OPEN ACCESS
Scholars International Journal of Obstetrics and Gynecology
Abbreviated Key Title: Sch Int J Obstet Gynec
ISSN 2616-8235 (Print) |ISSN 2617-3492 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com/journal/sijog/home

Original Research Article

Ormeloxifene: A Selective Estrogen Receptor Modulator in Medical Management of Dysfunctional Uterine Bleeding

Malathi Jonna[1*], Vijayalakshmi P[2]

[1]Assistant Professor, Department of Obstetrics and Gynaecology, Sri Padmavathi Medical College for Women, SVIMS, Alipiri Road Beside Bharathiya Vidya Bhavan School SVIMS University, Andhra Pradesh 517507, India
[2]Professor, Department of Obstetrics and Gynaecology, Sri Padmavathi Medical College for Women, SVIMS, Alipiri Road Beside Bharathiya Vidya Bhavan School SVIMS University, Andhra Pradesh 517507, India

DOI: 10.36348/sijog.2019.v02i06.003 | **Received:** 09.06.2019 | **Accepted:** 18.06.2019 | **Published:** 30.06.2019

***Corresponding author:** Malathi Jonna

Abstract

OBJECTIVE: The study was done to evaluate the efficacy of ormeloxifene in medical management of dysfunctional uetrine bleeding. ***METHODS:*** Thirty women in reproductive age group who have completed child bearing, attending the outpatient gynaecology department with complaint of heavy menstrual flow were recruited for the study over a period of one year. Ormeloxifene (60 mg) was given orally twice a week for first 12 weeks and then once a week for up to next 12 weeks. Menstrual blood loss measurement was done using pictorial blood loss assessment chart (PBAC), blood haemoglobin (gm/ dl) levels and endometrial thickness was the main measurements to evaluate the efficacy of therapy. The data obtained was analyzed using the mean and p values of less than 0.05 were accepted as indicating statistical significance. ***RESULTS:*** There was a significant reduction in PBAC score from pre-treatment and post-treatment with ormeloxifene ($p<0.001$).There was also significant reduction in the endometrial thickness after treatment ($p<0.001$).The difference in mean haemoglobin concentration of 2.02 gm/dl between pre-treatment and post-treatment.no major adverse effects were seen in the study. ***CONCLUSION:*** The results in this study showed that ormeloxifene, a non-hormonal, non- steriodal agent provides effective and favourable medical management with least side effects, suitable for the treatment of dysfunctional uterine bleeding.

Keywords: SERM, ormeloxifene, dysfunctional uterine bleeding, menorrhagia, PBAC score, polymenorrhagia.

INTRODUCTION

Menorrhagia is defined as a cyclic bleeding with blood loss of >80 ml or more than 7 days duration. It affects 10 to 30% of reproductive age women in their lives [1-3]. In the majority of the cases, abnormal genital tract bleeding with no organic disease and the bleeding is termed dysfunctional uterine bleeding [4]. Over the years, menorrhagia has become a very common presenting complaint.

Now a days the total span of menstruating years has increased either due to early menarche or late menopause. Women are unwilling to accept any minor menstrual disturbances. Women are looking at ultimate cure, which is hysterectomy. Recently concern about long term complication about hysterectomy has been expressed like premature ovarian failure, urinary dysfunction and cardiovascular disease.

The discovery that pharmacologic agents can be estrogenic in some tissues while antiestrogenic in others had led to intense interest in better understanding the mechanism by which molecular structure interacts with cellular receptors to selectively affect DNA trasncription in different organs. Appreciation for these selective estrogen receptor modulators (SERM's) has inevitably given to the hope of developing one that could confer all the benefits of estrogen without any of its risks.

The ideal SERM should function as an anti-estrogen in the breast and utreus and a partial estrogen agonist in the skeletal, cardiovascular, CNS, gastrointestinal tract and vagina.

Ormeloxifene is a third generation selective estrogen receptor modulators, a class of medication which acts on the estrogen receptor. It is devoid of progesterone, androgenic and anti-androgenic activities [5]. Ormeloxifene is a non –hormonal, non- steroidal agent that provides effective and favourable pharmacological management option for the treatment

of dub [6]. It has no apparent adverse effects on endrocrine, hematologic, liver and lipid function [5]. SERM's are a new class of drugs avaiable today for the management of disorders resulting from disturbances of estrogen secretion. The effect of SERM on the vascular endothelium leads to reduced blood loss and thereby decreasing the symptoms in DUB.

Ormeloxifene not only preferred as oral contraceptive, but also useful for management of dysfunctional uterine bleeding and advanced breast cancer [7].

The present study was done to evaluate the efficacy of ormeloxifene in medical management of dysfunctional uterine bleeding.

MATERIALS AND METHODS

This is a prospective study of one year duration, on 30 women with dysfunctional uterine bleeding who attended to out-patient department of obstetrics & gynaecology. Newly diagnosed dysfunctional uterine bleeding who have completed child bearing above the age of 20 years was included in the study.

The exclusion criteria included those patients with pelvic pathology like Pelvic inflammatory disease(PID), Fibroids, Endometriosis, known case or suspected of genital tract malignancy, those with heavy bleeding necessitating emergency treatment, and those who were on any kind of hormonal treatment like progesterone, estrogen, testosterone, prostaglandin or danazol and any allergy to ormeloxifene.

Informed consent was taken and detailed history regarding menstrual cycle was taken and patient was examined. Routine haematological investigations like haemoglobin, coagulation profile, thyroid profile, ultrasound pelvis, endometrial biopsy and liver functions test were done.

