Research Paper

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Study of Efficacy of Ormeloxifene in The Medical Management of Menorrhagia

Medical Science

KEYWORDS : Ormeloxifene, Menorrhagia.

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ABSTRACT

Background: Selective Estrogen Receptive Modulators (SERM) like Ormeloxifene could be useful in DUB.
Objective: To study efficacy of Ormeloxifene in medical management of menorrhagia.
Methodology: 140 eligible participants were recruited for treatment with Ormeloxifene over 1.5 years in a tertiary care hospital.
Observations: Haemoglobin levels increased from pre-treatment (7.827 gm%) to post treatment (9.814 gm%); the mean increase being 1.98 gm%. Endometrial thickness decreased from 11.65mm to 7.39mm, with mean difference of 4.26mm. The median PBAC score pre-treatment was 106 (range- 168 to 70) & post-treatment was 63 (range- 84 to 36); the difference being highly significant (<0.01).
Conclusion: Ormeloxifene is a highly efficacious drug for the medical management of menorrhagia.

INTRODUCTION

Investigations in various developing countries reveal that Menstrual dysfunctions are common & troubling part of a majority of women's lives; yet little attention is paid to understanding or ameliorating it.[1] Menstrual dysfunction, like other neglected aspects of reproductive health, is not included in the Global Burden of Disease estimates.[2]

Menorrhagia is one of the commonest menstrual dysfunction, affecting 10-33% of women at some stage of their lives; besides being major cause of iron deficiency anaemia in females after nutritional anaemia.[3] Menorrhagia is defined as cyclical bleeding at normal intervals which is excessive in amount (blood loss greater than 80 ml) or duration (lasting longer than 7 days).[4] Around half of the women who present with menorrhagia have blood losses within normal range. With judicious selection of cases of DUB, The medical management is more effective in ameliorating the symptoms & surgery can be avoided.

Various medical therapies have been used for the treatment of Menorrhagia. NSAIDs and tranexamic acid offer a simple therapy to be taken during menses, with poor to fair reductions in menstrual blood loss (MBL). Danazol and the Gonadotropin- releasing hormone analogues are highly effective, but side-effects make them suitable only for short-term usage. Combined oral contraceptive pill and the levonorgestrel intrauterine system give fair to good reductions in MBL, but with an additional contraceptive cover. Cyclical progestogens are the most commonly prescribed therapy in UK, but are ineffective for management of ovulatory menorrhagia unless taken at high doses (10-15mg/day) for 3 weeks.

All these issues lead to the call for a newer effective class of drug with minimum side-effects: Selective Estrogen Receptor Modulators (SERM). SERM are unique compounds that have attracted great interest lately. They have affinity to the oestrogen receptors and act like oestrogens in some tissues and have anti-oestrogenic effects in others. Ormeloxifene is one such SERM which has shown anti-oestrogenic effect in uterus that forms pharmacological basis of its use in Menorrhagia.[5] Various researchers have generated evidence for the use of Ormeloxifene in DUB & it's superiority over other treatment modalities. Present study was undertaken with the objective of studying efficacy of Ormeloxifene in medical management of menorrhagia in our set up.

METHODOLOGY

- **Study Design:** Institution based prospective observational study
- **Study setting:** Department of Obstetrics & Gynaecology, Tertiary care Medical College Hospital.
- **Study duration:** December 2012 to August 2014.

Participant Selection:

Inclusion Criteria-

- Aged 35-45 years
- Multiparous women having completed their families
- Complaints of heavy menstrual flow (willingness to undergo premenstrual dilatation and curettage to rule out organic cause of bleeding)
- Willingness to adhere to the treatment for six months
- Willingness for follow up

Exclusion Criteria- Presence of any of the following-

- Atypical endometrial hyperplasia or malignancy
- Endometrial polyp
- Uterine size >6 weeks
- Fibroid uterus
- Adenomyosis
- Pregnant uterus
- Pelvi-abdominal mass
- Pelvic inflammatory disease
- Cervical dysplasia
- Bleeding dyscrasia
- Clinical evidence of hepatic dysfunction
- Postmenopausal bleeding
- Hypersensitivity to the drug

Participants were randomly recruited from the OPD & were evaluated for mentioned selection criteria. Detailed history was taken along with general, systemic, per-vaginum & per-speculum examination and Dilatation & Curettage. Blood investigations & pelvic ultrasonography were also performed. After screening by the mentioned selection criteria by above means, a total of 140 participants were recruited for the study. The participants were adequately counselled regarding the drug Ormeloxifene, its side-effects & cost. Pictorial Blood Loss Assessment Chart (PBAC) scoring system was used in the present study. It is a simple, pictorial tool used in women with menorrhagia to assess menstrual blood loss.[6] A PABC score $\geq$100 was considered a menstrual loss > 80 ml and diagnostic of menorrhagia.[6] PBAC was also explained to the participants in detail.

Ormeloxifene was given to the participants in following dosage after all the criteria were fulfilled: 60 mg twice/week for first three months and then once/week for next three months. Total duration of treatment was 6 months. Patients were to take the drug on specific days every week i.e. Wednesday and Sunday in first three months and then every Sunday in next three months. Participants were followed up every 3 months. PBAC score, haemoglobin concentration and endometrial thickness using TVS were assessed before and after treatment.

Written informed consent was elicited from each participant before recruitment for the study.

