Original Article

Effectiveness of Mefenamic Acid on Premenstrual Syndrome in Women of Reproductive Age

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Abstract

Objectives: The study aim was to assess the effectiveness of mefenamic acid in treating premenstrual syndrome in women of reproductive age.

Methodology: A non-randomized (quasi) study was conducted in Obstetrics & Gynecology department of Federal Govt. Services Hospital, Islamabad from January to December 2023. The study included 100 participants. Participants were instructed to take mefenamic acid for a period of 3 months and were then followed up 3 months additionally. After the follow-up period, the persistence of symptoms and the efficacy of the treatment were recorded.

Results: The mean age of the patients was 30.14±8.38 years. The most prevalent symptoms of PMS were nausea (87%), GIT disturbances (86%), and headaches (82%), followed by tenderness in breast (80%) and vomiting (76%). The effectiveness of mefenamic acid in alleviating symptoms was observed to be 72%. Significant improvements in the symptoms of headaches, dysmenorrhea, tenderness of breast, and irritability of mood were observed ($p \leq 0.05$). No clinically significant differences were found between marital status, education, occupation, and improvement duration of symptoms ($p \geq 0.05$).

Conclusion: The study concluded that the mefenamic acid is effective in relieving symptoms in patients with premenstrual syndrome.

Keywords: Efficacy, Mefenamic acid, Premenstrual syndrome, Reproduction.

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Introduction

Premenstrual syndrome (PMS) is a condition that occurs during the luteal phase of the menstrual cycle, characterized by symptoms severe enough to interfere with daily life and occurring in a predictable pattern relative to menstruation.[1] The incapacitating symptoms recur with each menstrual cycle, commonly including headaches, swelling of breast and tenderness, fatigue, bloating, irritability, and depression.[2] The prevalence of symptoms associated with PMS can vary depending on the population under study and the assessment methods employed. A 70-90% range is an estimation of percentage of women experiencing PMS symptoms during their reproduction. The prevalence of PMS in women varies across different populations: 38% in Arab, 18% in Japan, 25%-97% in Brazil, and 41% in America. It is lower in Europe, ranging from 10% to 12%, while the highest 98% in Asia.[3] Additionally, women about 5-8% with hormone disturbance experienced moderate to severe symptoms.[4]

Women with PMS have a higher risk of developing

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perimenopausal and postnatal depression.[5] A 22%-28% women with PMS have decreased efficiency of work, 82% in relationships with husbands, 60% with children, and 42% in social activities.[6,7]

A study suggests possible link between early-life abuse (physical, sexual, or emotional) and a higher risk of experiencing PMS in women during their middle-to-late reproductive years.[8] Alternative therapies for PMS that do not involve medication include dietary changes, stress management, exercise, and social support are effective.[9] Pharmacological interventions for PMS include GnRH analogs, danazol, spironolactone, mefenamic acid, alprazolam, fluoxetine, and gamma-linolenic acid.[10] Alprazolam, an anxiolytic drug, has been shown to be highly effective than placebo for treating the syndrome. However, prolonged use of benzodiazepines is considered uninvited.[11] A study found mefenamic acid alleviated many symptoms that related with PMS.[12] Mefenamic acid is particularly effective when PMS is related with menorrhagia or dysmenorrhea.[1]

The study objective was to assess the effectiveness of mefenamic acid in treating PMS, as it's not carried the risk of dependence as seen with some other medications. The study significance lies in its efforts to raise awareness among women and offer improved methods for alleviating PMS symptoms.

Methodology

A non-randomized (quasi) study was conducted in Obstetrics & Gynecology department of Federal Govt. Services Hospital, Islamabad from January to December 2023. Following approval from hospital ethics committee and obtaining written consent, a consecutive 100 patients was enrolled in this study. The sample was determined using WHO calculator, with 95% confidence interval, an alpha error of 5%, and incidence of PMS was 7%.[4] The study included women aged 14-40 years who had regularly menstruation for the past 3 months and had been symptoms for at least 3 months. The study also included women who experienced at least 3 of the following symptoms, whether physiological and/or psychological: vomiting, nausea, headache, GIT disturbance, dysmenorrhea, irritability, and tenderness in breast. The study excluded pregnant women, perimenopause, women with irregular menstruation, women underwent hormone replacement, and who had used oral contraceptives.

