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STUDY OF ORMELOXIFENE IN MANAGEMENT OF AUB IN A TERTIARY CARE CENTRE

Gynaecology

Sujata Kumari Assistant Professor, Deptt. Of OBG , P.M.C.H, Patna.
Dr Anamika* Senior Resident, Deptt. Of OBG , P.M.C.H, Patna.*Corresponding Author

ABSTRACT

BACKGROUND: In today's world where women represent a major sector of paid work force in both the developing and developed countries, any regular source of debility like Heavy menstrual bleeding(HMB) , the most common presentation of Abnormal uterine bleeding(AUB) has important economic and personal consequences. **AIMS AND OBJECTIVES:** To determine the efficacy of ormeloxifene in reducing blood loss in AUB as assessed by PBAC score, endometrial thickness and hemoglobin.**MATERIAL AND METHOD:** This was a hospital based prospective study done on 42 patients of AUB visiting the gynaecological opd of P.M.C.H, Patna from January 2019 to December 2019. **RESULTS:**The mean age of patients was 39.64%(range 35-50 years). Most of women were multiparous. Mean PBAC score after treatment was 73 and overall reduction in menstrual blood loss was 85.71%. The mean endometrial thickness was 7.81 before treatment and was 4.94% after treatment. Mean hb was 9.64% before treatment and 10.84% after treatment which shows stastistically significant increase in Hb%. There was 87.71% reduction of HMB and 90% reduction in passage of blood clots.11.9% failed to respond to ormeloxifene. The side-effects were amenorrhoea-9.5%, delayed or decreased menses-7.14% and GI symptoms-2.38%. **CONCLUSION:**Ormeloxifene is non-hormonal drug efficacious in reducing HMB in AUB with minimum side-effects.

KEYWORDS

AUB, HMB, Ormeloxifene, SERM, non-hormonal.

INTRODUCTION

AUB is defined as bleeding from uterine corpus that is abnormal in volume, character, frequency and duration and occurs in absence of pregnancy-ACOG. About 5% of women in the age group of 35-50 years of age seek medical help for heavy menstrual bleeding (HMB) which accounts for 12% of gynaecological referrals.[1] HMB is objectively defined as monthly blood loss of more than 80 ml. Monthly blood loss in excess of 60 ml may result in iron deficiency anaemia.[2] There are variety of approaches to medical management of AUB ranging from hormonal treatment in the form of combined oral contraceptive pill (COCPs), Progestogens, Danazol and Gonadotropin Releasing Hormone (GnRH) agonists to non hormonal drugs like prostaglandin synthetase inhibitors, antifibrinolytics and Non-steroidal Antiinflammatory Drugs (NSAIDs). Medical treatment needs to be individualized and is not suitable for all ages. It is noticed that the symptoms reappear once the therapy is stopped. And may not be very compliant as it is associated with many of side effects.

Hormonal treatment, which is the most widely used (Progestogens or Oestrogen + Progestrone) is associated with side effects, which include fatigue, mood changes, weight gain, nausea, bloating, oedema, headache, depression, loss of libido, irregular bleeding and atherogenic changes in the lipid profile.[3]

Patients not responding to medical treatment are offered surgical line of treatment. But it is invasive procedure not suitable for all ages. It is also more expensive and associated with post op morbidity.

So, ideally a medical approach should be considered as first line of treatment in AUB but without the side effects of hormonal drugs. This brings in picture a designer drug which can block the action of estrogen on endometrium but not its beneficial effect on other organs which cause side effects in case of hormonal steroids -"SERMS(selective Estrogen Receptor Modulator)". Ormeloxifene is an optimally designed SERM with such response. The current study thus evaluates how efficacious the drug is in improving HMB and its side effects.

MATERIAL AND METHODS

This was a hospital based prospective study done on 42 patients of AUB visiting the gynaecological opd of P.M.C.H, Patna from January 2019 to December 2019.

Inclusion criterion

Women aged 35-50 years with diagnosis of AUB with heavy menstrual bleeding were included.

Exclusion criterion

- Pregnancy/desirous of pregnancy, lactation.
- women with infections, malignancy, liver or kidney disease, severe anemia, coagulopathy.
- history of drug allergy.
- patients with pelvic pathology, fibroid, PCOD, cervical hypertrophy, endometrial thickness >12mm.

METHOD

Patient enrolled in study underwent history taking, physical examination and investigations-TVS , Haemolglobin.

Tab. Ormeloxifene was given in dose of 60 mg twice a week for 3 months (after informed consent), starting it within day 5 of cycle each month/ day of visit if there was history of bleeding pv > 10 days.

2 pre-treatment baseline cycles were compared to 3 consecutive treatment cycles.

They were advised to attend opd on monthly basis or earlier if needed.

Monthly PBAC score forms were filled to assess the amount of blood loss each menstrual cycle.

In this study HMB was defined as PBAC score >100.

At end of 3 months mean PBAC score was calculated, Hb % was evaluated and TVS was repeated for endometrial thickness(ET).

Stastical analysis

Microsoft excel.

RESULTS

The mean age of patients was 39.64%(range 35-50 years). Table 1.

