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A Comparative Study Of Ormeloxifene Versus Oral Contraceptive Pill In Treatment Of Menorrhagia In Reproductive Age Group:A Randomized Control Study

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Abstract

Background : Abnormal uterine bleeding (AUB) is the most common menstrual disorder of women in any age group and is a diagnosis of exclusion. Management of menorrhagia is a difficult task as there are wide variations in the available drugs and a lot of different regimes are available.

Methods: The study was conducted in the Department of Obstetrics and Gynecology, S.P.Medical College & AGH, Bikaner, Rajasthan. This was an Hospital based prospective randomize control study. We included 40 patients in each group for present study. Group A was given tablet ormeloxifene 60mg twice a week for 12 weeks followed by once a week for next 12 weeks and Group B was given low dose OCP (30 microgram Ethinyloestradiol and 150 microgram levonorgestrel)from day 1 to day 21 of menstrual cycle for 6 months.

Result: We found that in group A [ORM] pre-treatment mean haemoglobin was 7.29±0.94 gm% and post treatment mean haemoglobin was 9.77±0.89 gm%, while in group B[OCP] pre-treatment mean haemoglobin was 7.48±0.83gm% and post treatment haemoglobin was 8.43±0.73gm% .The difference was found statistically significant (P-value <0.0001). In our study, In group A[ORM] pre-treatment mean PBAC score was 273.2±42.2 and post treatment mean PBAC score was 91.5±17.89. While in group B [OCP] pre-treatment mean PBAC score was 276.95±35.52 and post treatment mean PBAC score was 187.63± 24.31.The difference in reduction of PBAC score post treatment was found statistically significant(p- value<0.0001).

Conclusion: It can be concluded that both ormeloxifene and OCPills significantly reduce blood loss in patients of reproductive age group AUB evidenced by decrease of PBAC score, rise in hemoglobin levels and decrease in ET. However, ormeloxifene was found to be superior to OCPills in reducing the menstrual blood loss.

Keywords: Dysfunctional uterine bleeding, Ormeloxifene, Oral contraceptives.

Introduction

Menorrhagia is abnormal vaginal bleeding from genital tract .1,2,3 Average menstrual blood loss is between 30- 40 ml per cycle. An early population - based study concluded that upper limit of normal menstrual blood loss was between 60-80 ml, with the upper limit subsequently adopted as classic definition of menorrhagia.1 It affects 10-30% of women at some stage in their life. 1, 4

The patho-physiology of dysfunctional uterine bleeding is largely unknown but occurs in both ovulatory and anovulatory menstrual cycles .3 A number of the local factors are thought to be involved in the local control of menstrual blood loss and abnormality in these factors that may cause menorrhagia.5 Once a diagnosis has been reached with aid of history, examination, hematological and endocrine investigations, and dilatation and curettage when appropriate, medical treatment is the usual first line approach.

The treatment of menorrhagia is a demanding task and various drugs like antifibrinolytics, non-steroidal anti- inflammatory drugs (NSAIDs), progesterones, combined estrogen and progesterones, danazol, gonadotrophin releasing hormone analogues and levonorgesterol-releasing intrauterine system have all been used with different results in the management of menorrhagia. Oral contraceptives have long been used clinically to decrease menstrual flow Oral contraceptives (OCs), also known as "the pill", are the most popular method of contraception among female adolescents. The primary mechanism of action is that it suppress hypothalamo- pitutary axis to inhibit ovulation , reduce fertility and produce atrophy of endometrium. Ormiloxifene(also known as centchroman) is one of the selective estrogens receptor modulators (SERM).6 It is a non-steroidal , non hormonal, oral contraceptive which is taken once in a week. However, Ormeloxifene acts as estrogen antagonist in uterus (endometrium), breast tissues which lead to endometrial atrophy hence the decreases menstrual blood loss.7 The safety profile of Ormeloxifene is excellent with very few side effects like nausea, headache, weight gain, delayed or prolonged menstrual period. There is well known effect of both OCP and ormeloxifene on AUB , however there are very few studies comparing the effect of ormeloxifene and OCP in reproductive age group AUB , so we decided to conduct this a comparative analysis of both OCP and ormeloxifene.

