The Efficacy and Safety of Ormiloxifene, A Selective Estrogen Receptor Modulator in AUB(E)

Padma Rao[1], Shabina Khan[2]

ABSTRACT

Introduction: Abnormal uterine bleeding (AUB) is one of the most common cause for which women consult to their gynaecologists. The study of this drug was done to evaluate the efficacy along with adverse reactions of ormeloxifene in patients with abnormal uterine bleeding.

Material and methods: This was 3 months prospective study on 40 patients with complaints of abnormal uterine bleeding having PBAC Score more than 100. Ormeloxifene 60 mg twice a week was given for 3 months and follow-up at 4th, 8th ,12th week to assess for endometrial thickness by USG, Haem level, PBAC score and adverse effects of drug therapy.

Results: A total 40 patients with the mean age of 32.91±6.82 were taken. There was statistically significant decrease in, haemoglobin level, endometrial thickness and PBAC score.

Conclusion: Thus Ormeloxifene, cost effective, a non-steroidal, non-hormonal agent, with its convenient dose schedule provides effective and favourable medical treatment of AUB(E).

Keywords: Abnormal Uterine Bleeding, PBAC Score, Ormeloxifene.

INTRODUCTION

AUB is the term used to describe any shift from normal menstruation or from a normal menstrual cycle pattern which includes regularity, frequency, heaviness of flow, and duration of flow with wide variability[1]Chronic AUB is "bleeding from the uterus which is of abnormal induration, volume, and/or frequency and has been present for the majority of the last 6 months." AUB in adolescence results from anovulation and coagulation defects, in perimenarchal girls and perimenopausal women bleeding from HPO axis dysfunction and bleeding after menopause due to atropty of vagina or endometrium or polyps. Most common drugs which are used for medical management of AUB are NSAID- nonsteroidal anti-inflammatory drugs, progesterone, antifibrinolytics, estrogen progesterone combinations, GnRHanalogues, Danazol. Combined oral contraceptive pills, GnRH analogues, Danazol which are commonly used in AUB has certain side effects so not commonly used. Medical management is always the first option for management and surgery like hysterectomy should be the last option in the management of AUB.[1]

Ormeloxifene (SERM) is a benzopyran Selective Estrogen Receptor Modulator, blocks the cytosol receptors by binding competitively over estradiol. It acts as agonist on bone, vagina and antagonist in breast and uterus. The effect of SERM is on the vascular endothelium and it decreases loss of blood (AUB)so improvement of symptoms of AUB.[2-6] Current research aimed to study the acceptability efficacy, and adverse effects of ormiloxifene in AUB.

MATERIAL AND METHODS

A prospective study was carried out in Rohilkhand Medical College, Bareilly on 40 patients with AUB over the age of 35 years who have completed their family, and recorded over a period of 3 (10 October 2020 to 10 January 2021). SPSS 24 version was used for statistical analysis.

Inclusion Criteria: Patients presenting with abnormal uterine bleeding after excluding uterine pathology, congenital malformation and other organic causes for AUB.

Exclusion Criteria

Leiomyoma, liver dysfunction, heart disease. coagulopathies, endometriosis, malignancies of genital tract. pregnancy, lactating women in the first 6 months of postnatal period, history of abortion within last 3 months, renal disease, IUCD or pill users, thyroid disorder

Treatment Evaluation: Pre and Post

Three baseline menstrual cycles were compared before and after treatment with ormiloxifene. These parameters are:

A. Estimation of haemoglobin,
B. Thickness of endometrium in proliferative phase assessed by sonography transvaginaly
C. Total menstrual loss of blood by (PBAC) pictorial blood loss assessment chart.

PBAC more than 100 and blood loss greater than or equal to 80ml and was considered diagnostic of menorrhagia. Scoring was based on area of soakage, number and presence of clots.

Treatment Protocol: Tablet ormiloxefene 60 mg twice a week (according to day1 of menses) for 12 weeks and patients were advised to come for follow-up at 4th, 8th ,12th week.

