ORIGINAL RESEARCH PAPER

Medical Science

TO EVALUATE THE EFFICACY AND SAFETY OF ORMELOXIFEN IN TREATMENT OF MENORRHAGIA

KEY WORDS: Pelvis, Sexual Dimorphism, Sciatic Tubercle.

Dr Rajkishori Dandotiya Senior Resident, G.R.Medical College, Gwalior, Madhya Pradesh

Dr Paribhashita Mishra* Assistant professor, G.R.Medical College, Gwalior, Madhya Pradesh *Corresponding Author

ABSTRACT

OBJECTIVE: 1.To evaluates the efficacy of Ormeloxifene in the medical management of menorrhagia.2. To findout side effects of Ormeloxifene.

STUDY DESIGN AND SETTING: The descriptive observational study was conducted in Department of Obstetrics and Gynecology, G.R.Medical College and Kamla Raja Hospital, Gwalior (Madhya Pradesh) from January 2017 to December 2017.

MATERIAL AND METHOD: One hundred women of reproductive age group with menorrhagia were recruited for the study. These patients were given ormeloxifene 60 mg twice a week for 12 weeks from first day of periods and once a week for next 12 weeks. Parameters assessed were Mean blood loss (MBL) by PBAC score, duration of bleeding, presence of blood clots and mean rise in hemoglobin after 6 months of treatment and changes in these parameters were analyzed by student's paired' tests using SPSS 16.0 version ,p value ≤ 0.05 was taken as significant.

RESULT: The mean pre-treatment MBL (PBAC score) was 450.5 which reduced to 60 at 6 months with ormeloxifene and was found to be statistically significant (p-value ≤0.001). Mean duration of bleeding pretreatment was 7.4days which was reduced to 2 days after 6 months of treatment with ormeloxifene. This reduction in duration of bleeding was statistically significant (P<0.001).The mean rise in hemoglobin was 1.4 which was also statistically significant. The decrease in endometrial thickness in patients on ormeloxifene was 1.13 which was not significant (p-0.09).

CONCLUSION: Ormeloxifene is very effective in treatment of menorrhagia. It decrease duration of bleeding, passage of blood clots and improve hemoglobin effectively. Ormeloxifene is accepted well and has good patient compliance due to its minimal adverse effects, low cost and simple dosage schedule.

INTRODUCTION

Menorrhagia is defined as cyclical bleeding which is excessive in amount **(** blood loss ≥ 80 ml) or duration (lasting 7 days) or a PBAC score of 100.[1]Menorrhagia is a common and treatable gynecological condition affecting more than 10 million women every year out of which 60% will require hysterectomy within 5 years, accounting for up to 75% of all hysterectomies performed worldwide**.**[2]American College of Obstetricians and Gynecologists (ACOG) also recommends that in absence of evidence of organic disease, medical treatment should be the first line of management but therapy should be changed according to patient profile. Multiple factors taken into account include the patient's age, desire for future fertility, uterus preservation etc.[3]Annually 5-10% of woman of reproductive age seek medical care for menorrhagia.[4] A wide range of treatment modalities are available which include medical therapy, minimal invasive surgeries and definite surgical interventions. Medical management has always been the first therapeutic option to be tried and if it fails to show results, one can choose surgical interventions. Medical management can be hormonal or non-hormonal.[5,6] Ormeloxifene is a new addition to medical therapy developed at Central Drug Research Institute, Lucknow. It is non-hormonal and non-steroidal, Selective Estrogen Receptor Modulator (SERM).[10] The chemical name of ormeloxifene is 3, 4 Trans 2, 2 dimethyl-3, phenyl-4(p)-beta pyrolidinoethoxy phenyl-7-methoxy chroman hydrochloride. It is easily absorbed from the gut, and it reaches a peak serum concentration in 30 minutes and its half-life is7 days.[6,7] It has got antioestrogenic effect on uterine and breast tissue and stimulatory effect on vagina, bone, cardiovascular system. It has anti-proliferative effect on endometrium, hence used as a quick and effective endometrial hemostat for menorrhagia and exerts contraceptive effects.[8] Side effects mostly seen with hormonal contraceptives like nausea, vomiting, headache, moodswings, acne, hirsutism, mastalgia weight gain, hypertension etc. not usually seen with Ormeloxifene. Amenorrhoea, delayed menses, scanty flows are the only limitations.[9] Contraindications of treatment includes renal or hepatic disorder, hypersensitivity to drug and it is not teratogenic**.**[11,12] It**.** has an excellent therapeutic index and is considered safe for the treatment of menorrhagia**.**[13]

MATERIAL AND METHOD: The descriptive observational study was conducted in Department of Obstetrics and Gynecology, G.R.Medical College, Gwalior (Madhya Pradesh) from January 2017 to December 2017.