Material And Methods

The study was conducted in the Department of Obstetrics and Gynecology, S.P.Medical College & AGH, Bikaner, Rajasthan. This was Hospital based prospective randomize control study conducted form November 2020 to October 2021

Study Design: Hospital based randomized control study

Study Location: This was a tertiary care hospital based study done in department of Obstetrics and Gynecology, S.P.Medical College & AGH, Bikaner, Rajasthan, India

Study Duration: November 2020 to October 2021

Sample Size:. 80 patients

S**ample Size Calculation:** Sample size was estimated on the bases of a single proportion study design. Sample size was estimated using MEDLAC 16.4 version software power of study 80% ,allowable error 5%, sample size obtain for this study was 40 patients in each group (group A – patient prescribed tab ormeloxifene, group B patient prescribed oral contraceptive pill), expecting approx.10% drops out .

Subject And Selection Method: Women in reproductive age group attending outpatient department (OPD) with subjective symptoms of excessive MBL irrespective of bilateral tubal ligation were included in study. Group A[ORM] was given ormeloxifene tablet 60mg twice a week for 12 weeks, followed by once a week for next 12 weeks. Group B[OCP] was given low dose OCP containing 30 micrograms ethinyloestradiol and 150micrograms levonorgestrel from day1 to day 21 of menstrual cycle for 6 cycles and followed for 6 months.

Inclusion Criteria: women of reproductive age group with excessive menstrual bleeding willing to give informed consent to participate in study.

Exclusion Criteria:

1. Patients with any organic pelvic pathology or pregnancy
2. Acute heavy bleeding,
3. Haemodynamically unstable patients
4. Postmenopausal bleeding
5. Recent history or clinical evidence of jaundice, renal disease
6. Polycystic ovary syndrome
7. Chronic cervicitis or cervical hyperplasia
8. Chronic illness for example, tuberculosis
9. Past history or family history of thromboembolic diseases
10. Known or suspected cancer of breast or other estrogen-dependent cancers
11. Hypersensitivity to drugs.

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Data-analysis: The data collected were analysed and comparison of values between the groups was performed using students "t" for quantitative data and

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chi-square will be used for qualitative data. Statistical significance will be considered at p value <0.05.

Method Of Collection Of Data :

Informed consent was taken from all the patients. A detailed history and clinical examination was done. As AUB is a diagnosis of exclusion investigation were done to rule out any other possible cause for abnormal uterine bleeding. These included complete blood cell count including hemoglobin 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 , numbers and size of clots passed , and if dysmenorrhea experienced . The pictorial blood loss assessment chart (PBAC) scoring were done accordingly to assess menstrual blood loss. PBAC is a simple procedure for objective assessment of menstrual blood loss. A PBAC score more than 100 indicates a menstrual loss >80 ml and is considered diagnostic for menorrhagia.

The women were allocated into two groups using randomization by chit and box method .Cases were taken until each group had 40 cases, who were ready for follow-up. Group A was given ormeloxifene tablets 60mg twice a week for 12 weeks and group B was given low dose OCP (30 microgram ethinyloestradiol and 150 microgram levonorgestrel) from day 1 to day 21stof the menstrual cycle for 6 cycles. Patients was followed up to 6 months and during each visit a detailed menstrual history was taken, PBAC score was calculated. Haemoglobin concentration and endometrial thickness was measured after 6 months of treatment. Any side effects during therapy was also noted .

Result

Total number of patients participating were 80 , 40-40 patients belong to each group . Haemoglobin level,

PBAC score endometrial thickness were measured before starting therapy and at the end of 6 month of therapy. Statistical parameter used as mean±SD.

Sociodemographic and clinical parameters were almost similar except for minor difference in few variables. In both group majority of cases belong to parity two. Mean age in group A[ORM] was 30.2±7.92 year and in group B [OCP] was 33.25±6.89 years. In group A[ORM] more patients belong to urban area and in group B [OCP] 50% patients belong to urban area

We found that 83.33% cases in group A [ORM] and 91.18% cases in group B show dysmenorrhoea before starting treatment. Also, 74.7% cases in group A[ORM] and 64.71% cases in group B[OCP] show irregular cycle before starting the treatment. In Group A [ORM] 33 patients showed improvement in dysmenorrhoea and 35 patients showed regular cycle post treatment. While in group B [OCP] 34 patients showed improvement in dysmenorrhoea and 37 patients showed regular cycle post treatment. Results of present study are comparable to other studies conducted previously.9,10,11,13

When comparing post treatment result the mean blood loss following treatment show reduction in both groups however significant reduction was seen in ormeloxifene group as in table no 3. Mean haemoglobin level shows improvement in both groups post treatment, however ormeloxifene group showed significantly better improvement in comparison to OCP group as in table no 3. Mean endometrial thickness also showed reduction in both study group but significant (p value<0.05) was observed in group A[ORM].

