participants were divided into two groups of 45, each receiving either chamomile capsule 100 mg or MA 250 mg three times a day, for an interval beginning from the 21st day of menstrual cycle till the next onset. Descriptive and inferential statistics were used in order to analyze data.

Results: A significant decrease ($P < 0.0001$) was found in average mastalgia between pre and post intervention after first and second cycles in those treated with chamomile Extract (10.5 ± 21.7 and 13.7 ± 20.4 percent) and among MA treated subjects (12.1 ± 624.7 and 13.8 ± 24 percent). There was no significant difference in MAPMS symptom in chamomile extract-treated and MA groups after first and second cycles ($P > 0.05$).

Conclusions: Chamomile reduces the severity of MAPMS during treatment. Consumption of chamomile seems to be similar to MA in relieving the intensity of MAPMS.

Keywords: Chamomile; Mefenamic Acid; Mastodynia

1. Background

Mastalgia (breast pain) is a symptom that usually affects 70% of women at any given point during their life time (1). Mastalgia is a multi-faceted and inhomogeneous clinical condition with poorly understood etiology (2). Breast pain can either be cyclical which is intensified before menstrual period or non-cyclical and unrelated to the menstrual period (3). Cyclical mastalgia occurs in 60% of the women with mastalgia. The mean age of presentation is in the third and fourth decades. Cyclic mastalgia frequently presents as part of the premenstrual syndrome (PMS) (4). Increasing in severity in the days preceding menstruation and then decreasing after the onset of menses. It is usually described as a bilateral pain or heaviness affecting the upper outer quadrants of the breast. Cyclical mastalgia may also be unilateral and focal in nature. Mild premenstrual mastalgia lasting 1-4 days can be considered normal. However, up to 30% of women

may experience severe pain for more than five days and in 15% it limits daily activities (5). Medical treatment of breast pain includes complicated methods of which some are doubtful to have any effect at all, and most chemical treatments have considerable side effects (6). Various supportive therapies have been recommended to alleviate mastalgia. These include vitamin B₂, B₆, E and C, diuretics, non-steroidal inflammatory drugs (NSAIDs), progestational agents, thyroxin, Danazol, Bromocriptine and Tamoxifen and plant extracts like vitexagnus castus, evening primrose oil (EPO) (7).

Some clinical trials have revealed that mefenamic acid (MA) affects PMS and mastalgia, through inhibition of the enzymes involved in prostaglandin synthesis, more significantly than placebos during the week before menstrual period (8). This medication has varying side effects on the blood, gastrointestinal tract, kidney skin, and thus

Implication for health policy/practice/research/medical education:

This project evaluated effectiveness of *Matricaria chamomila* (chamomile) extract on the Intensity of mastalgia associated with premenstrual syndrome.

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it should be administered as 250-500 mg every 6-8 hours daily (8-10). The use of herbal treatments in the management of pain is well documented (11). Some reported studies indicate the efficacy of chamomile on some ill conditions related to menstruation such as dysmenorrhea and PMS (12). It is among the best, effective and widely used traditional medications (13). Chamomile with the scientific name, *Matricaria chamomila*, belongs to Compositae family which is a plant native to the Mediterranean region, but now with a wide distribution (14-16). 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 (17).

Women constitute half of the world's population. More than 30% of Iran's population is women of 14-45 years of age. The increase of women's role in the society and workplaces has changed their roles, lifestyle and family patterns. Now, women are more interested and responsible for their health care and they demand better health care services (18). Periodical breast pain and tenderness is a problem that most women experience before their menstruation (19). Chronic or recurrent mastalgia and lack of reliable remedies can severely impact a patient's quality of life. Psychological morbidity such as depression, helplessness and loss of self-esteem in patients with mastalgia are well documented (20). Given the high prevalence of this problem (1) and considering the associated harmful adverse effects of synthetic drugs.

2. Objectives

The present study was designed to determine the effect of chamomile essential oil on the intensity of Mastalgia associated with premenstrual syndrome and compare it with that of MA.

3. Patients and Methods

The present research was a prospective, randomized, double blind trial of two groups that was carried out after getting approved by the international branch of ethics committee of Shahid Beheshti University of Medical Sciences. The study was conducted on 90 students, who had submitted their written informed consent, and resided in Fatemeh and Kowsar dormitories at Kazerun Islamic Azad University, southern Iran. The participants were divided into two groups of 45 who either received Chamomile capsule 100 mg or MA 250 mg three times a day from 21st day of menstrual cycle till the next onset. The data were gathered from September 2011 to March 2012.

The inclusion criteria consisted of single women aged from 18 to 35 years, with normal body mass index, and regular menstrual cycle from 21 to 35 days. They were also diagnosed with mastalgia associated with PMS, with at

least two months history of symptoms, had no physical or psychological disorders, and were not on such medications as hormonal, vitamins, herbal, antidepressant, aspirin, or warfarin, and had no history of allergy to herbal drugs. The exclusion criteria were allergy to drugs, improper use of capsules and those with a significant disease, and taking medications during the study.

