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Original Research Article

Role of Ormeloxifene in Management of Abnormal Uterine Bleeding

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Abstract: The objective is to study the efficacy, safety and acceptability of ormeloxifene in the medical management of AUB. This is a Hospital based interventional study which included a sample size of 52 Samples. 52 cases of AUB were recruited. Each was given 60 mg of ormeloxifene twice weekly for 3 months and then once a week for next month. Follow up was done at 1,3 and 4 month. Primary outcome measures were menstrual blood loss, haemoglobin concentration and endometrial thickness. Secondary outcome measures were the acceptability and side effects of ormeloxifene. The mean pretreatment HB concentration was significantly increased and means pretreatment endometrial thickness was reduced. Thus ormeloxifene is safe and effective drug for medical management of AUB. It is non-steroidal, pharmacologically and metabolically safe oncologically protective and cost effective too.
Keywords: ormeloxifene, AUB, HB

INTRODUCTION

Menorrhagia is usually defined as menstrual blood loss of >80 ml/cycle or a PBAC score (pictorial blood loss assessment chart) of >100 [1]. Abnormal uterine bleeding is defined as a state of bleeding which can be described by PALM COEIN

CLASSIFICATION

P- Polyp
A- Adenomyosis L- Leiomyoma
M-Malignancy
C- Coagulopathy
O-Ovulatory dysfunction E-Endometrial
I-Iatrogenic
N- Not yet decided

It is the most common menstrual disorder that can affect any women from menarche to menopause [2]. In an objective study measuring menstrual loss [3], it was determined that the mean menstrual blood loss is 43 ml/cycle. Many drugs for AUB are available, but response to treatment varies. Success with 1st generation ablative procedures varies from 80-97%, but they require skill for hysteroscopy. 2nd generation procedures have similar success rates and complication profiles, take less time to perform and are technically easier to conduct, but are expensive [4]. Various drugs used are NSAIDS, tranexamic acid, Hemostatic progestins, oral contraceptives, Antifibrinolytics, Danazol. The role of levonorgesterol intrauterine system (LNG IUS) in menorrhagia is well established and is now considered to be the reference treatment in medical management, but its cost limits its widespread use [2, 5].

Ormeloxifene (centchroman) is a non-steroidal, non-hormonal, pharmacologically inert, selective estrogen receptor modulator (SERM) [6]. It has anti-estrogenic and anti-proliferative effect on endometrium, hence used as a quick and effective endometrium hemostat for abnormal uterine bleeding[6].Its dose is 60 mg twice a week for 3 months and then a dose of 60 mg once a week for a month[2].Bleeding usually stops or becomes normal within 2 to 3 days of first dose followed by regular or delayed cycles which are normal or scanty in flow in 85 to 87% of subjects [7]. Ormeloxifene in the above mentioned dose acts as estrogen antagonist in the uterus and breast. It has mild estrogenic action on vagina, bone density, CNS and serum lipids. It has no progestational, androgenic or anti-androgenic properties

besides it is oncologically protective (protects against breast and endometrial carcinoma) [6].

SIDE EFFECTS OF ORMELOXIFENE [8]

- Vague abdominal pain
- Headache
- Gastric dyspepsia
- Cervical erosion and discharge
- Ovarian cyst

AIMS AND OBJECTIVES

1. To study the effect of ormeloxifene on menstrual blood loss with 4 months of treatment
2. To study the effect of ormeloxifene on blood haemoglobin levels.
3. To study the effect of ormeloxifene on endometrial thickness.

MATERIAL AND METHODS

Study area: Study was conducted in department of Obstetrics and Gynaecology, Zenana Hospital, SMS Medical College, Jaipur

Study design: Hospital based interventional study.

Sample size: 52

Inclusion criteria

- All cases of abnormal uterine bleeding

Exclusion criteria

- Uterine size 8 wks, fibroids, adnexal mass detected on ultrasonography.
- Presence of any pelvic pathology
- Active bleeding necessitating emergency treatment
- Renal or hepatic dysfunction
- Associated infertility
- Post-menopausal bleeding

PROCEDURE

After all relevant investigations done, baseline clinical profile, cycle length, duration of bleeding and PBAC Score for each women was noted and they were given PBAC charts before giving ormeloxifene. Patients were asked to keep records of their menstrual patterns, bleeding days and amount of mean blood loss. Follow up were made at 1, 3 and 4 months of therapy and after 3 months of completion of treatment to assess improvement of symptoms. Thus the total duration of study was 7 months. At each visit days of bleeding, cycle length, PBAC score and any side effects were noted in detail. Haemoglobin and ultrasonography were repeated after 4 months of treatment.

RESULTS AND DISCUSSION

As table-1 shows majority of the patient's i.e.67.35% had no associated complaints except menstrual problems.

As seen in the table-2 majority (85.71% i.e.42/49)of the patients had PBAC score in the very heavy range (>300) at the time of recruitment. Thus 81.63% patients were relieved of menorrhagis at the end of study. This finding is similar to the study done by Kriplani *et al.;* in 2007 [10] where they found that centchroman use cured menorrhagia in 78%patients.