The study was conducted after necessary approval from the Institutional Ethics Committee.

OBSERVATIONS

Of total 140 study participants; most belonged to 35-40 years category (88.57%), were literate (82.15%), from urban locality (81.43%) & from lower-middle socio-economic status (42.14%).

History of bleeding for 8-9 days (41.42%) was the most common presentation pre-treatment, whereas 52.85% had bleeding for only 1-2 days after treatment. Distribution by cycle length showed as being 20-40 days in majority (57.85%) of participants pre-treatment; which shifted to >40 days category (62.86%) post-treatment. Major improvement was noted in presence of clots, which were there in 61.4% participants pre-treatment & reduced to only 21.42% post-treatment. Similar trend was noted in the complaints of dysmenorrhoea (70.7%) in pre-treatment & (21.43%) post-treatment.

Haemoglobin estimation of participants revealed statistically significant improvement in the mean levels from pre-treatment (7.827 gm%) to post treatment (9.814 gm%); the mean increase being 1.98 gm%. Iron wasn't supplemented during this period.

Endometrial thickness decreased from 11.65mm to 7.39mm, which was statistically significant, with mean difference of 4.26mm.

Table 1: Comparison of Hemoglobin & Endometrial Thickness before & after Ormeloxifene Therapy

	Pre-Therapy	Post-Therapy	Mean Difference	P-Value
Mean Hemoglobin in gm% (Standard Deviation)	7.827 (+/- 1.0341)	9.814 (+/- 0.8041)	1.98	<0.01
Mean Endometrial Thickness in mm (Standard Deviation)	11.65 (+/- 1.858)	7.39 (+/- 1.203)	4.26	<0.01

The median PBAC score pre-treatment was 106 (range- 168 to 70) & post-treatment was 63 (range- 84 to 36). By applying Wilcoxon Signed Rank Test, P-value was calculated which was highly significant (<0.01).

Table 2:Comparison of PBAC score before & after Ormeloxifene Therapy

	PBAC (Pre-Therapy)	PBAC (Post Therapy)
MEDIAN		
25	106	63
PERCENTILES	100	56
50	106	63
	114.75	69.75
75		

Wilcoxon Signed Ranks test P value <0.01

As for subjectivity of complaints of the patients, as many as 78.57% participants reported marked improvement after treatment; while no patient reported aggravation of symptoms.

DISCUSSION

Our study reported shifting of majority in bleeding days per cycle from 8-9 days to 1-2 days post-treatment and in more than half of the participants, cycle length increased from 20-40 days to >40 days. This is in-line with the **Grover et al study**[7], which reported decrease in total number of bleeding days/year by 76% with Ormeloxifene treatment. In another study by **Agarwal et al**[5], 90.4% reduction in the menstrual blood loss was reported. A study by **Chandra et al**[8] observed 85.7% improvement in heavy blood flow. In **Kriplani et al study**[9], there was significant decrease in the menstrual blood loss after two months and four months. In the **Chitrangadha et al study**[10], the menstrual blood loss decreased by 20.7% at the end of two months, 43.4% at the end of four months and 59.5% at the end of six months in case of Ormeloxifene group as compared to Norethisterone group. Similar improvements were reported across studies w.r.t. presence of clots & dysmenorrhoea.

The mean increase in Hb concentration was reported to be 1.98gm% in our study. The findings sit well with the study by **Grover et al**[7], in which mean increase in Hb concentration was reported at 0.43gm%. **Chandra et al**[8] observed an increase of 1.3gm% in their study. While **Agarwal et al**[5] reported mean Hb concentration increase by 1.82gm% after similar duration of Ormeloxifene therapy. **Gupta et al**[11], also found statistically significant increase in Hb concentration from 8.26gm% to 10.59gm% (mean increase of 2.33gm%). **Kriplani et al study**[9] also reported similar finding.

The statistically significant reduction in mean endometrial thickness reported in present study with Ormeloxifene therapy (4.26mm) is in coherence with findings from other similar studies. **Agarwal et al**[5] observed mean reduction of 8.13mm, while **Grover et al**[7] reported it at 1.2mm. In studies by **Chandra et al**[8] & **Gupta et al**[11] also, similar findings were reported amongst almost 90% of participants.

In our study, the median PBAC score pre-treatment was 106 (range- 168 to 70) & post-treatment was 63 (range- 84 to 36) and the reduction was found to be statistically significant. In **Kriplani et al study**[9]**,** the pre-treatment median PBAC score was 388 (range 169-835). PBAC reduced to 80 (range 0-730) and 5 (range 0-310) at 2 and 4 months respectively (P-value <0.01). In **Chandra et al study**[8], the median pre-treatment baseline PBAC score was 272.0 with a range of 123 to 865. The median post-treatment PBAC score was 107.8 with a range of 60.7 to 415. Sixty out of eighty-five patients recorded a mean PBAC score of <100 at the end of study. In **Agarwal et al**[5] **study,** the mean pre-treatment PBAC score was 334 with a range of 123-643. After 3 months of treatment with Ormeloxifene, it reduced to 111 (range 42-201) and after 6 months to 32 (range 0-75), all the results being statistically significant. So our study further substantiates the available evidence w.r.t. PBAC score.

CONCLUSION

Ormeloxifene is a highly efficacious & safe drug for the medical management of menorrhagia.

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