In this study, the method of sampling was first purposive, followed by selection of individuals based on random sampling, using the Random Allocation software. First, the researcher provided the students at girls' dormitories with a questionnaire that described the inclusion criteria. A total of 221 students entered the study. The eligible participants then filled the daily form of mastalgia intensity for two consecutive cycles, following the instructions on how to fill out the forms. The daily symptoms were then recorded in the research unit. The mastalgia intensity were indicated in the forms as none to severe and given 0 to 3 scores accordingly.

The total pain intensity rate was determined from seven days before the first day of menstruation divided by the number of persisting days, and expressed by converting the mean severity into percentage. Based on the percentages obtained, the participants were divided into three groups including those with mild symptoms (below 33%), medium group (between 33% and 66%), and severe group (above 66%). From this initial stage to the following two menstrual cycles, 99 participants were excluded from the survey due to incorrect filling of the forms. The remaining 122 subjects were then randomly divided into two groups of 61 based on the symptom severity and respective demographic data, using Excel software. Having obtained the written consents, all participants received questionnaire No. 1 which consisted of six demographic items as year of education, semester, father's and mother's occupation, average family income, eating at university canteen, and three questions related to the menstrual age (menarche), mastalgia emergence time, and the length of menstruation period.

Chamomile extract was prepared from the plant purchased from Tehran based Zarband company. The extract was then mixed with starch; capsules containing 100 mg of the extract and 150 mg of starch were placed in capsules resembling MA capsules, in the laboratory of School of Pharmacy, Shahid Beheshti University of Medical Sciences. MA capsules 250 mg were purchased from Al-Havi pharmaceutical company, Tehran, Iran. The two types of capsules were packed and coded separately by the assistant researchers who along with participants were blinded to the type of the ingredients. The capsules were then administered three times a day for two cycles to appropriate groups of participants from the 21st day until the next onset of menstruation. Concurrent with either chamomile or MA regimens, each participant received a daily form of mastalgia intensity to fill in for the next two consecutive days. At the end of each course, questionnaires on the efficacy and side effect of the capsules

Table 1. Comparison of Demographic and Menstrual Related Variables Associated With Chamomile and MA Consumption (n = 45)^a

Variable	Chamomile	Mefenamic Acid	Independent T-Test Results
Age, y	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, d	28.87 ± 1.59	28.79 ± 1.54	P = 0.63
Menarche age, y	13.22 ± 1.29	13.36 ± 1.43	P = 0.64
Mastalgia emergence time, d	4.96 ± 2.05	4.62 ± 1.94	P = 0.43

^a Data are presented as Mean ± SD.

Table 2. Comparison of Demographic Related Variables Associated With Chamomile and MA Consumption^{a, b}

Variables	Chamomile	Mefenamic Acid	P Value
Semester			0.29
Higher than 4th semester	18 (40)	23 (51.1)	
Lower than 4th semester	27 (60)	22 (48.9)	
Degree			0.88
Associate	1 (2.2)	0	
Bachelor	42 (93.3)	44 (97.8)	
Doctrate degree	2 (4.4)	1 (2.2)	
Father's occupation			0.93
unemployed	1 (2.2)	1 (2.2)	
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			1
Housewife	43 (95.6)	43 (95.6)	
With occupation	2 (4.4)	2 (4.4)	
Family average income			0.82
One million toman or above	30 (66.7)	31 (68.9)	
Less than one million toman	15 (33.3)	14 (31.1)	
Using university canteen			0.79
Have	9 (20)	10 (22.2)	
Not Have	36 (80)	35 (77.8)	

^a Data are presented as No. (%).

^b P < 0.05.

were distributed among the participants to rate their satisfaction. 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 including frequency tables, means values, and standard deviations to evaluate the efficacy of the treatments and associated side effects on the recipients. Inferential statistical tests such as independent t-test, Chi-square, and Wilcoxon test were used to make intergroup and intragroup com-

parisons in terms of intensity of mastalgia and the corresponding background characteristics of the two groups. P-value less than 0.05 was considered significant. Content validity was used in order to determine validity of the questionnaires. To determine the reliability, repeated test was used and intra class correlation coefficient (ICC) was calculated for each item and found to be above 0.75.

4. Results

Of the 122 participants in the survey, 12 individuals from

Table 3. Comparison of Mean Percent of Mastalgia Associated with PMS Intensit^{a, b}

Treatment Phase	Chamomile	Mefenamic Acid	P Value ^c
Prior to treatment	30.2 ± 29.78	25.4 ± 23.6	0.39
After first phase of treatment	19.71 ± 27.2	13.32 ± 24.3	0.24
After second phase of treatment	16.5 ± 23.96	11.6 ± 24.1	0.33
Reduction following the first phase	10.5 ± 21.7	12.1 ± 24.7	0.74
Reduction following the second phase	13.7 ± 20.4	13.8 ± 24	0.98
Intra group difference	P < 0.0001	P < 0.0001	Wilcoxon test

^a Data are presented as Mean ± SD.

