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ROLE OF MEFENAMIC ACID IN MANAGEMENT OF HEAVY MENSTRUAL BLEEDING OF ENDOMETRIAL ORIGIN

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ABSTRACT

Background: Heavy menstrual bleeding (HMB) is a common clinical problem among reproductive women .Anemia which may be difficult to treat even with continuous iron therapy is the most common complication, in addition to adverse impact on women's physical psychological and social life .The abnormal uterine bleeding of endometrial dysfunction is thought that is the result of increased blood loss from vasodilation due to prostaglandins or from increased fibrinolytic activity within the endometrium .So we suggest that Nonsteroidal anti-inflammatory drugs (NSAIDs) which prevent formation of prostaglandins, have high efficacy in reducing menstrual blood loss and also pain **Objective** Main purpose: study the efficacy of mefenamic acid in management heavy menstrual Bleeding Second purpose : 1-the prevalence of primary dysmenorrhea in our study's patients. 2-study the efficancy of MFA in reducing the severity of abdominal pain in patients with dysmenorrhea .3-Adverse side effects during treatment .**Methods** :An experimental pilot study (prospective) covered 50 patients among 19-33 years old ,presented with heavy menstrual bleeding after excluding pregnancy, structural and iatrogenic causes coagulation defects and ovulatory disorders at Tishreen university Hospital in Lattakia between 2021- . Complete menstrual history was taken pregnancy test was done, physical examination and Ultrasound were performed.We gave them mefenamic acid 500 mg tablets three times daily from the first to the fifth Day of menstrual bleedi .Pictorial bleeding assessment chart (PBAC) number of pads ,cycle Duration and Hemoglobin level.were used for assessing blood loss volume. Visual Analog Scale (VAS) was used for assessing the severity of pain. **Results**: The current study showed that after initiation of treatment by Mefenamic acid, a decrease in bleeding loss volume (PBAC score) was observed with statistically significant differences. The decrease after a month was 19%, after 2 months was 34% ,after three months was 38% .There was a significant decrease in number of pads as follow (17% after 1st month, 32% after 2nd month, 35% after 3rd month) There was a decrease in cycle duration without statistically differences. The hemoglobin level was increased significantly (4%). 88%Of patients had dysmenorrhea along with heavy menstrual bleeding and a statistically significant decrease in VAS score was observed after 3 months of treatment (75%). **Conclusion**: Mefenamic acid has high efficacy in reducing menstrual bleeding and reducing pain and is available, short-term treatment with few side effects.

KEYWORD: Heavy menstrual bleeding, Dysmenorrhea, Mefenamic acid.

INTRODUCTION

Heavy menstrual bleeding (HMB) is a common clinical problem among reproductive age women with approximately 5-10% of women seeking medical attention annually.[1]

Social inconvenience and anemia which may be difficult to treat even with continuous iron therapy are the most common complications of HMB in women.[2]

HMB of endometrial origin is clinically defined as regular menstrual periods lasting more than 7 days and /or blood loss greater than or equal to 80 ml in the absence of other causes of abnormal uterine bleeding (PALM-COEIN).[3,4]

Heavy menstrual bleeding is also defined as blood loss in a manner that interferes with physical, psychological and social quality of one's life.[5]

Laboratory investigations indicate that heavy menstrual bleeding is associated with two main factors:
1- An increase in fibrinolysis within the endometrium.[6]
2-An imbalance in prostaglandins (PGs) It has been demonstrated that women who experience heavy menstrual bleeding have relatively high serum levels of prostaglandin E2 and prostacyclin which induce vasodilation and prevent the local accumulation of platelets.[7] And lower levels of prostaglandin F2a, which cause vasoconstriction.[8]

Furthermore, women with HMB have more prostaglandin E receptors in their uteri than women who have lighter menstrual periods.[9]

Therefore, it has been suggested that prostaglandin synthesis inhibitors could be an effective and appropriate treatment for heavy menstrual bleedig.[10]

Non-steroidal anti-inflammatory drugs (NSAIDs) are highly effective in the reduction of menstrual bleeding.[11,12]

Mefenamic acid is the most commonly studied NSAIDS for heavy menstrual bleeding.[13,14]

Mefenamic acid is amember of the anthranilic acid derivatives class of Nonsteroidal anti-inflammatory drugs(NSAIDS). It inhibits both isoforms of the enzyme cyclooxygenase (COX1-COX2) this prevents formation of prostaglandins.[15,16]

So it was used for the menstrual pain as well as menorrhagia.[17,18]

METHODS

This was an experiment pilot study (prospective), appearing the efficacy of Mefenamic acid in management of heavy menstrual bleeding.

