



EFFECT OF ORMELOXIFENE ON HAEMOGLOBIN STATUS IN ABNORMAL UTERINE BLEEDING

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ABSTRACT

AIM: Abnormal Uterine Bleeding (AUB) is the commonest presenting symptom in Gynaecology out-patient department. The Aim is to study the efficacy, safety and acceptability of ORMELOXIFENE in improving Haemoglobin concentration in patients with Histopathological reports like Secretory phase, Proliferative phase, Late Proliferative phase and Surface Hyperplasia in AUB. We also tried to observe the Incidence of various pathologies in different age groups presenting with AUB, AUB being the major contribution to anaemia, non-surgical management of the problem should be the main stay of treatment.

Methods: This is a Hospital based Prospective study which included a sample size of 50. 50 cases of AUB were observed. Each patient was given 60 mg. of Ormeloxifene twice weekly (Sunday & Wednesday) for a period of 3 months and then weekly once (Sunday) for another 3 months. Primary outcome measures were menstrual blood loss, Haemoglobin concentration and Histopathological type.

Results: The Mean post treatment HB concentration and PBAC score were significantly increased.

Conclusion: 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 : Abnormal Uterine Bleeding (AUB), Hemoglobin (HB), Spotting (S), Dysmenorrhoea (D), Clots (C), Irregular cycles (IC), Menorrhagia (MNG), polymenorrhoea (PMG)

INTRODUCTION:

Abnormal Uterine Bleeding is a common condition for women of all ages to consult the gynaecologist. It includes non-organic causes of uterine bleeding. Endometrial biopsy on curettage could be a safe and diagnostic step in evaluation of abnormal uterine bleeding after ruling out medical causes of AUB and to determine the specific pathology in different age groups.

Menorrhagia is usually defined as menstrual blood loss more than 80 ml./cycle or a PBAC score (Pictorial Blood Loss Assessment) of more than 100.(1)

In this Prospective study measuring menstrual loss, it was determined that the Mean Menstrual blood loss is 43 ml./cycle. It is the most common menstrual disorder that can affect any woman from Menarche to Menopause (2). 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 like dilatation and curettage have similar success rates and complication profiles, take less time to perform and are technically easier to conduct, but are expensive(3). Various drugs used are NSAIDS, Tranexamic acid, Haemostatic agents, Progesterones and Danazol.

The role of Levonorgestrel intrauterine system (LNGIUS) in Menorrhagia is well established, but its cost limits its widespread use. Ormeloxifene dose is 60 mg. twice weekly for 3 months and then a dose of 60 mg. weekly for another 3 months. Bleeding usually stops or becomes normal within 2 or 3 days of first dose followed by regular or delayed cycles which are normal or scanty in flow in 85 to 87% of subjects (4). Ormeloxifene (Centchromon) is a non steroidal, non hormonal, pharmacologically inert, selective estrogen receptor modulator (SERM) (5). It has anti estrogenic and anti proliferative effect on endometrium, hence used as a quick and effective endometrium hemostat for AUB. Ormeloxifene 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.

AIMS AND OBJECTIVES:

To study the effect of Ormeloxifene on menstrual blood loss with 6 months of treatment and follow up for 6 months. To study the effect of Ormeloxifene on improvement of HB levels.

MATERIAL AND METHODS:

This was a prospective study conducted on patients presenting with AUB from JAN 2016 to Dec. 2016 in the Outpatient Department of

Gynaecology and Obstetrics, KING GEORGE HOSPITAL, Visakhapatnam.

Patients were selected based on clinical details, who underwent diagnostic curettage and Histopathological evaluation.

STUDY DESIGN: Hospital based Prospective study

SAMPLE SIZE: 50

INCLUSION CRITERIA: All cases of AUB

EXCLUSION CRITERIA:

- Uterine size 8 weeks or more, Fibroids, Adenexal mass detected on USG,
- Presence of any PID.
- Active bleeding necessitating emergency treatment.
- Renal and Hepatic dysfunction
- Associated Infertility
- Post menopausal bleeding

PROCEDURE:

After recording all relevant investigations, baseline clinical profile, cycle length, duration of bleeding and PBAC score for each woman were 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 blood loss. Follow ups were made at 1,3 & 6 months of therapy and after completion of 3 months of treatment to assess improvement of symptoms and HB concentration. The total duration of study was 12 months. At each visit, days of bleeding, cycle length, PBAC score and any side effects were noted in detail. HB was repeated after 6 months of treatment.

RESULTS:

In this study 23 patients (46%) were in the age group of 40-50 years, 12 patients (24%) in the age group of 30-40 years and 15 patients (30%) in the age group of 20-30 years.

Depending on symptoms majority of patients 28 (56%) were suffering from polymenorrhagic cycles. 13 patients (26%) were suffering from menorrhagic cycles. Out of 50, 5 patients (10%) were with continuous bleeding and 4 patients (8%) with irregular cycles.

Majority of patients 30 (60%) were suffering from passage of clots associated with dysmenorrhoea. 8 patients (16%) were with dysmenorrhoea only and 8 patients (16%) were with passage of clots only. 4 patients (8%) were noted without dysmenorrhoea and clots.