Table 1: Distribution Of Cases According To Sociodemographic Parameters

Mean		Group A[ORM]	Group B[OCP]
Age		30.2±7.92	33.25± 6,89
Parity		2	2
	Urban	22	20

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Residance	**Rural**	**18**	**20**

Side effects of therapy were also recorded in both treatment groups patients in group A[ORM] reported amenorrhoea(15%) as more common side effect, headache(14%) and GI symptoms(7.5%) reported by few subjects.OCP group reported weight gain (7.5%), head ache (20%) as more common side effects. Overall none of the participants from either group reported intolerable side effects

Table 2: Comparison Of Cases According To Pretreatment And Posttreatment Symptoms In Both Groups

Symptoms	Group A[ORM]		Group B [OCP]	
	Pre-treatment	Post treatment	Pre treatment	Post treatment
Dysmenorrhoea	34	7	36	6
Irregular cycle	29	5	25	3
P-value	<0.0001			

Table 3: Comparison Of Cases According To Pre And Post Treatment Pbac Score, Haemoglobin Level And Endometrial Thickness

Mean±SD	Group A[ORM]		Group B[OCP]	
	Pre treatment	Post treatment	Pre treatment	Post treatment
PBAC	273.2±42.2	91.5±17.89	276.95±35.52	187.65±24.31
Haemoglobin(gm/dl)	7.29±0.94	9.77±0.89	7.48±0.83	8.43±0.73
Endometrial thickness(in mm)	12.16±2.92	7.92±1.64	11.63±2.25	10.21±1.91
P-value	<0.0001			

Discussion

The traditional surgical treatment for menorrhagia is hysterectomy, which even though, offers an effective cure, involves major surgery with significant postoperative morbidity. Another alternative is endometrial ablation techniques with considerably reduced postoperative morbidity. It is always hard to quantify mean blood loss objectively and is usually defined subjectively in clinical practice. We opted to use PBAC chart as used by Higham et al8 It is a simpler and faster method, not requiring preservation of sanitary products and avoids costly chemical assay.

In the present study reduction in menorrhagia represented by decrease in post treatment PBAC score. Before starting treatment mean PBAC score in Group A[ORM] was 273.2±42.2, after 6 month of treatment significant reduction (p-value<0.05) in PBAC score 91.5±17.89 was seen. In Group B [OCP] there was also reduction in PBAC score from 276.95±35.52 to 187.65±24.31 was seen but reduction in menorrhagia is less compare to patients taking ormeloxifene. In similar study conducted by

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khare et al13 mean PBAC score before starting treatment and 6 month after treatment with ormeloxifene was 108.70 and 63.8 while in OCP group was 113.87 and 94. The result of our study with regards to PBAC score following treatment with ormeloxifene and OCP are comparable with earlier studies. Result of present study showed there was significant rise in haemoglobin level of 2.48gm/dl after 6 month of treatment with ormeloxifene compare to 0.95gm/dl rise in haemoglobin level seen with treatment with OCP. Rise in mean Hb level in individuals of both treatment groups in present study is in corroboration with the findings of earlier studies conducted by Aruna devi V et al10, Lakkhawar NJ et al14 and others15,16 . The mean endometrial thickness was also decreased in both the study groups following therapy. At the end of 6 month of treatment with ormeloxifene showed better result comparison to treatment with OCP and these findings are similar with the earlier studies.

Satisfaction among the patients was observed in both the treatment groups however ormeloxifene therapy was reported to be more effective, side effects were minimal and tolerable in both the groups. More common side effects seen with ormeloxifene was amenorrhoea (15%). Side effects like weight gain(7.5%) , head ache(20%) seen in OCP therapy more commonly then ormeloxifene group. Ormeloxifene can be a good option with its property of creating a hypoestrogenic environment without disturbing other estrogen positive effects. It is also devoid of androgenic side effects such as acne, hirsutism. Metabolic side effects of OCP are also not found with ormeloxifene. Thus there seems to be enough evidence to consider ormeloxifene a better drug for the pharmacological management of abnormal uterine bleeding.

Conclusion

It can be concluded that both ormeloxifene and OCPills significantly reduce blood loss in patients of reproductive age group AUB evidenced by decrease of PBAC score, rise in hemoglobin levels and decrease in ET levels. However, ormeloxifene was found to be superior to OCPills in reducing the menstrual blood loss. Ormeloxifene was also tolerated better compared to OCPills with fewer side effects experienced by patients. Compliance with the drug, dosage schedule and effect on quality of life was also better with ormeloxifene compared to OCPills .So Ormeloxifene could be the drug of choice in patients of AUB in the reproductive age group.

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