

Efficacy of Ormeloxifene in the Management of Dysfunctional Uterine Bleeding

Swati Gett¹, Shruti Singh²

Author's Affiliation:

^{1,2}Senior Resident,
Dept. of Obstetrics and
Gynecology, Kasturba Hospital,
Delhi- 110006, India.

Corresponding Author:

Swati Gett,
Senior Resident,
Dept. of Obstetrics and
Gynecology, Kasturba Hospital,
Delhi- 110006, India.
E-mail: swatiget@gmail.com

Received on 30 December 2017

Accepted on 19 January 2018

Abstract

Introduction: Dysfunctional Uterine Bleeding is the most common cause of abnormal vaginal bleeding during a woman's reproductive years. 'Ormeloxifene' a nonsteroidal selective estrogen receptor modulator (SERM), is currently undergoing clinical evaluation for the treatment of heavy menstrual bleeding. It normalizes the bleeding from the uterine cavity by regularizing the expression of estrogen receptors on the endometrium. *Aim and Objectives:* To study the efficacy of Ormeloxifene in the management of dysfunctional uterine bleeding. *Material and Methods:* A total of 50 women between 20 to 50 years of age presenting with abnormal or dysfunctional uterine bleeding during a period of one year included in the study. During each visit a detailed menstrual history was taken and PBAC score was calculated. All patients of DUB under study treated with Ormeloxifene and the treatment outcome measured. *Results:* Among a total of 50 patients, there were 25 (50%) patients belonged to 31-40 years age group with 37.9 years to be a mean of all ages. The mean Hb level recorded was 7.3gm%. The mean PBAC score prior to treatment was 274 which was found to be decreased upto 91.7 after a treatment of 3 months with Ormeloxifene. *Conclusions:* DUB is considered to be caused because of the hormonal imbalance, eventually leading to hyperestrogenic state, which can be quite successfully treated by the medical management, like Ormeloxifene.

Keywords: Dysfunctional Uterine Bleeding.

Introduction

Dysfunctional Uterine Bleeding (DUB) is defined as a state of abnormal uterine bleeding without any clinically detectable organic pelvic pathology like tumour, inflammation or pregnancy and is a diagnosis of exclusion. It is the most common cause of abnormal vaginal bleeding during a woman's reproductive years [1].

DUB may be ovulatory or anovulatory. In 80-90% of DUB, bleeding results from dysfunction of HPO axis which leads to anovulation and as anovulatory cycles produce no progesterone to stabilize cyclic withdrawal of the estrogen prepared endometrium, bleeding episodes become irregular and amenorrhoea, metrorrhagia and menorrhagia are common. In other

10-20% women with DUB, ovulation occurs cyclically and menorrhagia is thought to originate from defects in the control mechanism of menstruation [2].

Ormeloxifene (also known as centchroman) is one of the selective estrogen receptor modulators. It is a non-steroidal, non-hormonal oral contraceptive which is taken once in a week [3]. In India, Ormeloxifene has been available as a birth control product since the early 1990s. It is developed as centchroman by Indian Central Drug Research Institute, Lucknow, India and it is currently marketed here under the trade name, Saheli [4]. It mediates its effects by high affinity interaction with estrogen receptors, antagonizing the effect of estrogen on uterine and breast tissue and stimulating effect on vagina, bone, cardiovascular system and central nervous system [5]. Ormeloxifene is not only preferred

as an oral contraceptive, but also useful for management of dysfunctional uterine bleeding and advanced breast cancer [6].

Aim and Objectives

To study the efficacy of Ormeloxifene in the management of dysfunctional uterine bleeding

Material and Methods

In the present study, patients presenting with dysfunctional uterine bleeding (DUB) to Department of Obstetrics and Gynaecology, Sardar Patel Medical College, Bikaner during the specified period from September 2015 to August 2016 were taken up for study. We included 50 women between 20 to 50 years presenting with abnormal or dysfunctional uterine bleeding without any organic, systemic or iatrogenic cause were enrolled.

Inclusion Criteria

- All patients with DUB of 20-50 years of age were included in the study.
- All patients who were ready for follow up.

Exclusion Criteria

- Patients who were pregnant, lactating, with history of heart disease, hypertension, migraine, Polycystic ovarian disease, liver and kidney impairment and thyroid dysfunction were excluded.
- Patients with fibroid uterus, adenomyosis, atypical endometrial hyperplasia, bleeding disorders were also excluded.

Informed consent was taken from all the patients.

After obtaining an approval from institutional ethics committee, a detailed history and clinical examination was done. As DUB is a diagnosis of exclusion, investigations were done to rule out any other possible cause for abnormal uterine bleeding. These included complete blood cell count including hemoglobin (Hb) level, thyroid stimulating hormone, coagulation profile, PAP smear, pelvic ultrasound to measure endometrial thickness and rule out any pelvic pathology and endometrial sampling.