As shown in table-3 41 patients had endometrial thickness in the range of 5-8mm, 5(10.21%) patients in the range of >8-11mm and 3(6.12%)patients had Et>11mm.

As can be seen from the above table-4 majority of patients had dysmenorrhoea of varying intensity before treatment. 31 patients out of 49 i.e.63.26% had dysmenorrhoea 6 patients had severe 11 moderate and 14 had mild dysmenorrhoea. Biswas Subhas Chandra *et al.;* in 2002 [9] also observed improvement in dysmenorrhoea in 78.26%.Kriplani *et al.;* in 2007 [10] observed that 56.7%and 66.7% patients, were free of pain at the second and fourth months of treatment.

As the table-5 shows 36(73.46%) patients had a history of passage of clots during periods which decreased substantially to 20 Patients just after 1 month of treatment. The improvement continued and at the end of 4 months of treatment only 3 patients gave history of passage of clots. Kriplani *et al.;* in 2007 [10] observed improvement of 88.89%.

As shown by the table-6 majority of patients (57.15%) had no adverse effects with ormeloxifene with 4 months of treatment. Study by Kriplani *et al.;* in 2007 [10] noted ovarian cyst (7.1%), cervical erosion and discharge (7.1%), gastric dyspepsia (4.8%), vague abdominal pain (4.8%) and headache as adverse effect.

As the table-7 shows majority (53.06%) of patients had duration of bleeding>8 days.

Table-1: Distribution according to type of associated complaints of the subjects before starting treatment

Type of complaints	No.	%
Low backache	7	14.29
Pain abdomen	4	8.16
Weakness	2	4.08
White discharge	2	4.08
Heaviness in lower abdomen	1	2.04
None	33	67.35
Total	49	100.00

Table-2: Distribution according to PBAC score of the subjects at various intervals

PBAC Score	Before treatment	After 1 month	After 4 months	After 3 months follow up
Very heavy (>300)	42 (85.71%)	16 (32.65%)	2 (4.08%)	0 (0.00%)
Heavy (>100<300)	7 (14.29%)	26 (53.06%)	7 (14.29%)	1 (2.17%)
Moderate (11-100)	0 (0.00%)	6 (12.24%)	11 (22.45%)	15 (32.61%)
Scanty (<10)	0 (0.00%)	0 (0.00%)	2 (4.08%)	8 (17.38%)
Amenorrhoea	0 (0.00%)	1 (2.04%)	27 (55.10%)	22 (47.83%)
Total	49 (100.00%	49 (100.00%)	49 (100.00%)	46 (100.00%)

Table-3: Distribution according to endometrial thickness of subjects

Endometrial thickness(mm)	Before treatment		After 4 months of treatment	
	No.	%	No.	%
5-8	41	83.67	43	87.76
>8-11	5	10.21	4	8.16
>11	3	6.12	2	4.08
Total	49	100.00	49	100.00

Table-4: Distribution according to Dysmenorrhoea of the subjects at various intervals

Dysmenorrhoea	Before treatment	After 1 month	After 3 months	After 4 months
Nil	18(36.74%)	28(57.14%)	34(69.39%)	39(79.59%)
Mild	14(28.57%)	10(20.41%)	8(16.33%)	8(16.33%)
Moderate	11(22.45%)	7(14.29%)	5(10.20%)	2(4.08%)
Severe	6(12.24%)	4(8.16%)	2(4.08%)	0 (0.00)
Total	49 (100.00%)	49(100.00%)	49(100.00%)	49(100.00%

Table-5: Distribution according to passage of clots of the subjects at various intervals

Passage of clots	Before	After 1 month	After 3 months	After 4 months	After 3 months
Passage of clots	36/49 (73.46%)	20/49 (40.81%)	11/49 (22.45%)	3/49 (6.12%)	3/49 (6.12%)

Table-6: Distribution according to side effects of ormeloxifene after 4 months of treatment

Side effects	No.	%
White discharge per vaginum	8	16.33
Gastric dyspepsia	4	8.16
Vague abdominal pain	4	8.16
Ovarian cyst	3	6.12
Headache	2	4.08
None	28	57.15
Total	49	100.00

Table-7: Distribution according to duration of flow of menstruation

Duration(in	No.	%
<7	23	46.94
>8	26	53.06
Total	49	100.00

CONCLUSION

Ormeloxifene is a safe and effective drug for the medical management of abnormal uterine bleeding. The other benefits are that it is non-steroidal, pharmacologically and metabolically safe and oncologically protective. It causes no major or persistent side effects and is well tolerated. Also it is cost effective and dose schedule of the drug results in good compliance. Thus oral centchroman may be used as a first line medical management of AUB especially for patients who wish to preserve fertility and in whom steroidal treatment is not recommended and or contraindicated. It is especially a better choice in: 1. Perimenopausal women to tide over that period and in whom amenorrhoea is welcome and in 2 young women who desire contraception and in ...3. Patients who are high risk of surgery.

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