Our study covered 50 patients, presented with HMB and matched the inclusion and exclusion criteria, they were recruited from gynecology clinic at Tishreen university hospital in Lattakia, Syria during 2021-2022.

Inclusion criteria were as follows:
1. Age 18-40 years.
2. Regular ovulatory cycles.
3. Stable hemodynamically.
4. Normal findings on physical examination and Ultrasound.
5. Negative Pregnancy test.

Exclusion criteria included
1. Other causes of uterine bleeding (PALM-COEIN) except Endometrial etiology.
2. Vaginitis, endometritis, and pelvic inflammatory disease.
3. History of hepatic or renal impairment.
4. Presence of endocrine disorders or ovulatory disorders.
5. Presence of coagulation disorders.
6. Use of copper IUD.
7. Taking hormone drugs during the last three months or Depot Medroxyprogesterone acetate during the last six months.
8. Taking drugs that affect the HPO axis, drugs that cause hyperprolactinemia, anticoagulant drugs or tamoxifen.
9. Contraindication of use Mefenamic acid.

First we explained the trial to the patient and we answered her questions.

Then, the patient consented to take part in the study, signed an informed consent form and was assured that her information would be kept confident.

After that, we took menstrual history, any other associated symptom, sexual history, medical history, surgical history and contraceptive history.

Later physical examination, ultrasound, Speculum examination and pregnancy test were performed.

Our study included two phases:
First one: the month before treatment (control cycle) we recorded:
- The volume of bleeding on the pictorial Blood Assessment chart (PBAC).
- Number of sanitary pads used during menstrual period.
- Duration of menstrual period.
- Hemoglobin level.
- The severity of pain on Visual Analog Scale (VAS).

Second one: The three months of treatment (intervention cycles), the patients received tablets containing 500 mg Mefenamic acid three times a day after meals for five days from the first day in the menstrual cycle.
All patients were followed up for three consecutive cycles (intervention cycles) we asked the patient about:
- BPAC score (after 1^{st},2^{nd}, 3^{rd} month) of treatment.
- Number of pads used (after 1^{st},2^{nd}, 3^{rd} month) of treatment.
- Duration of menstrual period (after 1^{st},2^{nd}, 3^{rd} month) of treatment.
- Hemoglobin level after three months of treatment.
- The severity of pain after three months of treatment.
- Any adverse effects during treatment.

Statistical analysis
- The data were expressed as proportions and means.
- Friedman test and paired T-student were used.
- Data was analyzed with SPSS version 20.
- A p-value of < 0.05 was considered statistically significant.

RESULTS

This study was involved 50 patients among 19-33 years old, and the mean age was 25+-3.
The distribution of patients as martial status, 56% were single and 44% were married.

- There was a marked decrease in BPAC score during the months of intervention in the patients receiving Mefenamic acid (19 % after 1st month, 34% after 2nd month ,38% after 3rd month) with p-value <0.05.
- There was a marked decrease in number of pads used during the months of intervention (17% after 1st month, 32% after 2nd month, 35% after 3rd month) with p-value <0.05.
- Duration of menstrual period decreased (1% after 1st month, 1% after 2nd month, 4% after 3rd month), but this decrease wasn't significant (p-value=0.095).
- Hemoglobin level increased significantly (4% after three months of intervention) with p-value <0.05.

Dysmenorrhea

- 44 out of 50 patients (88%) had dysmenorrhea along with HMB before treatment and the distribution as Severity of pain (6% no pain, 13% mild, 46 % moderate, 16% severe).
- After intervention the distribution was as (31% no pain, 12% mild, 7% moderate, 0% severe).
- The severity of pain (Vas score) had a marked decrease after three months of intervention 75% with P-value <0.05.
- Side effects during the three months were reported in 6 patients out of total (12%) and Nausea was the most common.

Table-1: menstrual blood loss (BPAC score) before and after intervention.