Inclusion Criteria

One hundred women of reproductive age group attending the gynecological outpatient department of obstetrics & gynecology with complaint of heavy and prolonged menstrual flow with/without short cycles were selected for the study.

Exclusion Criteria

1. Suspected genital tract malignancies
2. Pelvic inflammatory disease
3. Pelvic pathology such as uterine fibroids
4. Endometriosis
5. Medical disorders such as platelet disorder or coagulopathy
6. Pregnancy
7. IUCD or oral contraceptives pills user
8. Hypersensitivity to the drug
9. Hepatic, renal diseases and thyroid dysfunction

One hundred women were selected at random sampling from outpatient Department of Obstetrics and Gynecology after taking informed consent. Detailed clinical and menstrual history was taken. General physical examination was done. A pelvic examination was done to rule out pregnancy and to find out pelvic pathologies like fibroid, adenomyosis or adnexal masses.

Endometrial biopsy and Pap's smear was taken. A TVS was done for endometrial thickness and to rule any other pelvic pathology. The drug was administered orally in the form of 60 mg tablet twice weekly for the first 12 weeks and then once a week for another 12weeks. Hemoglobin estimation was done at every month during follow up. To measure the menstrual blood loss (MBL) Pictorial blood loss assessment chart (PBAC) was used. Changes in PBAC scoring, endometrial thickness (ET) and hemoglobin levels (Hb) were analyzed by students paired' tests using SPSS 16.0 version. P value ≤ 0.05 was taken as significant.

Result:

Table 1: Pre and post treatment PBAC Score 50

PBAC Score	Pre-treatment (n=100)	3months (n=98)*	6months (n=86)**
<100	0 (0%)	36(36.7%)	76 (88.3%)
100 —200	0(0%)	38 (38.7%)	12 (13.9%)
201 —300	14 (14%)	12 (2.2%)	0 (0%)
301 —400	22(22%)	6 (6.1%)	0(0%)
401 — 500	18(18%)	2(2.0%)	2(2.3%)
501 —600	18(18%)	2(2.0%)	0 (0%)
601 —700	10 (10%)	0 (0%)	0 (0%)
701 — 800	10(10%)	2 (2.0%)	2 (2.3%)
801 — 900	8 (8%)	0 (0%)	0 (0%)

PBAC score was >200 in pretreatment women and 86% had significantly high PBAC score of > 300.After 3 months post-treatment PBAC score was reduced to 100 in 36.7% of patients and after 6 months post-treatment PBAC score was reduced to 100 in 88.3% of cases.

Table 2: Analysis of PBAC Score

Pre-Treatment	Post-Treatment 6 months				
Minimum Score	Maximum Score	Median Score	Minimum Score	Maximum Score	Median Score
230	845	450.5	0	720	60

Pre-treatment PBAC score in our study ranged from 230 - 845 with a median 450.5. Median PBAC score was reduced to 60 after 6 months of treatment with Ormeloxifene which was found to be statistically significant (p<0.001).

Table 3: Efficacy of ormeloxifene in reducing menstrual blood clots

Passage of blood clots	No. of cases
Pre-treatment	86
Post-treatment	14
No. of patients improved	72(83.7%)

Out of 100 cases 86patients had presence of blood clots and by the end of 6 months of therapy there was reduction in passage blood clots in 83.7% of patients who were treated with ormeloxifene (z score=8.1; P<0.001)

Table 4: Duration of bleeding

Duration of bleeding in days	No. of patients before treatment (n=100)	No. of patients 3 months after treatment (n=86)
0	0	22(25.5%)
1-2	0 (0%)	26 (30.2%)
3-4	2 (2%)	14 (16.2%)
5-6	24 (24%)	24 (27.9%)
7-8	44 (44%)	0
9-10	24 (24%)	0
>10	6 (6%)	0

Median duration of bleeding pretreatment was 7.4days with range of 3-12days. Median duration of bleeding after treatment was 2 days with range of 4-6 days. This reduction in duration of bleeding after six months treatment with ormeloxifene was statistically significant (P<0.001).

Table 5: Pre-treatment and post-treatment hemoglobin level.

