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Original Research Article

Efficacy of ormeloxifene in comparison to norethisterone in the management of abnormal uterine bleeding

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is the most common complaint worldwide. In India, most of the women present with menorrhagia and majority of them are anemic and require medical management to avoid its consequences. Hence this study is done to compare the efficacy of ormeloxifene with norethisterone in women presenting with AUB.
Methods: In this study 61 women suffering from AUB were included. This prospective randomized double blinded study was done on women between the age group of 19-45 years and were allocated randomly into two groups, one group was given ormeloxifene and the other was given norethisterone for a period of 3 months. Haemoglobin levels, endometrial morphology on ultrasound were assessed before and after the treatment in both the groups.
Results: It is observed in our study, that both ormeloxifene and norethisterone reduced menorrhagia. The rise in hemoglobin concentration was significantly more with ormeloxifene than norethisterone (8.3 g/dl to 10.3 g/dl versus 9.0 g/dl to 10.4 g/dl). In our study, the significant reduction in the endometrial morphology was more with ormeloxifene than norethisterone (9.3 mm to 7.8 mm versus 8.3 mm to 7.2 mm).
Conclusions: Ormeloxifene is a new modality drug and is found to be a better option in reducing menorrhagia compared with norethisterone in respect to a greater success rate, better compliance and cost effectiveness. Hence our study concludes ormeloxifene as a better choice over norethisterone in the treatment of AUB.

Keywords: Abnormal uterine bleeding, Ormeloxifene, Norethisterone, Endometrial thickness

INTRODUCTION

Abnormal uterine bleeding (AUB) is the most common complaint. AUB is the term used to describe any departure from normal menstruation or from normal menstrual cycle pattern.[1] In India, the prevalence of AUB is about 9-30% in pre-menopausal women and 50%in peri-menopausal women.[2] Ormeloxifene is a newer non-steroidal drug, emerging as a safe and effective management of abnormal uterine bleeding. It reduces the menstrual blood loss by regularizing expression of estrogen receptors on endometrium. It also reduces premenstrual symptoms, dysmenorrhea and mastalgia. It is very effective in reducing up to 70% of blood loss with minimal side effects, also has an easy dosing schedule and cost efficient.[3] Hence this study is undertaken to evaluate the effectiveness of ormeloxifene in comparison with norethisterone in the medical management of AUB.

METHODS

This prospective randomized double blinded study was conducted from May 2019 to April 2020 in a tertiary care hospital, Shri Sathya Sai Medical College and Research

Institute, Tamil Nadu, India. The study group consisted of 61 women suffering from AUB.

The inclusion criteria are all women aged between 19-45 years with diagnosis of AUB. The exclusion criteria are women with hypersensitivity to the drug, medical disorders, liver disorders, heart diseases, renal disease, thyroid disorders, and women desirous of fertility. After getting informed and written consent, patient's demographic data, detailed history was obtained. General physical examination, per speculum and pervaginal examination was done.

Baseline laboratory investigations like hemoglobin levels, bleeding time, clotting time, total leucocyte count, platelet count, blood grouping and typing were done for all the patients. Transvaginal ultrasound was done using 7.5mhz voluson P8 transvaginal probe to study the endometrial morphology (ET). It was measured at the thickest part including both the endometrial layers in the longitudinal plane, before the start of the treatment.

Women with AUB were allocated randomly into two groups and the patients in the ormeloxifene group were asked to take orally tablet ormeloxifene 60 mg twice a week on every Wednesday and Saturday for 3 months and the patients in the norethisterone group were asked to take 5 mg of tablet norethisterone twice daily for 21 days followed by 7 days of pill free period for 3 months. Patients were advised to keep record of number of days of bleeding, interval at which periods are coming, number of pads soiled, history of passage of clots and dysmenorrhoea. They were asked to come for follow up every month.

On each follow up they were asked about improvement in blood loss and also for any other complaints. Then hemoglobin concentration, endometrial thickness was measured after 3 months of therapy in both the groups.

Statistical analysis

The data collected were analyzed using statistical package for the social sciences (SPSS) software version 23 and p value estimated.

RESULTS

In this study 61 women with AUB were considered and the data were analyzed. The age distribution shows that 29% of cases in NET group and 30% in ORM group belonged to age group between 36-40 years and >41 years while 22.7% of cases in NET group and 26.7% of cases in ORM group were between 30-35 years of age. The two groups were comparable to each other (Table 1).

In our study, the hemoglobin concentration was between 9-11 gm% in 54.8% of patients in the NET group and 40% of patients in the ORM group, and between 6-8 gm% in 38.7% of patients in NET group and 33.3% of patients in the ORM group. Mean haemoglobin level before start of treatment in NET group was 9.0 gm% and in ORM group was 8.3% (Table 2).