[1]JR-III, Post Graduate Student, Department of Obstetrics and Gynecology, Rohilkhand Medical College and Hospital, Bareilly, [2]Professor, Gynecology, Rohilkhand Medical College and Hospital, Bareilly, India

Corresponding author: Dr. Padma Rao, G - Block, Room No. 3, Rohilkhand Medical College Campus, Bareilly, India

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RESULTS

The descriptive statistics of pre- and post-PBAC, endometrial thickness (ET) and hemoglobin (Hb) levels before and after treatment and side effects of drugs have shown in Tables.

Table no-1 showing there is significant reduction of flow during menses, the duration of cycle length increased after treatment of three months with ormiloxifene. P value is (<0.001) shows significant improvement as number of days of flow decreased and cycle length increased. The mean duration of bleeding was 6 to 9days before treatment which was reduced to 3 to 5 days after 3 months treatment to test group. There is significant reduced flow after treatment with ormiloxifene for 3 months.

There was significant improvement of Hb level after giving the treatment for three months of ormiloxifene in patients of AUB (table-2).

Pictorial blood loss assessment chart shows there is significant reduction of flow after treatment of ormiloxifene (figure-3).

There is significant reduction of thickness of endometrium after treatment of ormiloxifene. Thickening of endometrium was initially 11.07 mm and become 10.10 mm after treatment of ormiloxifen of 3 months (figure-4).

Figure-5 shows that out of 40 patients 5.5% shows amenorrhoea,6% shows hypomenorrhoea, nausea showen by 4%, and headache by 3%, no significant major side effects were shown by any patient.