	PBAC (mean ± SD)	Change by	Min value	Max value
Before treatment	121.6 ± 8.9	0%	102	139
After 1 month	98 ± 7.1	19%	84	111
After 2 months	80.5 ± 7.9	34%	63	96
After 3 months	75.4 ± 7.1	38%	61	90
p-value	< 0.0001			

Table-2: Number of pads used during menstrual period before and after intervention.

	Number of Pads (mean ± SD)	Change by	Min value	Max value
Before treatment	23.1 ± 5.2	0%	15	39
After 1 month	19.1 ± 4.2	17%	13	31
After 2 months	15.8 ± 3.9	32%	9	27
After 3 months	14.9 ± 3.5	35%	10	25
p-value	< 0.0001			

Table-3: Duration of menstrual period before and after intervention.

	Duration of menstrual period (mean ± SD)	Change by	Min value	Max value
Before treatment	8.3 ± 1.8	0%	6	13
After 1 month	8.2 ± 1.9	1%	5	12
After 2 months	8.2 ± 1.6	1%	5	12
After 3 months	1.4±8	4%	5	11
p-value	0.095			

Table-4: Hemoglobin level before and after intervention.

	Hemoglobin level (mean ± SD)	Change by	Min value	Max value
Before treatment	9.9 ± 0.5	0%	8.8	11
After 3 months	10.3 ± 0.6	4%	9	11.4
p-value	< 0.0001			

Table-5: Distribution of patients according severity of pain before and after intervention.

	No pain	Mild pain	Moderate pain	Severe pain
Before treatment	6 (12%)	13 (26%)	23 (46%)	8 (16%)
After 3 months	31 (62%)	12 (24%)	7 (14%)	0 (0%)

Table-6: VAS score before and after intervention.

	VAS (mean ± SD)	Change by	Min value	Max value
Before treatment	4 ± 2.3	0%	0	7
After 3 months	1 ± 1.5	75%	0	4
p-value	< 0.0001			

Table-7: Side effects during intervention.

Side effects	Heartburn	Nausea	Diarrhoea	Nervosness	Abdominal pain	Total
Number	1	2	1	1	1	6

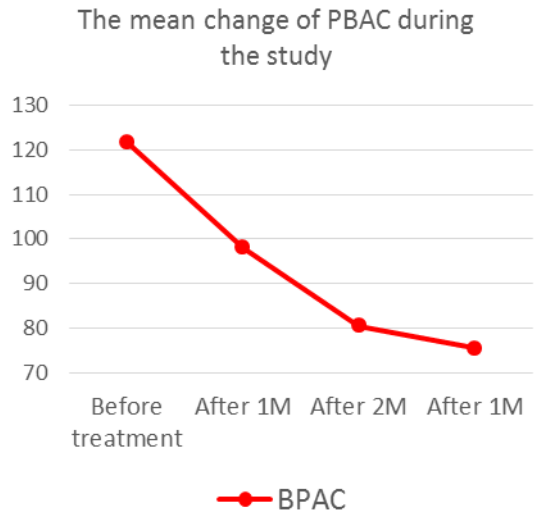

Figure 1: menstrual blood loss (BPAC score) before and after intervention.

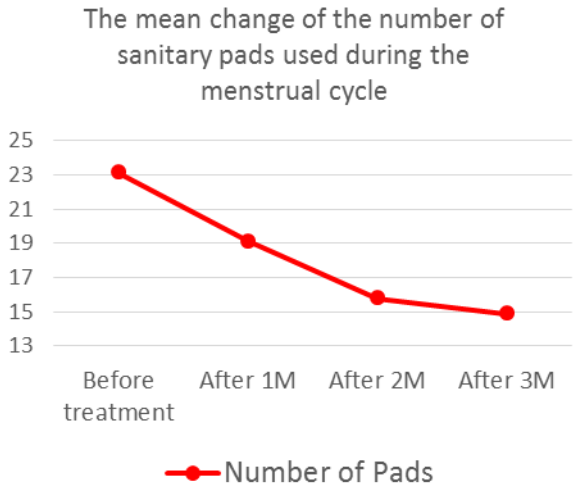

Figure-2: Number of pads used during menstrual period before and after intervention.

