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STUDY OF EFFICACY AND SAFETY OF ORMELOXIFENE IN THE MANAGEMENT OF DYSFUNCTIONAL UTERINE BLEEDING

Gynaecology

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ABSTRACT

BACKGROUND: Dysfunctional uterine bleeding is the major presenting complain in the patients of reproductive age group. Nonsteroidal anti-inflammatory drugs, tranexamic acid, ethamsyalate and norethisterone are the primary drugs which we use to treat the DUB cases. SERM like Ormeloxifene is a safe and effective drug to treat the Dysfunctional uterine bleeding. The objective of the study is to evaluate the efficacy and safety of Ormeloxifene in cases of DUB.

METHODS: We selected 34 patients of Dysfunctional uterine bleeding in the study after taking the consent. All the patients were given Tab Sevista(ormeloxifene) 60 mg biweekly for initial 3 months then they all were switched on Tab Sevista 60 mg weekly for next 3 months. All the patients were followed up for 1 year. The result and outcome were measured by reduction of menstrual blood loss in each cycle(assessed by PBAC score), rise of Hemoglobin concentration and endometrial thickness. Patients were also evaluated for the side effect and acceptability of the drug.

RESULTS: At the end of study our two patients undergone for hysterectomy due to excessive menstrual blood loss and we lost follow up of two patients. Result of the study evaluated in rest 30 patients. In our study we found significant reduction of menstrual blood loss, rise of haemoglobin concentration and endometrial thickness was also found to be significantly reduced.

CONCLUSION: Ormeloxifene is a safe and effective drug without any major side effect. This drug can be used in treatment of Dysfunctional uterine bleeding.

KEYWORDS

SERM, DUB, Ormeloxifene

INTRODUCTION

Abnormal uterine bleeding is one of the commonest gynaecological complain of our patients attending to our OPD. AUB is defined as any uterine bleeding that is not regular, noncyclical, with varying degree of frequency, amount and duration. It can present in the form of menorrhagia, polymenorrhoea, intermenstrual spotting or post coital bleeding. The cause of AUB could be organic, systemic; any pathology of pelvic organ or it could be because of coagulopathy.

Dysfunctional Uterine Bleeding is a state of abnormal uterine bleeding without any clinically detectable organic, systemic and iatrogenic cause. DUB is a diagnosis made by excluding other causes and it is one of the most common causes of AUB. Near about 1/3 of patients of AUB are due to dysfunctional uterine bleeding. DUB can be treated by medical therapy and by surgical interventions.

Medical therapy should always be tried first in cases of DUB and if medical management fails then only we should try for surgical option. Hysterectomy should be the last option in the treatment of DUB.

Medical therapy can be hormonal or non-hormonal. As DUB is more frequently found in an ovulatory cycle than non ovulatory cycle so hormonal therapy with progesterone, oestrogen or combined therapy has been found very effective in case of DUB.

Other hormonal agents like GnRh agonist and SERMs and LNG IUD are also highly effective. Non hormonal drugs like tranexamic acid, ethamsylates and NSAIDS are very effective as first line therapy and they reduce the menstrual bleeding up to 50 %. Danazol is now not in use as it has very high androgenic side effects.

Ormeloxifene, also known as centchroman is SERM (Selective oestrogen receptor modulator) acts on oestrogen receptors. It is a non-steroidal oral contraceptive. In India it is available as birth control pill since the early 1990s. It has anti oestrogenic action on endometrium, uterus and breasts and oestrogenic action on bones, vagina, liver, cardiovascular and CNS. Ormeloxifene may be used as a weekly oral contraceptive. Its other uses are in the treatment of mastalgia, fibroadenosis and menorrhagia.

Ormeloxifene does not cause uterine stimulation, prevent bone loss, has no adverse effect on lipids and cardiovascular system. There is no increase risk of breast cancer. The only side effect is delayed menstruation in the woman using it for DUB. It has a long half life, cheap, easily available.in the initial three months it is given biweekly then dose can be reduced weekly.

METHOD

A prospective study was conducted in Sir Sunder Lal hospital, BHU, Varanasi on the patients attending the OPD of Dept. of Obstetrics & Gynaecology over a period of 12 month from January 2018 to December 2018.

34 women presenting with abnormal uterine bleeding without any organic, systemic or iatrogenic cause were included in the study. A detailed medical, surgical and obstetrical and gynaecological history was taken from all the patients. They were asked about the symptoms like menorrhagia, dysmenorrhoea, dyspareunia, lower abdominal pain or any abdominal mass. After taking history both general and systemic examination was done. All these procedures were done after taking written informed consent by the patients.

INCLUSION CRITERIA :-

Women of reproductive age group 18-45 years with abnormal uterine bleeding without any organic or pelvic pathology were included in the study. Other causes of menorrhagia like coagulopathies, fibroids and drugs were ruled out.

EXCLUSION CRITERIA :-

Those patients who were having any pelvic pathology, polyp, any cervical lesion, liver or renal disorder, hypo or hyperthyroidism, child birth within 1 year and patients having history of abortion in previous 3 months were excluded from the study.