^b The first phase of treatment, one cycle after chamomile and MA consumption; the second phase of treatment, two cycle after chamomile and MA consumption.

^c It is independent t-test results.

the Chamomile and 9 from MA group were excluded from the study because of leaving the dormitory, avoiding to return the filled forms (chamomile group), improper use of the capsules, and not filling the forms (MA group) in the first stage of treatment. In the second stage, four participants were excluded from Chamomile group because of improper use of the capsules and seven were eliminated from MA group due to GI disorder and improper use of capsules. In the end, the data related to 90 participants including 45 persons in each group were evaluated and statistically analyzed.

The average age of participants in chamomile group was 22.42 ± 2.55 SD and in MA was 21.71 ± 2.17 SD years. The BMI indices (Kg/m²) for chamomile and MA groups were 22.08 ± 1.78 and 21.78 ± 1.76 respectively and the respective durations of the menstrual period were 28.87 ± 1.59 and 28.79 ± 1.5 days, which were not significantly different. The first menstrual age (menarche) for most participants was 13 years and over and the length of mastalgia prior to menstruation was longer than four days. The two groups were not significantly different in terms of parents' occupation and education, average family income, number of residents in the dormitory room and eating at university canteen (Table 1) and (Table 2). A significant decrease in average mastalgia was observed between Chamomile Extract and MA-users in pre and post intervention after first and second cycles. However, no significant difference in average MAPMS symptoms was observed between chamomile Extract-users after first and second cycles (Table 3). The side effects after two periods of treatment included menstrual bleeding in nine (20%) patients receiving chamomile and GI complications in 13 (28.9%) subjects in MA treated group, and the difference between the two groups was statistically significant (P < 0.0001).

5. Discussion

As the results indicate Chamomile extract and MA could relieve mastalgia intensity, but in this respect there was no significant difference between the two groups. This is consistent with other reports where decreasing breast pain was observed in both chamomile and MA treated

groups (12).

Our findings were in agreement with those of other studies that reported the relief of dysmenorrheal pain following chamomile consumption (21, 22). Another report supported the relieving effect of chamomile on colic in milk-fed children (23) which is similar to our findings where chamomile alleviated breast tenderness. Consumption of climex, composed of Angelica and chamomile tea, in menopause women can help relieve hotness and flushing (24). The topical administration of NSAIDs over a three-month period can relieve the mastalgia with minimal adverse effects (25), a finding similar to the present study.

The causes of mastalgia have not been well known, but it seems that prostaglandins are mainly the mediators responsible for the emergence of PMS-related symptoms (5, 6) Taking into account the findings of present study, it can be suggested that the anti-inflammatory effect of chamomile on estrogen receptors and pain relief are due to Chamazulene and alpha bisabolol (17, 26), and anti-prostaglandin effect of MA alleviates mastalgia (8, 10). In our study, the treatment with chamomile continued for only seven days, while in other studies on other medicinal herbs the treatment courses were longer. For example, evening primrose oil was used through the entire cycle beginning from the onset of one menstrual period to the next for relieving of mastalgia (27). Furthermore, Chamomile is a common, well known and accessible herbal medicine in Iran (13), so it can be recommended for decreasing periodical breast pain.

Excessive menstrual bleeding was reported to be a side effect of treatment with Chamomile, and as indicated in traditional medicine (26) it could be attributed to its type of Coumarins (17). GI complications as the side effect of MA use in our study were also observed in previous studies (9, 10). In previous studies, the menstrual bleeding did not increase following chamomile consumption (21). However, in a study on anticoagulant medicine conducted in 2006, women were cautioned against the use of chamomile (27). Nevertheless, chamomile has been recommended for relieving mastalgia intensity. However, regarding chamomile consumption, consulting with

physicians is necessary in cases of anemia or anticoagulant medication. Also, prospective studies are needed to further support the use of chamomile in reducing mastalgia. The strength of the present study lies in its randomized fashion, prospective nature, large sample size (90 subjects), and double blindness with regards to the effects of the two medicines on the subsets of symptoms. The present study, as observed in some other similar ones, suffers from certain limitations noticeably data collection through self-report.

As demonstrated in this study, chamomile acts similarly to MA in relieving mastalgia associated with PMS intensity. In the present study the treatment course of one week proved to be sufficient for both agents. Therefore, the use of such medications is not suggested for the whole menstrual period.

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Authors' Contribution

Study concept and design: Farangis Sharifi, Masoumeh Simbar; acquisition of data: Farangis Sharifi; analysis and interpretation of data: Hamid AlaviMajd, Farangis Sharifi, Masoumeh Simbar; drafting of the manuscript: Farangis Sharifi; critical revision of the manuscript for important intellectual content: Masoumeh Simbar; statistical analysis: Hamid AlaviMajd, Farangis Sharifi; administrative, technical, and material support: Faraz Mojab, Farangis Sharifi; study supervision: Masoumeh Simbar.

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