Depending on pattern of menstrual flow, majority of patients 38 (76%) had menstrual flow for 5 to 10 days. Menstrual flow for more than 10 to 20 days was found in 6 patients (12%) and for more than 20 days was

found in 6 patients (12%) before taking treatment with Ormeloxifene. After treatment with Ormeloxifene for 6 months, reduced menstrual blood flow for less than 5 days was noted in 40 patients (80%). Menstrual flow for 5-10 days was noted in 10 patients (20%).

Before treatment PBAC score was noted between 200-300 in 5 patients (10%) and between 300-400 in 20 patients (40%). 14 patients (28%) have shown score of 400-500 and 10 patients (20%) have shown a score of 500-600. Only one patient (2%) was with score between 600-700.

After treatment maximum patients 29 (58%) were with PBAC score between 100-200. 20 patients (40%) have shown reduced score to less than 100 and only one patient (2%) was with score 200-300 (Table-II).

Before treatment HB concentration was noted and 10 patients (20%) were noted with HB percentage of 8 to 8.99 and 36 patients (72%) had HB percentage of 9 to 9.99. Only 4 patients (8%) were with HB percentage of 10 to 11.

After treatment with Ormeloxifene for 6 months, gross increase in HB concentration was found in majority of the patients i.e. 37 patients (74%) have shown HB levels between 10-11% and 13 patients (26%) were with HB levels between 9-9.99% (Table-I).

Depending on Histopathological report 27 patients (54%) have shown secretory phase of endometrium. 13 patients (26%) have shown Proliferative phase of endometrium. 6 patients (12) were with late proliferative endometrium and only 4 patients (8%) were with surface epithelial hyperplasia without atypia.

Discussion:

AUB is one of the most common gynaecological complaints with which women attend the outpatient department. Ormeloxifene which is a potent antiestrogen with weak agonist properties has a pharmacological profile which is very effective in AUB.

In the present study, the mean age of distribution of AUB was between 41-50 years. In a study by Sutherland (1949) 39% of patients were above the age of 50 years.

In the present study, there was a significant response on the passage of clots from 80% prior to treatment to 22% post treatment. This was in concordance with the study by Subhash Chandra et.al, Darjeeling and Alka Kriplani et.al New Delhi, where the passage of clots reduced from 74% cases and 64.3% cases before treatment to 12% and 7.1% respectively post treatment.

Present study shows significant improvement dysmenorrhoea from 78% cases prior to treatment to 23% cases at the end of treatment. This correlates well with the studies by Subhash Chandra et.al, Darjeeling and Alka Kriplani et.al, New Delhi, where there was improvement in dysmenorrhoea in 27% and 71.4% cases prior to study to 5% and 23% at the end of study respectively.

In the present study the mean increase in HB level was 0.9 gm%. In the study by Subhash Chandra et al Darjeeling, the mean increase in HB level was 1.3 gm%. In study by Alka Kariplani et al, New Delhi it was 0.6 gm%.

In the present study mean PBAC score before treatment was 402.70 which decreased significantly to 104.42 after treatment with Ormeloxifene. In studies by Subhash Chandra et al and Alka Kriplani et al, the mean PBAC scores prior to treatment were 272.0 and 388 respectively which reduced to 107.8 and 80 after treatment respectively.

Amenorrhoea was the most common side effect in all the studies. In the present study, amenorrhoea was reported in 8% of cases. In the study by Subhash Chandra et al, Darjeeling amenorrhoea was seen in 17.64% cases and in study by Alka Kriplani et al, New Delhi, it was reported in 3.6% cases.

CONCLUSION:

Abnormal uterine bleeding is one of the most common gynaecological symptom that makes a patient consult a Gynaecologist. Medical treatment of Abnormal Uterine Bleeding should aim to relieve symptoms, improve quality of life and avoid the risk of surgery.

Despite a decrease in mean blood loss by 50% many woman remain menorrhagic when treated with Tranexamic acid, Mefanamic acid, Ethamsylate or Nor ethesterone and many are non compliant due to daily dosage. Ormeloxifene is a safe and effective drug for the medical management of AUB. 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. It is also cost effective and dose schedule of the drug results in good compliance.

At the recommended dose, ormeloxifene doesn't exhibit progestational, androgenic or antiandrogenic properties. Likewise, it doesn't affect the secretion of pituitary, thyroid or adrenal hormones.

Ormeloxifene may be considered for the medical management of idiopathic, menorrhagia, especially for patients who prefer non steroidal treatment, wish to preserve fertility and when steroidal treatment is either not recommended not desired.

Ormeloxifene is a good option for young females who desire contraception. It is better choice in perimenopausal women to tide over that period and in patients who are high risk for surgery.

Table - 1: HB% Before and After Treatment with ormeloxifene

Before HB%	After	
	No. of patients	No. of Patients
8-8.99	10	0
9-9.99	36	13
10-11	4	37

Mean HB level Before Rx 9.3

Mean HB Level After Rx 10.2

The improvement in the Hemoglobin concentration after intervention is found to be statistically high significant of 95% confidence internal levels.

P Value 0.0001

Table 2: PBAC Score Before and After Treatment with Ormeloxifene

SCORES	BEFORE	AFTER	TOTAL
< 300	5	50	55
>300	45	0	45
Total	50	50	100

PBAC Score before Rx 402.70

PBAC Score after Rx 104.42

Improvement in the PBAC Scores after treatment was 104.42 was found to be statistically highly significant.

P Value 0.0001

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