In our study, most of the of the patients had endometrial thickness the in the range of 10.1 to 15 mm (90% in NET group and 70% in ORM group), 5.1 to 10 mm in 9.7% of NET group and 30.0% of ORM group (Table 3).

Table 1: Age distribution.

Age (years)	Drug	
	NET n (%)	ORM n (%)
19-25	1 (3.2)	0 (0)
26-30	5 (16.1)	4 (13.3)
30-35	7 (22.7)	8 (26.7)
36-40	9 (29)	9 (30)
>41	9 (29)	9 (30)
Total	31 (100)	30 (100)

Table 2: Haemoglobin.

Hb	Drug	
	NET n (%)	ORM n (%)
<6	1 (3.2)	2 (6.7)
6-8	12 (38.7)	10 (33.3)
9-11	17 (54.8)	12 (40.0)
>12	1 (3.2)	6 (20.0)
Total	31 (100)	30 (100)

Table 3: Endometrial thickness.

ET	Drug	
	NET n (%)	ORM n (%)
5.1-10	3 (9.7)	9 (30.0)
10.1-15	28 (90.3)	21 (70.0)
Total	31 (100)	30 (100)

Our study shows that the pretreatment mean hemoglobin concentration in NET group was 9 gm%, which was increased to 10.4 gm% with a mean of 1.4 gm% at the end of 3 months.

The pretreatment mean hemoglobin concentration in ORM group was 8.3 gm%, it increased to 10.3 gm% with a mean of 2 gm% at the end of 3 months. On comparing both groups, rise in hemoglobin levels was more in the ormeloxifene group and the difference is statistically significant ($p<0.05$).

The mean endometrial thickness was reduced from 9.3mm to 7.8mm after 3 months with ormeloxifene and with Norethisterone, it was reduced from 8.3mm to 7.2mm at the end of 3 months of therapy (Table 4).

Table 4: Comparison of pre– and post– treatment variables.

Characteristics	Drug			
	NET Mean±SD	P value	ORM Mean±SD	P value
Pre HB	9.0±2.2	<0.0057	8.3±1.4	<0.0001
Post HB	10.4±1.6		10.3±0.9	
Pre ET	8.3±1.4	<0.0022	9.3±1.6	<0.0004
Post ET	7.2±1.3		7.8±1.5	

P<0.05 statistically significant

DISCUSSION

AUB affects 9-14% of women once in their lifetime from menarche to menopause and it has the greatest impact on quality of life affecting women physically, emotionally and socially.

In the present study, 29% of cases in NET group and 30% in ORM group belonged to the age group between 36-40 years and >41 years, these findings were similar to Shahab et al, Girija et al, Ravibabu et al, Grover et al and Agarwal et al, all of them had maximum number of patients between the age group of 30 to 40 years.[4-8] In the present study there is statistically significant improvement of haemoglobin concentration in both the ormeloxifene and norethisterone groups, but it is more significant with ormeloxifene.

In the study conducted by Agrawal et al, in the ORM group mean rise in haemoglobin levels was 2.3 gm%, in the NET group mean rise in haemoglobin levels was 1.3 gm% which is similar to our study where the mean rise in haemoglobin in the ormeloxifence group is 2 gm% with pre and post treatment values in ORM group are 8.3 gm% and 10.3 gm% respectively and 9.0 gm and 10.4 gm% pretreatment and after 3 months of therapy in NET group with mean rise in haemoglobin in norethisterone group is 1.4 gm/dl, both of them are statistically significant.[9] In the study done by Surabhi the rise of haemoglobin was 2.49% in the ormeloxifene group as compared to norethisterone group which documented 1.31 gm% improvement in the haemoglobin levels which is similar to the present study.[10]

In the present study, there is significant reduction in ET from 8.3 mm to 7.2 mm with p value <0.0022 in the norethisterone group and 9.3 mm to 7.8 mm with p value <0.0004 in the ormeloxifene group after 3 months of therapy which is similar to Jacob et al study where they also had in the ormeloxifene, a significant reduction in the endometrial thickness from 7.8 mm to 5.3 mm that is 2.47 mm with p value <0.001 compared to norethisterone which decreased by 0.8 mm from 6.7 mm to 5.9 mm with p value of 0.109.[11]

CONCLUSION

The present study shows that, compared with norethisterone, ormeloxifene had a significant effect in reducing the endometrial thickness and significant increase in mean haemoglobin level. There is also good patient compliance because of convenient dosage schedule with ormeloxifene. Hence the present study concludes ormeloxifene as a better choice over norethisterone in the treatment of AUB.

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