The cases were advised to maintain a menstrual diary to record the total number of days of bleeding, number of sanitary pads used, degree of soaking of each pad, number and size of clots passed, and if dysmenorrhoea experienced. The Pictorial Blood loss Assessment Chart (PBAC) Scoring was then done accordingly to assess menstrual blood loss. PBAC is a simple procedure for objective assessment of menstrual blood loss. A PBAC score ≥ 100 indicates a menstrual blood loss ≥ 80 ml and is considered diagnostic for menorrhagia. All women under study were given Ormeloxifene tablet 60 mg twice a week for 12 weeks. Patients were followed upto 3 months. During each visit a detailed menstrual history was taken, PBAC score was calculated. Hemoglobin concentration and endometrial thickness were measured after 3 months of the treatment. Any side effects, if experienced, were also noted.

The primary outcome measures were reduction in amount of menstrual blood loss which was assessed by fall in PBAC score, rise in hemoglobin level and reduction in endometrial thickness done in proliferative phase by an ultrasound.

All outcome measuring parameters were presented as Mean and were analyzed using the Z technique. Statistical significance was taken as $p \leq 0.05$.

| | PBAC Scoring | |
|----------------------------|-------------------|------|
| Sanitary napkins/Tampons | Lightly soiled | (01) |
| | Moderately soiled | (05) |
| | Saturated | (20) |
| Clots | Small | (01) |
| | Large | (05) |
| Duration of flow (in days) | | |

Results and Observations

The Table 1 shows distribution of patients according to age, parity, their residence and the duration of overall symptoms the patient is suffering from. Among the total 50 patients, there were 25 (50%)

patients belonged to 31-40 years age group with a mean of all ages 37.9 years. About parity status, a maximum patients 23 (46%) were having ≥ 04 parity status with overall average of 3.4. Maximum patients belonged to rural communities 28 (56%) and more than half number of patients were having less than 09 months duration of symptoms with an average duration of 6.8 months.

Table 2 shows results of various investigations carried out prior to treatment with Ormeloxifene. About 72% of patients were having haemoglobin level between 6-8gm%. The mean Hb level recorded was 7.3gm%. On USG examination, the mean endometrial thickness found to be 11.9mm with a maximum number of patients in the range of 10.1mm to 15mm. The PBAC score estimated among the patients with uterine bleeding shows that, maximum patients were belonged to intermediate group ranges between 201 to 300 and mean score was found to 274 among the patients studied. After treating the patients with ormeloxifene, they were followed up further for a period of 03 months and again various investigations were performed in order to review the treatment outcome among the patients. The various parameters studied were found to show a favourable outcome with a significant improvements in their clinical status. The mean values estimated, depicted in

theTable 03 shows a comparative improved condition among overall patients studied.

Discussion

Table 1 shows age distribution of the study participants (20-50 years) with mean age of 37.90 years. This study age groups are comparable with previous studies by Debasmita Mandal et. al. [7], Dhananjayan D et. al. [8] and Neha Agarwal et. al. [9]. The reason could be that in younger years of the reproductive life, the heavy menstrual bleeding might not cause much of a trouble to the affected women as most of the times the bleeding is temporarily halted during the pregnancies and the health status of young women is mostly better than the women in their later years of life, so they usually present late to the hospital. The distribution of patients according to the duration

Table 1: Distribution of variables among study subjects

| Patient Characteristics | | Number of patients N=50; (%) | Mean Values |
|-------------------------------|-------|------------------------------|-------------|
| Age Intervals (Years) | 20-30 | 9 (18%) | 37.90 |
| | 31-40 | 25 (50%) | |
| | 41-50 | 16 (32%) | |
| Parity Status | 01 | 1 (02%) | 3.4 |
| | 02 | 12 (24%) | |
| | 03 | 14 (28%) | |
| | ≥ 04 | 23 (46%) | |
| Residence | Urban | 22 (44%) | ---- |
| | Rural | 28 (56%) | |
| Duration of Symptoms (months) | 0-3 | 11 (22%) | 6.8 |
| | 4-6 | 17 (34%) | |
| | 7-9 | 12 (24%) | |
| | 10-12 | 9 (18%) | |
| | >12 | 1 (02%) | |

Table 2: Results of various investigations prior to treatment with Ormeloxifene

| Results of Investigations (prior to treatment) | | Number of patients N=50; (%) | Mean Values |
|--|---------|------------------------------|-------------|
| Hemoglobin (gm%) | <6 | 3 (06%) | 7.3 |
| | 6-8 | 36 (72%) | |
| | 8.1-10 | 11 (22%) | |
| Endometrial thickness on USG (mm) | 0-5 | 1 (02%) | 11.9 |
| | 5.1-10 | 12 (24%) | |
| | 10.1-15 | 32 (64%) | |
| | 15.1-20 | 5 (10%) | |
| PBAC score | 100-200 | 3 (06%) | 274 |
| | 201-300 | 33 (66%) | |
| | 301-400 | 14 (28%) | |