The evaluation and data collection process involved a thorough examination and history-taking to rule out any underlying pathology. Related investigation was conducted as part of the evaluation. Patients with symptoms were given mefenamic acid 250mg tablets at least 3 months, starting 3 days before and for the first 3 days of the menstruation, in two daily doses. A minimum 3 months patients follow up was done. MINEMAR was administered both before and after the treatment period. A proforma was organized to record all the data, including patient's bio-data, severity and duration of symptoms, reliving factors, follow-up details, and the effectiveness of treatment.

Data analysis was performed using SPSS v 25. Quantitative variables such as age and duration of symptoms were expressed as mean ± SD. Qualitative variables such as symptoms of PMS, marital status, education, and efficacy of mefenamic acid were measured as frequencies and percentages. A probability p value ≤ 0.05 was considered significant. Effect modifiers, such as age, marital status, symptoms of PMS, duration of symptoms, and level of education were tested by stratification. Chi-square was applied for stratification.

Results

In this study, one-hundred (n=100) women experiencing at least 3 of the symptoms defined in the methodology were included. Mostly women were housewives, married and educated. The mean age of women was 30.14±8.38 years (range, 14-42 years). Women's ages were divided into two categories, with the most common age category for PMS being ≤ 28 years. Among 100 women, 62% were ≤ 28 years, while 38% women were in a range of 29-42 years. The most common symptoms of PMS were nausea, GIT disturbances, and headaches, followed by tenderness of breast and vomiting (Table I). The mefenamic acid efficacy in relieving symptoms was noted in 72% women, whereas 28% women showed no efficacy.

The mefenamic acid efficacy showed according to age distribution in improving PMS symptoms among women of age categories was similar. An efficacy of 75.8% was noted among women aged 28 years or younger. In women aged 29-42 years the reported efficacy was 65.8% (Table II).

Significant improvements were noted in headache, irritability, dysmenorrhea, and tenderness in breast (Table III). However, no significant improvement was

found among education, marital status, duration of symptom, and occupation (Table IV).

Table I: Common PMS symptoms. (n=100)

Symptoms		N	%
Nausea	Yes	87	87.0%
	No	13	13.0%
GIT disturbances	Yes	86	86.0%
	No	14	14.0%
Headaches	Yes	82	82.0%
	No	18	18.0%
Tenderness of breast	Yes	80	80.0%
	No	20	20.0%
Vomiting	Yes	76	76.0%
	No	24	24.0%
Irritability	Yes	70	70.0%
	No	30	30.0%
Dysmenorrhea	Yes	60	60.0%
	No	40	40.0%

Table II: Efficacy of mefenamic acid according to age distribution. (n=100)

		Efficacy		Total	p value
		Yes	No		
Ages (year)	14-28	47 (47.0%)	15 (15.0%)	62	.131
	29-42	25 (25.0%)	13 (13.0%)	38	
Total		72 (72.0%)	28 (28.0%)	100	

Table III: Mefenamic acid efficacy at PMS symptoms. (n=100)

		Efficacy		p value
		Yes	No	
Nausea	Yes	66 (75.9%)	21 (24.1%)	.281
	No	9 (69.2%)	4 (30.8%)	
GIT disturbances	Yes	60 (69.8%)	26 (30.2%)	.193
	No	6 (42.9%)	8 (57.1%)	
Headaches	Yes	64 (78.1%)	18 (21.9%)	.019
	No	8 (44.4%)	10 (55.6%)	
Tenderness in breast	Yes	68 (85%)	12 (15%)	.003
	No	8 (40%)	12 (60%)	
Vomiting	Yes	57 (75%)	19 (25%)	.593
	No	16 (66.7%)	8 (33.3%)	
Irritability	Yes	57 (81.4%)	13 (18.6%)	.001
	No	12 (40%)	18 (60%)	
Dysmenorrhea	Yes	50 (83.3%)	10 (16.7%)	.004
	No	16 (40%)	24 (60%)	