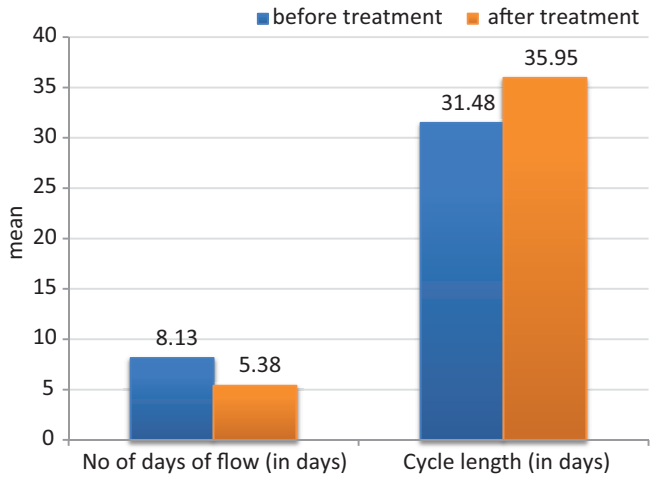

Figure-1: Comparison of menstrual cycle before and after treatment

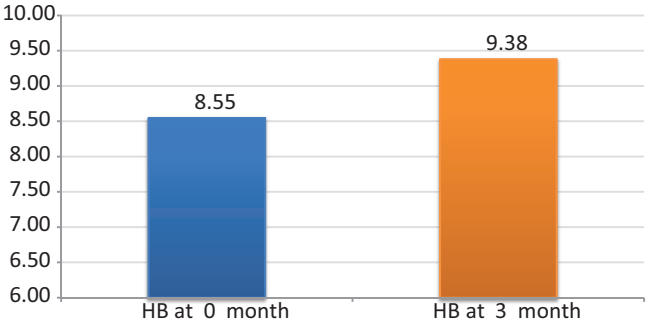

Figure-2: Comparison of HB- pre treatment and post treatment

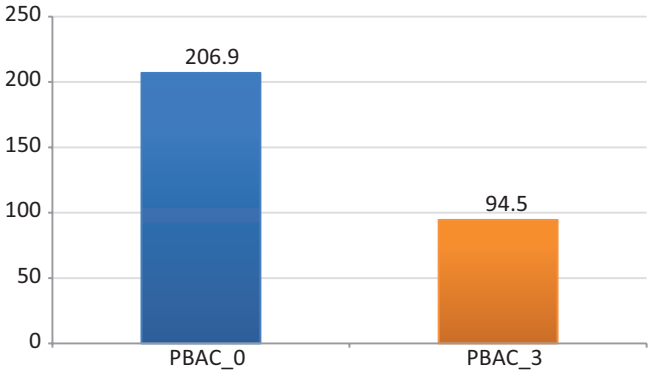

Figure-3: Comparison of PABC pretreatment & posttreatment of ormiloxifene

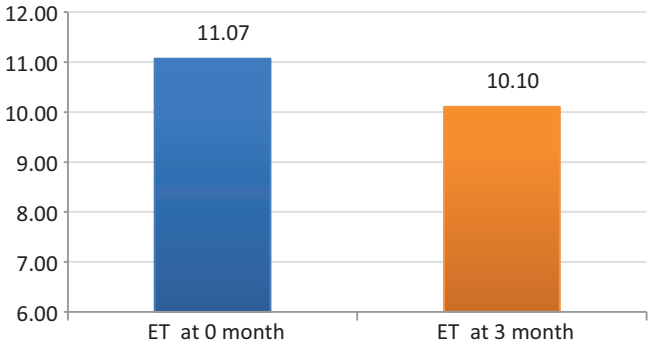

Figure-4: Comparison of endometrial thickness- pretreatment & posttreatment of ormiloxifene

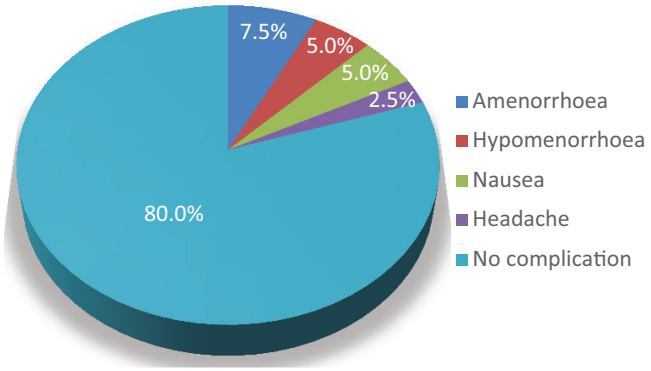

Figure-5: Complication

DISCUSSION

Medical management is the first line treatment for AUB and if there is no improvement by medical treatment than surgical intervention like endometrial ablation, hysterectomy become the last option. Hysterectomy causes surgical menopause and electrical ablation is unsuitable for women who wants to continue their reproductive and menstrual function. Medical management is basically for problems related to menstruation along with this preservation uterus and the ovaries. Pharmacological drugs like NSAIDs, progesterones, oral contraceptive pills, anti-fibrinolytic drugs, danazol, GnRH agonists - all reduces loss of blood during menses but the duration of treatment is limited. In our study we have analyzed the efficacy of ormeloxifene in patients with abnormal uterine bleeding and our results suggested that there was a significant reduction of menstrual blood loss after

taking the drug. Drugs used for medical management include hormonal pills, fibrin lysers and specifically developed antagonists to estrogen and progesterone. Among these Ormeloxifene,a site specific estrogen agonist-antagonist and an very effective option in patients of AUB and several studies have been conducted to test its efficacy.[7-10]

In a study conducted by Jacob KJ et al. Study show that reduction in mean PBAC score was (277.33 to 70.11), increase in hemoglobin level (9.68 gm% to 11.07 gm% and endometrial thickness 7.8 mm to 5.3 with ormeloxifene after 3 months of therapy.[11]

A study conducted by Geeta Rani et al[12] for 6 months. For the first 3 months ormiloxifen is given twice a week, next 3 months, once a week. Almost all patients had PBAC score less than 100, thus no menorrhagia following treatment. 11 patients developed amenorrhoea, a the most common side effect of Ormeloxifene, 82% of patients had decrease in endometrial thickness by more than 0.5 mm. Almost all patients had increase in haemoglobin level following treatment. Side effects seen during treatment were G.I side effects, headache, amenorrhoea.

CONCLUSION

Ormeloxifene is effective, quick acting and appears to be a good option for the management of abnormal uterine bleeding. It leads to marked reduction in menstrual blood loss, a significant increase in haemoglobin concentration and a marked decrease in endometrial thickness without any major side effect. It is very cost effective and has convenient dose schedule of one or twice a week. It has less side effects in comparison to other drug used in AUB. It can be used in any age group and oncologically protective to the breasts and endometrium. It is well tolerated and is a safe alternative for medical management of dysfunctional uterine bleeding.

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