Table 1:Age distribution

AGE(years)	Number(n=42)
35-40	24
40-45	8
45-50	10

Most of women were multiparous. Table 2.

Table 2: Parity distribution.

PARITY	Number(n=42)
0	2
1	1
2	16
3	15
4	5
5	3

PBAC score before treatment was 262.26%.Table 3.

Table 3:PBAC score before treatment

PBAC SCORE	Number(n=42)
100-200	5
200-300	21
>300	16

Mean PBAC score after treatment was 73 and overall reduction in menstrual blood loss was 85.71%. This was statistically significant.Table 4.

Table 4:Mean PBAC score after treatment

MEAN PBAC	Number(n=42)
<100	29
100-185	7
>185	1

The mean endometrial thickness was 7.81 before treatment and was 4.94% after treatment. The decrease in endometrial thickness was statistically significant.Table 5.

Table 5:Endometrial thickness before and after treatment

Endometrial thickness(mm)	Pretreatment	posttreatment
0-5	6	19
5-10	21	17
10-15	15	1

Mean hb was 9.64% before treatment and 10.84% after treatment. This was stastistically significant increase in Hb%.Table 6.

Table 6:Hemoglobin before and after treatment

HB	Pretreatment	posttreatment
6.5-7.5	1	0
7.5-8.5	4	0
8.5-9.5	11	3
>9.5	26	34

There was 87.71% reduction of HMB and 90% reduction in passage of blood clots.11.9% failed to respond to ormeloxifene. The side-effects were amenorrhoea-9.5%, delayed or decreased menses-7.14% and GI symptoms-2.38%. However none of the symptoms were severe enough to discontinue treatment.5.96% patients lost to follow up.

DISCUSSION

AUB is common and disruptive condition affecting the quality of life in women. Various medical therapies and surgeries have been advocated in its treatment . Present study was done to study efficacy and safety of ideal SERM ormeloxifene.

All patients were in age group 35-50 years. Majority of them belonged to 35-40 years. The mean age was 39.61%.

The majority of women were found to be multiparous. Most of them were of parity 2 or 3.

Blood loss during menstrual cycle was assessed by pictorial blood assessment chart(PBAC) score. In this study, PBAC score before treatment was 262.26. 88.1% of patients had PBAC score more than 200.

At the end of three months PBAC score had reduced by 87.83% which was stastically significant. Ormeloxifene competes with estradiol for binding with cytosol receptors. It not only blocks cytosol receptors but also causes their prolonged depletion and has long post withdrawal effect. Thus efficacy of drug improves with time which is depicted by increasing reduction in MBL with prolonged use.

The mean PBAC score at end of study was 73.7 reporting an overall reduction in MBL by 85.71%. Other studies done on sample size 50, 50 and 36 with same dosing reported stastically significant reduction in PBAC score.[4,5,6]

Present study showed side effects as amenorrhoea in 9.5%, decreased or delayed menses in 7.14% and GI symptoms in 2.38%. However studies by Neha et al showed no major side effects, Veena et al showed headache in 1, oligomenorrhoea in 8 and menopause in 4% and Mandal et al showed amenorrhoea in 5.56%, pain abdomen in 5.56%, gi symptons in 8.33% and headache in 2.78%.[4,5,6]

The mean endometrial thickness (in mm) before treatment was 7.81 and after treatment was 4.94. Hence there was reduction in ET which was a definitive objective evidence showing reduction in MBL. Ormeloxifene exhibits anti estrogenic activity like other drugs but also is more efficacious as it directly blocks estrogen receptor and thereby prevents mitogenic activity exhibited by eatrogen.

Studies using ormeloxifene in AUB have showed significant reduction in ET after treatment . Mean difference in ET was 2.87 in my study which was comparable to other studies.[4,6]

The mean hb was 9.64% before treatment and after treatment was 10.84%, a mean increase by 1.28%. This increase was almost similar to other studies.[4,6]

Another observation was that reduction in passage of clots was 90% at end of treatment.

11.9% failed to respond to treatment and it was observed that 80% who failed to respond had ET<=5 mm.

In various studies in majority of subjects menstrual cyclicity returned to normalcy after 3 months but the limitation of my study was lack to follow up after 3 months. So, it was not possible to comment upon return to normal cyclicity in my study.

Ormeloxifene is associated with other advantages. It can be started at any time of cycle. It controls bleeding within 48 hours. While preventing AUB it is concurrent contraceptive. It also offers perimenopausal bone and cardiovascular protection which is not found in other drugs treating AUB.

It has excellant safety index as reflected by lack of many side effects during clinical use.

Problems encountered with hormonal treatment can be averted by use of ormeloxifene which is non–steroidal, cost effective, can be started at any time of cycle in any type of AUB in all age groups from menarche to menopause.

CONCLUSION

Medical management of AUB should always be first line therapy. The preference should always be given to non-steroidal drugs like ormeloxifene, since steroidal drugs will only aggravate the existing endocrine dysfunction.

Ormeloxifene is highly efficacious in treatment of premenopausal AUB when given in dose of 60 mg biweekly for 3 months.

It is easy to administer, cost-effective, possess a high safety index and is associated with minimal side-effects. It can be started at any point of cycle and even during bleeding.

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