Original Article

An open clinical trial of Mefenamic Acid in Primary Dysmenorrhoea of Medical Students of Sylhet MAG Osmani Medical College, Sylhet

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Abstract

Background: Dysmenorrhea is one of the most common gynecological disorders among adolescent girls. **Material and Methods:** This was an open clinical trial conducted in the Department of Pharmacology and Therapeutics, Sylhet MAG Osmani Medical College, Sylhet from July 2018 to June 2019. It involved 45 unmarried female medical students of Sylhet MAG Osmani Medical College, Sylhet with primary dysmenorrhea and moderate to unbearable pain during menstruation (baseline VAS score 4cm or above). Diagnosis of primary dysmenorrhea was confirmed by gynaecologist. Visual Analog Scale (VAS), and Cox Menstrual Symptom Scale (CMSS) were used for grading of pain severity and duration of pain respectively before treatment. **Result:** Each participant received 250 mg Mefenamic acid every 12 hourly for 5 days. The treatment course continued for three menstrual cycles. VAS and CMSS were assessed in each cycle. The VAS score was significantly decreased from baseline (7.02 ± 0.72) to end of treatment at 3rd cycle (3.56 ± 0.55 ($p<0.001$). The CMSS also significantly decreased from baseline (3.96 ± 0.21) to end of treatment at 3rd cycle (1.33 ± 0.48) ($p<0.001$). Recorded adverse effects were nausea and or vomiting (24.4%), heart burn (31.1%) and dizziness (2.2%) were mild and no discontinuation was needed. **Conclusion:** Mefenamic acid is effective and safe in primary dysmenorrhoea.

Keywords: Primary dysmenorrhoea, Mefenamic acid, female medical students

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Introduction

Dysmenorrhea is one of the most common gynecological disorders among adolescent girls. Primary dysmenorrhea (PD) is defined as recurrent, crampy pain occurring with menses in the absence of identifiable pelvic pathology. It is unusual for symptoms to start within the first six months after menarche.[1] Symptoms typically accompany the start of menstrual flow or occur within a few hours before or after onset, and last for the first 24–48 hours.[2] It should be noted that 10-15% of women experience severe symptoms disrupting 1-3 days in their monthly life which are considered as the common causes of absenteeism from work and decrease the quality of life.[3]

Dysmenorrhea is caused by ischemia-associated uterine contractions and increases sensitivity in uterine nerves. It also happens in terms of prostaglandins, vasopressin and leukotrienes in the endometrium.[4]

Various ways have been recommended to treat the primary dysmenorrhea, such as yoga, massage, transcutaneous electrical nerve stimulation, vitamins, nutritional supplements and herbal medicine. Non-pharmaceutical treatments are acupuncture and surgery, of which some may have adverse effects or be contraindicated in certain groups of women. Prescribed medications include prostaglandin synthesis inhibitors and non-steroidal anti-inflammatory drugs (NSAIDs) to reduce the pain.[4]

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Mefenamic acid is a conventional and non-selective NSAID. It is easily accessible over the counter and is widely used by most local adolescents and adults for dysmenorrhoea. The dosage is 250 mg 12 hourly orally, to be taken three times/day after meal.[5]

In one uncontrolled trial, mefenamic acid, which inhibits PG synthesis and binding of PG to the cells, decreased uterine activity in dysmenorrhea with complete pain relief in 67 of 75 cycles treated.[6] In another study Nesa et al.[7] found that mefenamic acid decreases the severity of dysmenorrhea with adverse effects of gastrointestinal upset (2.0%) and respiratory distress (2.0%).

The present was designed to examine the clinical efficacy of mefenamic acid in the treatment of primary dysmenorrhea. Mefenamic acid was selected for this trial because of its pronounced inhibitory action on PG and the low incidence of mild side effects, as compared to the earlier aspirin-like substances.

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Material and Methods

This was an open clinical trial conducted in the Department of Pharmacology and Therapeutics, Sylhet MAG Osmani Medical College, Sylhet from July 2018 to June 2019. Forty-five unmarried female medical students of Sylhet MAG Osmani Medical College, Sylhet with primary dysmenorrhea and moderate to unbearable pain during menstruation (baseline VAS score 4cm or above) were included. Patients with a history of bronchial asthma, peptic ulcer disease, cholecystitis, pelvic inflammatory disease, previous history of abdominal or pelvic surgery; and those were using other medications such as sedative, anxiolytic, antidepressant, hormone preparation, antihistamine and The participants whose mean score of pain severity were less than 4 (based on VAS) were excluded from the study. Informed written consent was taken from the participants after explaining the process and purpose of the study in detailed. The clinical histories were taken. Each participant was examined thoroughly. All the findings, previous history and investigations were recorded. The diagnosis of primary dysmenorrhoea was made based on having characteristics of pain during menstruation and ruling out any history of pelvic disorders. The characteristics of pain in primary dysmenorrhoea are supra-pubic cramps which appeared in first two years of menarche, begin a few hours or just after the onset of menstruation, and last 48–72 hours.[8] Diagnosis was confirmed by gynaecologist.