The investigations we carried out in all the patients were:

- Complete blood count including platelet count
- Bleeding time and clotting time
- Thyroid profile
- USG abdomen and pelvis
- TVS for measurement of ET in proliferative phase

After the diagnosis of DUB made, all the patients were given Tab Ormeloxifene (tab sevista by torrent) at a dose of 60 mg biweekly for 12 weeks after then 60 mg weekly for next 12 weeks. Every patient was followed at monthly interval. At each OPD visit patients were asked about their menstrual history. Blood loss at each menstrual cycle was assessed by PBAC score (Pictorial blood loss assessment chart).

Outcome of the treatment given were measured by amount of menstrual blood loss, passage of blood clots, haemoglobin level and endometrial thickness by TVS.

RESULTS

The age and parity distribution is given in table 1. The mean age in our

study group was between 36-40 years age group (43.33%) with a range of 20-45 years. The parity distribution was mentioned in table 2. In our study 53.33% patients having parity of 3 (mean parity).

The mean haemoglobin of the patients at the beginning of treatment was 8.1gm/dl. After 6 months it was 10.4gm/dl. There was a significant improvement in mean haemoglobin (a rise of 2.3 gm/dl) after 6 months treatment with Ormeloxifene ($p < 0.05$).

Menstrual blood loss was assessed at the start of therapy then after 6 months of treatment with Ormeloxifene. There was a significant reduction in menstrual blood loss and passage of clots after 6 months of therapy. The mean PBAC score was 312 in the start of therapy and it was 48 after 6 months of treatment (p value < 0.05)

Endometrial thickness was also significantly reduced after the treatment.(previously it was 9.8mm and after treatment it reduced up to 6.2mm with p value <0.05).

DISCUSSION

Menstrual disorder specially menorrhagia is the major problem in our patients of reproductive age group. Apart from the organic and systemic causes, majority of cases are due to dysfunctional uterine bleeding. For the management of DUB, medical management is the first line treatment option. There are so many effective drugs available for the medical management of DUB. If medical management fail to show good result, then only one can try for surgical management. Hysterectomy is the major surgery and it should be the last option in management of dysfunctional uterine bleeding.

There are many effective drugs available for the treatment of menorrhagia like Tranexamic acid, NSAIDS, Nor ethisteron Acetate, Medroxy Progesterone Acetate, Ethamsylate in the market. No doubt, these drugs are very effective but sometimes they fails to reduce the menstrual blood loss completely.

In the other hand, we have other treatment modalities like ablation techniques and LNG-IUD but they are little bit costly and more ever this requires technical expertise and our every patient cannot afford it. Ormeloxifene is SERM, which selectively blocks the action of oestrogen on the endometrium. It is a research product of CDRI, Lucknow discovered in 1991 and it is marketed in INDIA since 1992 in the brand name of SAHELI, CHOICE,SEVISTA and Novex-DS. Primarily it was used as contraceptive but this drug is highly effective in patients of DUB who does not wants to conceive.

In our study, we used this drug in the patients of DUB, And it was found very effective in decreasing the blood loss during menses, improvement of Hb and reduction of endometrial thickness.

In our study, we found significant rise in Haemoglobin from 8.1 to 10.4 gm/dl (p value < 0.05),significant reduction of endometrial thickness(pre-treatment 9.8 to post treatment 6.2mm). Our study results are very much similar **to Dhananjay et al** (Hb increased to 8.26 to 10.59 gm/dl with p value < 0.01) and statistically significant decrease in ET (9.83 to 4.89 mm with p value <0.01) after 3 months of treatment with ormeloxifene.

Gandotra N et al found a reduction of menstrual blood loss assessed by PBAC score. The median pre- treatment PBAC score was 316 and it was reduced up to 52 after 6 months of treatment (p value 0.05). In our study we also found significantly reduction of menstrual blood loss (PBAC Score before treatment 312 and after 6 months of treatment 48 with p value <0.05).

Kriplani et al had done study on the efficacy and the safety of Ormeloxifene in the treatment of menorrhagia in 2009. It was a pilot study.

ACKNOWLEDGEMENT:

We are highly thankful to our patients for their support, help and cooperation in our study.

Limitation of the study:

Sample size of our patients included in study is small. Furthermore studies are required with more numbers of patients.

Tables and Figure

We selected 34 patients for this study out of these 34 patients, 2 patients were lost for follow up and 2 patients were undergone for hysterectomy.

Figure 1:-

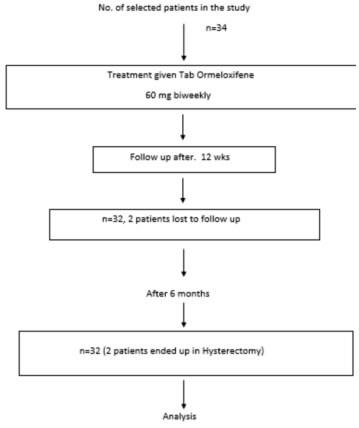

Table 1:-

The age and parity distribution of the subjects (n=30)

Age(Years)	Numbers	%
20-25	1	3.33
26-30	2	6.66
31-35	12	40
36-40	13	43.33
41-45	2	6.66

Table 2:-

Parity	Number	%
0	0	0 %
1	1	3.22 %
2	3	10 %
3	16	53.33 %
≥ 4	10	33.33 %

Table 3:-
Outcome of the study after 12 months

Parameter	Pre-treatment	Post treatment	P value
Mean Haemoglobin (gm/dl)	8.1	10.4	< 0.05
Mean PPAC	312	48	< 0.05
Endometrial thickness	9.8	7.2	< .005

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