Table 3: Comparison of results of investigations prior to and after treatment with Ormeloxifene

| Investigations | Mean Values after investigation | | P-value |
|----------------------------|---------------------------------|-----------------------------|---------|
| | Pre-Treatment | After 3 months of treatment | |
| Hemoglobin (gm%) | 7.3 | 9.6 | 0.0006 |
| Endometrial thickness (mm) | 11.9 | 7.9 | 0.0003 |
| PBAC score | 274 | 91.7 | 0.0004 |

of their symptoms, ranging from 2-15 months, with mean duration of 6.8 months. The mean duration of symptoms in our study was more, as seen in previous studies also [7,9], it might be because in our area more than 50% of the patients belong to rural population and are of low socioeconomic status and literacy rate, & are neglected, so they present late to the hospital.

Table 2 shows that, mean hemoglobin level of patients prior to treatment was 7.3gm% also, the mean endometrial thickness on USG prior to treatment was 11.9mm. These findings are similar to a previously conducted study [7]. This signifies the hyperestrogenic state in these women.

Table 3 shows the comparison in respect to pre- and post-treatment values of mean PBAC score, mean hemoglobin concentration and mean endometrial thickness, and all these were found to be significant in both the groups (p value <0.05). These findings are found to be similar to the previous studies [7,10,11,12]. This shows a decrement in the amount of menstrual blood loss. PBAC score is not routinely used to assess the menstrual blood loss in patients attending the hospitals, but it should be considered for this purpose. As seen in our study, PBAC score directly correlates to the hemoglobin levels in patients where the cause of anemia was only heavy menstrual blood loss. PBAC score can help in subjective quantification of blood loss during each cycle, and can be used as a helpful guide in patients requiring some kind of intervention, even before the development of anemia and before any significant effect on their quality of life. The PBAC scores, if mentioned, in previous records can be very helpful for comparison and quantification of blood loss.

Summary and Conclusions

Dysfunctional uterine bleeding (DUB) is a common problem seen in women of reproductive age group. The mean age of the patients was 37.90 years and most of the patients were multiparae. The duration of symptoms was high as these women are usually neglected, so they present late to the hospital. In patients on treatment with ormeloxifene, the hemoglobin levels increased significantly after 3 months of treatment, with percentage change in hemoglobin of 31.5% while, the endometrial thickness on ultrasonography decreased with percentage change in thickness of 25.2%. There was decrement in PBAC score after 3 months of ormeloxifene treatment, with percentage change in PBAC score of 66.53% noted.

To conclude, Dysfunctional Uterine Bleeding is considered to be caused because of the hormonal imbalance, eventually leading to hyperestrogenic state, which can be quite successfully treated by the medical management, like Ormeloxifene.

References

1. Haresh U. Doshi, Alka Kriplani. Clinical cases in Obstetrics & Gynaecology, first edition 2003. pp.250-51.
2. John O. Schorge, Joseph I, Schaffer et. al. Williams Gynaecology, Abnormal uterine bleeding; p.186.
3. V.L. Bhargava. Textbook of Gynaecology 2nd edition 2009.p.109.
4. Bouchard P. Current and future medical treatments for menometrorrhagia during the premenopause. *GynecolEndocrinol.* 2011;27:1120-25.
5. Shelly W, Draper MW, Krishnan V, Wong M, Jaffe RB. Selective estrogen receptor modulators: an update on recent clinical findings. *ObstetGynecol Surv* 2008;63:163-81.
6. Lal, J. Clinical pharmacokinetics and interaction of Centchroman- a mini review. *Contraception* 2010;81(4):275-80.
7. Debasmita Mandal et. al. Comparative study of low-dose oral contraceptive pill and ormeloxifene in the treatment of dysfunctional uterine bleeding. *Int J Health Allied Sci.* 2014;3(4): 225-31.
8. DeepikaDhananjayan and Mirunalini et. al. Comparative Study between Ormeloxifene and Norethisterone in the Improvement of Menstrual Blood Loss (MBL) In Abnormal Uterine Bleeding. *International Journal of Current Medical And Pharmaceutical Research*, 2016 Oct;2(10):758-761.
9. Neha Agarwal et. al. Comparative evaluation of the efficacy and safety of ormeloxifene and norethisterone in dysfunctional uterine bleeding. *Int J ReprodContraceptObstet Gynecol.* 2013;2(2):194-198.
10. Neha et al. Role of SERM in medical management of DUB. *Asian Obst and Gynecol. Practice* 2012;6:28-31.
11. Dr. S. Fayyaz Shahab et. al. Ormeloxifene: Boon to perimenopausal Dysfunctional Uterine Bleeding (DUB) women in avoiding hysterectomies. *International Journal of Medical Science and Education.* 2014 Jan- March;1(1):21-29.
12. Kriplani et al. Efficacy and safety of ormeloxifene in management of menorrhagia: a pilot study. *J Obstet Gynaecol Res.* 2009 Aug;35(4):746-52.