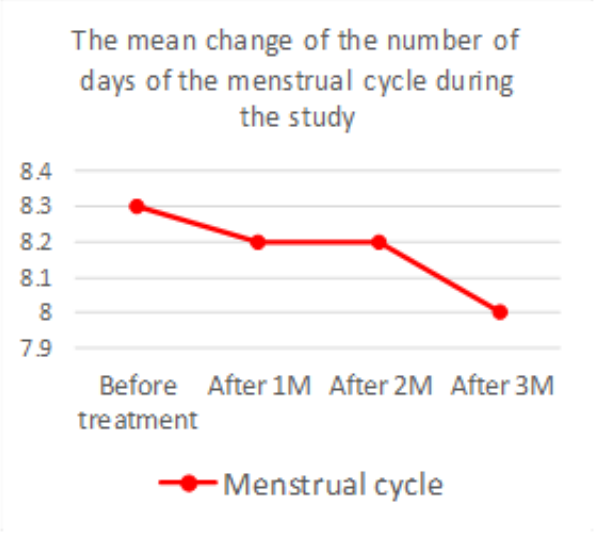

Figure 3: Duration of menstrual period before and after intervention.

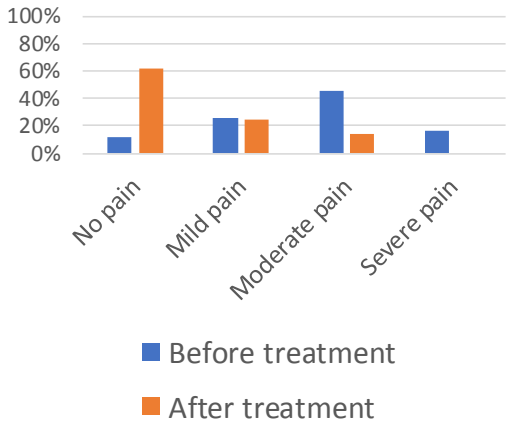

Figure 4: Distribution of patients according severity of pain before and after intervention.

DISCUSSION

Heavy menstrual Bleeding is one of the most common reasons why women consult gynecologists. Effective medical treatment will improve the patient's choice and provides an alternative to surgery.

In the present study it was observed that with Mefenamic acid there was a significant improvement in HMB for all the outcome parameters (BPAC score Number of pads, Hemoglobin level) compared to the baseline except uduration of menstrual period (The median reduction was 38%).

And there was a significant decrease in severity of dysmenorrhea (the median decrease was 75%).

M.khajehei et al, in Iran 2013, conducted a study on 40 patients with heavy menstrual bleeding who were treated with MFA. after 3 cycles, the blood loss volume reduced significantly (by 40%) which is consistent with our findings.[19]

Sohil kumar et al, in India 2018, conducted a study on 34 patients with dysfunctional uterine bleeding (DUB), showed that MFA reduces the menstrual bleeding volume (by 43.39%) and improves dysmenorrhea significantly.[20]

Tahereh Eftekhar et al, in Iran 2019, involved 30 patients with HMB who were given MFA and followed for two cycles. They have reported that:

The decrese of bleeding volume wasn't significant (p-value = 0.262),the duration of menstrual period decresed significantly (p-value =0.001), the Hemoglobin level didn't change significantly (these findings aren't consistent with ours).

The number of pads reduced significantly (p-value=0.001) there was a significant decrese in severity of dysmenorrhea (these findings are consistent with ours).[21]

CONCLUSION

Mefenamic acid is highly effective in reducing heavy menstrual bleeding and also is cheap, available, easy to use and the duration of treatment is short.

Moreover, MFA improves anemia and treats dysmenorrhea associated with HMB.

So we suggest MFA to be considered as first line therapy for HMB.