Hb Level (gm/dl)	Pre-treatment Level (n=1oo)	After 3 months of treatment(n=98) (n=49)	After 6 months of treatment(n=86) (n=43)
> 12	0	7 (7.1%)	20 (23.2%)
11.9 — 11	16(6%)	23 (23.4%)	24 (27.9%)
10.9 — 10	20 (20%)	30(30.6%) (28.5%)	30 (34.8%)
9.9 — 9	40 (40%)	28 (28.4%)	12 (13.9%)
8.9 — 8	20(20%)	10(10.2%)	0
7.9 — 7	4(4%)	0	0
<7	0	0	0

In pre-treatment assessment all patients had hemoglobin < 12gm/d1 and 64% had significant anemia. After 3 months post-treatment hemoglobin was increased to >11 gm/dl in 30.5%. And 6 months post-treatment hemoglobin was increased to >11gm/d1 in 51.1%.

Table 6: Analysis of hemoglobin level

Hb (gm/dl)	Pre-treatment level	Post-treatment at 3 months	Post-treatment at 6 months
Mean	9.51	10.9	10.9
Median	9.56	10.1	11
Highest	11.4	12.6	12.4
Lowest	7.2	6	9.2

After treatment with ormeloxifene, hemoglobin level rose from a median of 9.56 gm/dl to 11 gm/dl showing an improvement of 1.4 gm/dl which is statistically significant (p value<0.001).

Table 7: Thickness of endometrium on TVS

Endometrial thickness (mm)	Pre treatment (n=100)	After 3 months (n=98)	After 6 months (n=86)
<4	0	0	0
4 — 7.9	38 (38%)	40 (40.8%)	38 (44.1%)
8 — 11.9	49 (49%)	51 (52.04%)	48 (55.8 %)
12 — 15.9	8(8%)	7 (7.1%)	0
16 — 20	5 (5%)	0	0

In our study we found pre-treatment ET on TVS was >12mm in 13% of the patients. At 3 months post treatment with ormeloxifene 7.1% patients had ET >12mm.And none of the patient had ET > 12mm at 6 months of post-treatment.

Table 8: Analysis of endometrial thickness

Endometrial thickness(mm)	Pre-treatment	Post-treatment at 3 months	Post-treatment at 6 months
Mean	9.11	8.8	7.98
Median	8.55	8.4	8.2
Highest	16	14	11.5
Lowest	5.4	4.8	4.8

The mean pre-treatment endometrial thickness was 9.11mm. The mean post-treatment endometrial thickness was 7.98.The mean decrease of 1.13mm in endometrial thickness is statistically insignificant (p value=0.09).

DISCUSSION:

In our study main parameters assessed were mean blood losses by PBAC score, duration of bleeding, presence of blood clots and mean rise in hemoglobin after 6 months of treatment.

In present study we found that median score for blood loss was 450.5 which were reduced to 60 after 6 months of therapy.The median reduction in PBAC score was statistically significant and our result was similar to Biswas SC et al [14] study where they found median score was reduced from 272 to 107.8 after 6 months of therapy. In study conducted by Kriplani A et al[15] median PBAC score reduced from 388 to 50 after 4 months of treatment. In present study we found that out of 100 cases 86patients had presence of blood clots and by the end of 6 months of therapy there was reduction in passage of blood clots in 83.7% of patients who were treated with ormeloxifene (z score=8.1; P<0.001). Our result was similar to study done by Biswas et al in which they found absence of blood clots in 85.5% of patients by the end of therapy.

In our study we observe that median duration of bleeding reduced significantly from pretreatment duration of 7.4 days to 2 days after 6 months of therapy.(p-value 0.001) and the result was similar to pilot study conducted by Kriplani A et al in which they found median reduction in duration of bleeding from pretreatment value of 7 days to 3 days after 4 months of therapy.86% of the patients showed decrease in duration of bleeding in contrast to study done by Dutta RC et al[16] in 2002 where they found reduction in duration of bleeding in 25%.

In our study we found that mean increase in hemoglobin concentration was 1.4 which was statistically significant comparable to Dhananjay et al[17] study.

All the patients recruited in the study had TVS for endometrial thickness with mean pre-treatment ET of 9.11 which reduces to 7.98 after 6 months post-treatment.The decrease in ET was not statistically significant (p-value 0.9) which in contrast to Biswas et al study where they observed mean reduction of 3.6.

Therefore 60 mg of Ormeloxifene biweekly is effective and safe drug for the medical management of menorrhagia.

CONCLUSION:

Ormeloxifene is very effective in treatment of menorrhagia. It decrease duration of bleeding, passage of blood clots and improve hemoglobin effectively. Ormeloxifene is accepted well and has good patient compliance due to its minimal adverse effects, low cost and simple dosage schedule**.**

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