After selection of the participants and obtaining a written informed consent, the participants were given a form about their menstrual cycle; they were provided with instructions on how to fill out the form. Visual Analog Scale (VAS),[8,9] and Cox Menstrual Symptom Scale (CMSS) were used for grading.[10]

In order to assess pain severity, a 10 cm visual analog scale (VAS) was applied, which is a standard pain assessment tool.[9] The pain VAS is usually a horizontal line, 10 cm in length, defined by descriptive words of "no pain" (score of 0) and "very severe pain" (score of 10). Participants were asked to put a mark on the line that they felt represented the most severe pain that experienced during menstruation. The pain score was determined by measuring the distance between the score of 0 and the participants' mark in centimeters using a ruler. According to the 10-point VAS, mild dysmenorrhoea was defined as score of 0-3, moderate as score of 4-6 and severe as score of 7-10.[8]

Pain duration was measured from the onset of uterine cramps until they ended. CMSS was applied for the assessment of pain duration. Based on CMSS score, pain duration was categorized as follows: score 0: no pain; score 1: ≤ 0-0.5 hours of pain; score 2: 0.5-1 hours of pain; score 3: >1 hour of pain; score 4: >1 day of pain.[10] The participants were asked to record the longest duration of menstrual pain in the first three days of menstruation on special forms, based on CMSS score.

The demographic and menstrual condition of participants such as age, educational level, menstrual history consist of age at menarche, regularity and duration of menstrual cycles were recorded. In addition to this body mass index (BMI) was calculated from Height and Weight.

Each participant with primary dysmenorrhoea received 250 mg Mefenamic acid every 12 hourly for 5 days (5 days in a month, from two days before the menstruation until the first three days).

As soon as the treatment started, they were asked to record their most severe pain during menstrual period using VAS and its duration (onset of uterine cramps until they ended) in the first three days using Cox Menstrual Symptom Scale (CMSS). The participants were also asked if they were taken any analgesics for their pain; if so, the name and dosage of the medication were recorded in the treatment form.

The intensity of pain and duration of pain were assessed using the VAS and CMSS respectively at the end of the first, second and third menstrual cycles of treatment. Follow-up of participants for the assessment of menstruation characteristics were also done in this period. Likewise, participants' pain intensity was recorded before taking more analgesics whenever needed for additional relief.

The treatment course continued for three menstrual cycles, and then all the forms were collected. Any drug related adverse effects were noted in each follow up visit.

Ethical consideration:

(1) After explaining the purpose of study, informed written consent was taken from each participant. (2) Prior to the commencement of the study, approval of the ethical committee of Sylhet MAG Osmani Medical College, Sylhet, was taken.

Results

The mean age of patients was 20.02 ± 1.50 years (range, 17-23 years) and the mean BMI (Kg/M^2) of the patients was 22.83 ± 2.45 (range, 17.05-27.41).

The VAS scores were 7.02 ± 0.72, 5.91 ± 0.72, 4.76 ± 0.68 and 3.56 ± 0.55 at baseline, first cycle, second cycle and third cycle respectively. The VAS score was significantly decreased from baseline to end of treatment at 3rd cycle (F=343.764; p<0.001) (Figure-1).

The percentage reduction of VAS was 15.38%, 31.87% and 48.88% at first, second and third cycle respectively (Figure-2).

The Cox Menstrual Symptom Scale score significantly decreased from baseline to end of treatment at 3rd cycle (3.96 ± 0.21, 3.09 ± 0.42, 2.09 ± 0.47 and 1.33 ± 0.48 at baseline, first cycle, second cycle and third cycle respectively. The Cox Menstrual Symptom Scale score significantly decreased from baseline to end of treatment at third cycle (F=541.903; p<0.001) (Figure-3).

The percentage reduction of Cox Menstrual Symptom Scale score was 21.85%, 47.22% and 66.30% at first, second and third cycle respectively (Figure-4).