Discussion

This study enrolled 100 women with symptoms of PMS. The symptoms of nausea (87%), GIT disturbances (86%), and headaches (82%) were noted to be the leading symptoms of PMS, followed by tenderness in breast (80%) and vomiting (76%). The mefenamic acid efficacy in relieving symptoms was noted to be 72%. Significant improvements were noted in headache, irritability, dysmenorrhea, and tenderness of breast ($p \leq 0.05$). However, no significant improvement was found among education, marital status, duration of symptom, and occupation ($p \geq 0.05$). PMS is a combination of physical, psychological, and social symptoms that affect the daily lives of married women in their reproduction age. Approximately 80% of women in menstruation experienced symptoms of pre-menstruation, with the incidence of PMS estimated to be 20-40% according to American College of Obstetricians and Gynecologists (ACOG) criteria.[12,13]

Mefenamic acid is an approved medicine for dysmenorrhea and has been shown clinically to be effective in symptoms improving and altering the basic pathophysiology.[14] The dual mechanism of action of these medications enhances their effectiveness and results in a rapid onset of action. Furthermore, in vitro studies have shown that meclofenamate has the ability to inhibit 5-lipoxygenase action, different members of the propionic acid cluster, which exhibit slight or no inhibitory response.[15] Furthermore, increased prostaglandins production resulting cyclooxygenase-2 and other mediators has been revealed excessive contraction of uterine, leading to increased pain and discomfort.[16] The reported usage of these agents is 75-80%, with side effects such as nausea, abdominal pain and diarrhea to chronic kidney disease.[17] Correspondingly, we also found an efficacy of 72% in relieving premenstrual symptoms in physiologically and psychologically.

Table IV: Mefenamic acid efficacy at demographics. (n=100)

		Efficacy		p value
		Yes	No	
Marital status	Married	52 (74.3%)	18 (25.7%)	.591
	Single	21 (70%)	9 (30%)	
Occupation level	Working	30 (75%)	10 (25%)	.681
	Housewives	42 (70%)	18 (30%)	
Educational level	Uneducated	36 (69.2%)	16 (30.8%)	.430
	Educated	39 (81.3%)	9 (18.7%)	
Duration of symptoms (weeks)	≤ 1	44 (80%)	11 (20%)	.291
	≥ 2	32 (71.1%)	13 (28.9%)	

A study conducted in Indian and reported that 52% of participants experienced headaches, 28% experienced vomiting, and 30% experienced tenderness in breast as PMS symptoms. Additionally, 60% of participants preferred using the combination of mefenamic acid and dicyclomine for relieving the symptoms compared to using ibuprofen, paracetamol, hyoscine or dicyclomine alone.[18] Whereas, in our study the reported symptoms of headaches (82%), nausea (87%), vomiting (76%), and tenderness in breast (80%). These symptoms showed improvement ranging from 70% to 85% with the use of mefenamic acid alone. Furthermore, several studies have reported that mefenamic acid is the mostly used and effective drug among various medications used for self-medications.[19,20] It was also observed that mefenamic acid had a similar effect to celecoxib in relieving the symptoms.[21]

Several studies have been described the significant relief of dysmenorrhea associated with PMS, either when used alone or in combine with other treatments.[22,23] Nevertheless, mefenamic acid effect alone on PMS general symptoms has not been adequately evaluated, particularly among the population of Pakistan. Additionally, due to a lack of awareness about PMS symptoms and their management among the population, more individuals suffer from numerous symptoms without seeking medical attention. Hence, proper measures should be taken to arise awareness in women and give proper ways to improve the symptoms of PMS.

Conclusion

The study concluded that mefenamic acid is effective in treating premenstrual syndrome in women, with more treated individuals experiencing a satisfactory outcome. While there is still no definitive treatment procedure, the usage of mefenamic acid and its dose in PMS remains controversial. Based on our study, mefenamic acid may be considered as an effective treatment choice. However, further randomized trials involving larger cohorts are necessary to substantiate this claim.

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