REFERENCES

1. Philipp CS Antifibrinolytics in women with HMB Thromb Res., 2011; 127(Suppl 3): S113–S115.
2. Srinil S, Jaisamrarn U Treatment of heavy menstrual bleeding of endometrial origin with tranexamic acid. Med Assoc Thail, 2005; 88: 1.
3. Marret H, Fauconnier A, Chabbert-Buffet N, Cravello L, Golfier F, Gondry J et al Clinical practice guidelines on HMB: management of abnormal uterine bleeding before menopause. Eur J Obstet Gynecol Reprod Biol., 2010; 152(2): 133–137.
4. Munro MG, Critchley HO, Fraser IS: T e FIGO classification of causes of abnormal uterine bleeding in the reproductive years. Fertil Steril, 2011; 95(7): 2204.
5. Geirsson RT, Eggebø T. Core outcomes for reporting women's health. Acta Obstet Gynecol Scand, 2014; 93: 843–4.
6. Gleeson NC: Cyclic changes in endometrial tissue plasminogen activator and plasminogen activator inhibitor type 1 in women with normal menstruation and essential menorrhagia. Am J Obstet Gynecol, 1994; 171: 178.
7. Lethaby A, Augood C, Duckitt K, Farquhar C. Nonsteroidal anti-inflammatory drugs for heavy menstrual bleeding. Cochrane Database Syst Rev, 2007. issue 4: Art. No.: CD000400. [http://dx.doi.org/10.1002/14651858.CD000400.pub 2].
8. Sugino N. The role of oxygen radical-mediated signaling pathways in endometrial function. Placenta, 2007; 28(suppl 1): S133-S136. [http://dx.doi.org/10.1016/j.placenta.2006.12.002]
9. Hickey M, Fraser I. Clinical implications of disturbances of uterine vascular morphology and function. Baillieres Clin Obstet Gynaecol, 2000; 14(6): 937-951. [http://dx.doi.org/10.1053 /beog. 2000.0136]
10. Adelantado JM, Rees MCP, Bernal AL, Turnbull AC. Increased uterine prostaglandin E receptors in menorrhagic women. BJOG, 1988; 95(2): 162-165. [http://dx.doi.org/10.1111/j.1471-0528.1988. tb06846.x]
11. Sambrook AM, Cooper K. RCOG guidelines on menorrhagia – time for an update? Current Obstetrics & Gynaecology, 2005; 15(6): 382-386. [http://dx.doi.org/10.1016/j.curobgyn.2005.09.001]
12. Marjoribanks I, Proctor M, Farquhar C. Nonsteroidal anti-inflammatory drugs for primary dysmenorrhoea. Cochrane Database Syst Rev, 2003; 4: CD001751.
13. Lethaby A, Duckitt K, Farquhar C. Non-steroidal anti-inflammatory drugs for heavy menstrual bleeding. Cochrane Database Syst Rev, 2013. [cited 2017 Jan 24]. Available at: http://onlinelibrary. wiley.com /doi/10.1002/14651858.CD000400 .pub3/abstract;jsessionid=94F9FDAFF243FFBE504 877A60517E86C.f02t02.
14. Maybin JA, Critchley HO. Menstrual physiology: implications for endometrial pathology and beyond. Hum Reprod Update, 2015; 21: 748-61.
15. FDA Ponstel Label Updated February, 2008.
16. Drugs.com drugs.com international listings for mefenamic acid Page accessed July 3, 2015 prusakiewicz JJ, Duggan KC, Rouzer CA, Marnett LJ (August). "Differential sensitivity and mechanism of inhibition of COX-2 oxygenation of arachidonic acid and 2-arachidonoylglycerol by ibuprofen and mefenamic acid". Biochemistry, 2009; 48(31): 7353–5. Doi:10.1021/bi900999z. PMC 2720641. PMID 19603831.
17. Digital Medicines Information Suite". Medicines Complete. Doi:10.18578/bnf.855907230. Retrieved 2020-04-1873.
18. Austria-Codex (in German). Vienna: Österreichischer Apothekerverlag. Parkemed 500 mg-Filmtabletten, 2020.
19. M Khajehei, K Abdali,2 MSc; H Tabatabaee,3 MSc The effect of mefenamic acid and naproxen on heavy menstrual bleeding: A placebo-controlled study, 2013.
20. Sahil Kumar, Uma Tekur, Bhupinder Singh Kalra. Mefenamic acid and diclofenac in the treatment of menorrhagia and dysmenorrhea in dysfunctional uterine bleeding: a randomized comparative study, 2018.
21. Tahereh Eftekhar, Marjan Ghaemi, Aref Abedi, Mahboobeh Shirazi. Comparison of Misoprostol and Mefenamic Acid on Reducing Menstrual Bleeding in Patients Suffering From Heavy Menstrual Bleeding, 2019.