Recorded adverse effects were Nausea and or vomiting (24.4%), Heart burn (31.1%) and Dizziness (2.2%). Reported adverse effects were mild and no discontinuation was needed (Figure-5).

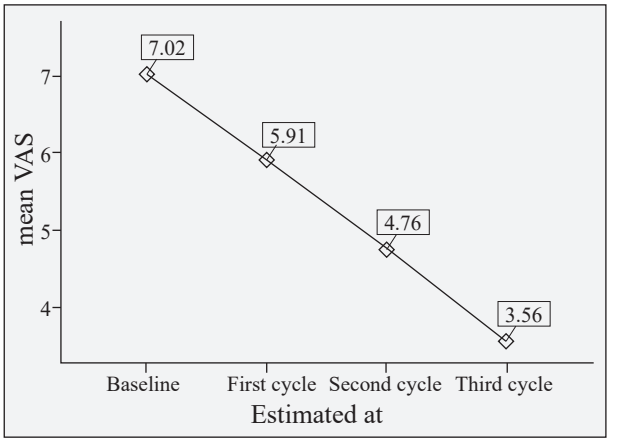

Figure-1: Visual analogue scale (VAS) score estimated before initiation of treatment and after 1st, 2nd and 3rd cycle of treatment (n=45)

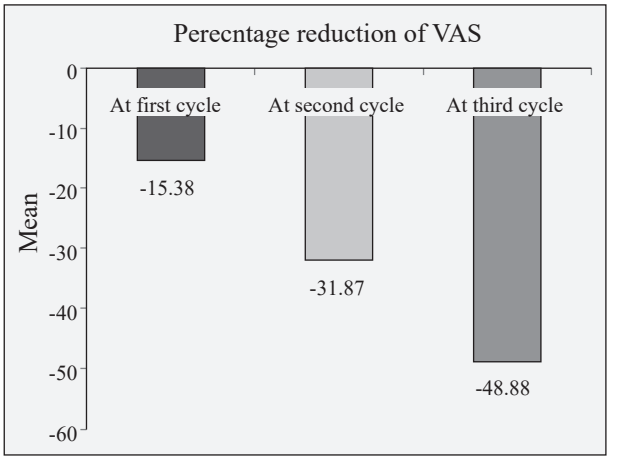

Figure No 2- Percentage reduction VAS score estimated after 1st, 2nd and 3rd cycle (n=45)

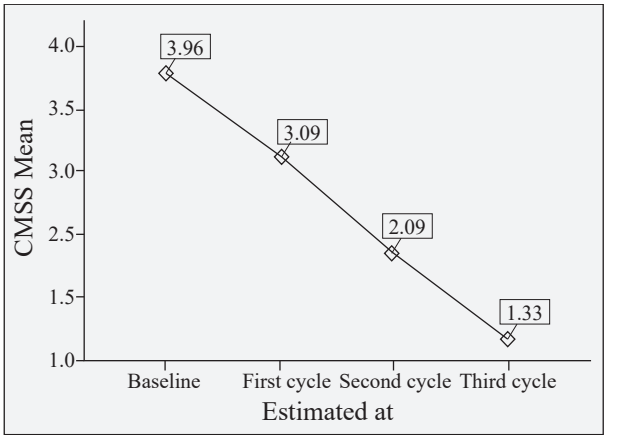

Figure-3: Cox Menstrual Symptom Scale (CMSS) score in estimated before initiation of treatment and after 1st, 2nd and 3rd cycle of treatment of Mefenamic acid (n=45)

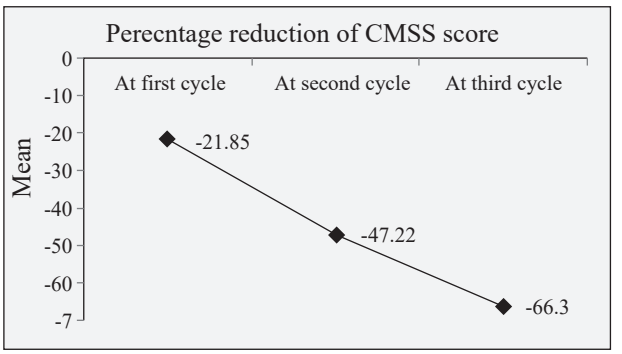

Figure No-4 Percentage change in CMSS estimated after 1st, 2nd and 3rd cycle (n=45)

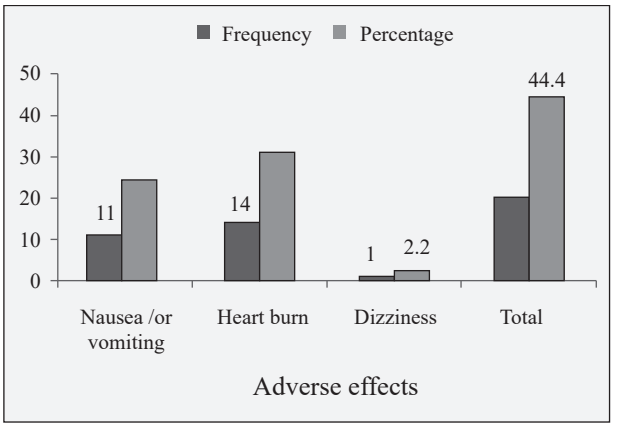

Fig 5: Distribution of patients by adverse effects (n=45) (Multiple response)

Discussion

Primary dysmenorrhea can be managed by three approaches, pharmacological, non-pharmacological and surgical. Best documented option by far is the pharmacological approach whereas all other approaches have variable evidences.[11] Higher concentration of PGF2α is present in menstrual fluid of women suffering from primary dysmenorrhea hence inhibition of Prostagladin synthesis has become the main treatment approach.[12] On account of the PG-based etiology of primary dysmenorrhoea, the current most common pharmacological treatment for dysmenorrhoea is non-steroidal anti-inflammatory drugs (NSAIDs).[13]

In this study the mean age of participants was 20.02 ± 1.50 years (range, 17-23 years). Similar mean age of the patients with primary dysmenorrhea was reported in several studies.[7,14-16] The mean BMI (Kg/M^2) of the patients was 22.83 ± 2.45 (range, 17.05-27.41). This result was consistent with other studies.[16,17] In this study the pain of dysmenorrhoea measured by VAS scores was significantly decreased from baseline to end of treatment at 3rd cycle ($p<0.001$). This finding was reduction of VAS after treatment of Mefenamic was reported in several studies.[4,14,15,17,18]

The Cox Menstrual Symptom Scale score significantly decreased from baseline to end of treatment at third cycle ($p<0.001$). After treatment with Mefenamic acid pain days were significantly decreased from baseline to end of treatment similar findings were observed in other studies.[15,19,20]

Mefenamic acid, which is a well-known medication for the treatment of dysmenorrhoea; the results are similar to the findings of the present study. One study shows that Mefenamic Acid is a suitable drug for the treatment of primary dysmenorrhoea, especially in those suffering from moderate pain.[21] In another study, Mefenamic Acid has been proposed as a dominant treatment for dysmenorrhoea.[22]

In this study recorded adverse effects were Nausea and or vomiting (24.4%), Heart burn (31.1%) and Dizziness (2.2%). Reported adverse effects were mild and no discontinuation was needed. Masoumi et al.[21] reported that adverse of Mefenamic acid were nausea (15%), vomiting (1.5%) and diarrhea (10.2%). In general, the reported side effects of mefenamic acid group included gastrointestinal complications reported in several studies.[7,15,17]

Our results have confirmed the view that the use of prostaglandin synthetase inhibitors and prostaglandin antagonists greatly relieves pain and other side effects of dysmenorrhea that may be caused by PG. For most patients, mefenamic acid constitutes safe and effective treatment of primary dysmenorrhea and its associated gastrointestinal symptoms. It represents a rational form of therapy for this distressing syndrome, advantageous because it is short-term treatment that inhibits PG synthesis and action during menses—the time of maximum release of preformed PG.[23]

Limitations in this study were (1) This open clinical trial was conducted in a single medical college, (2) Number of samples was small and (3) treatment period was only 3 months and long-term efficacy was not possible.

Conclusion

The results of this study showed that taking Mefenamic acid decreased the severity and duration of dysmenorrhea with mild gastrointestinal side effects. In conclusion, Mefenamic acid 250mg twice daily for 5 days is effective and safe treatment option in primary dysmenorrhea**.** Further clinical trial involving large sample with long duration and multicenter is needed to justify the effect of Mefenamic acid in primary dysmenorrhea.

Author Contributions:

Amirun Nahar and Md. Ansar Khan conceived and designed the study. Amirun Nahar prepared the material and acquired and analysed the data. Amirun Nahar wrote the first draft of the manuscript, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflict of interest: The authors declared no conflicts of interest.

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