Once the patient met the inclusion criteria, ormeloxifene tablet 60 mg was given twice a week for 12 weeks (wednesday and sunday) regularly and then once a week (sunday) for next 12 weeks. Treatment was continued irrespective of menstrual periods. The patients were advised to come for follow-up at 6^{th}, 12^{th} and 24^{th} week of treatment or earlier if needed. The main outcome was measured by haemoglobin levels, amount of menstrual blood loss and endometrial thickness at the end of 24^{th} week of study. Pictorial blood loss assessment chart (PBAC) was used to measure the menstrual blood loss [8]. The women were asked to use sanitary products which have been shown to have similar absorbent capacities, and the number of sanitary products used each day and the amount of soiling of each pad used were noted. Number and size of clots passed were recorded. Scores were assigned. 80 ml or more blood loss was considered when PBAC score is greater than or equal to 100 indicating a menstrual blood loss that is diagnostic for menorrhagia [8]. The data obtained was analysed using the mean and p values of less than 0.05 were accepted as indicating statistical significance

RESULTS

Table-1: PBAC Scoring

PADS	lightly soiled pad	1 points
	moderately soiled pad	5 points
	saturated pad	20 points
CLOTS	for each small clot	1 points
	for each large clot	5 points
	for each episode of flooding	5 points

Table-2: Demographic Factors

AGE (YEARS)	NUMBER(30)	PERCENTAGE (%)
20-30	2	6.6
31-40	12	40
41-50	16	53.4

Table-3: Symptoms of Dysfunctional Uterine Bleeding

SYMPTOMS	NUMBER(30)	PERCENTAGE (%)
Menorrhagia	8	26.6
Polymenorrhagia	8	26.6
Metropathia haemorrhagica	4	13.3
Oligomenorrhagia	7	23.3
Intermenustral spotting	3	10
Dysmenorrhoea	11	36.6

Table-4: Outcome of the Study

PARAMETERS	PRE TREATMENT	POST TREATMENT	P VALUE
PABC score	193.5	89.1	<0.001
Endometrial thickness (mm)	8.75	5.2	<0.001
Heamoglobin level (gm/dl)	9.09	11.1	<0.001

Table-5: Adverse Effects of Ormeloxifene

COMPLICATIONS	NUMBER(30)	PERCENTAGE (%)
Amenorrhoea	3	10
Spotting	2	6.6
Hypomenorrhea	3	10

Table-6: Main Outcome

TYPE OF BLEEDING	PRE TREATMENT(N=30)	POST TREATMENT (N=30)
Cyclical bleeding	09	23
Acyclical bleedig	19	07
Continous bleeding	2	0

Table-2 shows that age of the patients was between 20-50 years with most of the women belong to age group between 41-50 years with average age of 42.5 years (53.4%).

Table-3 shows most of the subjects presented with complaints menorrhagia (26.6%) and polymenorrhagia (26.6%). Dysmenorrhoea is a very frequent complaint (36.6%).

There has been a significant reduction in mean PBAC score ($p<0.001$) pre and post treatment with ormeloxifene. Significant reduction has also been seen in endometrial thickness ($p<0.001$). There has been significant improvement in haemoglobin levels after treatment with ormeloxifene from 9.09 gm/dl to 11.1gm/dl.

Only 3(10%) out of 30 subjects presented with amenorrhoea. 2(6.6%) had spotting and 3(10%) complained of hypomenorrhoea.

DISCUSSION

Dysfuntional uterine bleeding is very common complaint now a days among women, as it can occur any time between menarche and menopause. More common during the first five years after menarche and as she apporaches menopause. The use of ormeloxifene in DUB had very limited study. Women who wish to retain reproductive function; medical management is the best option. Pharmacological agents that helps to reduce menstrual blood loss such as NSAID's, antifibrinolytics, danazol, oral contraceptive pills, progestins, GnRH agonists.but their effects are defined to the period of treatment.

Ormeloxifene is a benzopyran serm. It blocks the cytosol receptors and hence it competitively binds over estradiol [9]. It has mild estrogenic activity on vagina, CNS and BMD. Ormeloxifene has suppressive and stimulatory effect on gonadotrophin release. This antiestrogenic effect excerts contraceptive benefit. It regularises the expression of estrogen receptors on endometrium and hence normalises the excessive blood loss.

The assesment of blood loss during menstrual cycle by counting napkins or by alkaline hematin test is cumbersome or costly. We opted for pictorial blood loss assesment chart (pbac) by Higham *et al.*, (Table-1), which is a simple and less time consuming procedure.

In our study, ormeloxifene has shown significant reduction in menstrual blood loss which is similar to studies by Biswas S C *et al.*, [9] and Kriplani A *et al.*, 10. There has been a significant rise in haemoglobin levels after treatment similar to study by Parveen Rajora P *et al.*, [11].

There is a significant reduction of endometrial thickness pre and post treatment with this drug.this results are similar to study by Jyotsna S *et al.*, [12].

Dysmenorrhoea is a very frequent complaint in our study (36.6%). it reduced to 13.3% after the treatment.

Limitation in our study was the small sample size. But there was significant reduction in menstrual blood loss. Ormeloxifene has good compliance because of convenient dose schedule (once or twice a week) and cost-benefit for the total therapy. Because of its anti-estrogenic action on the breast tissue, it does not increase the risk of breast cancer.

CONCLUSION

The results in this study showed that ormeloxifene, a non-hormonal, non- steriodal agent provides effective and favourable medical management with least side effects, suitable for the treatment of dysfunctional uterine bleeding. We conclude that in all age groups ormeloxifene is suitable for the treatment of

DUB, with least side effects and effective therapeutic efficacy. Because of convenient dosage schedule, the compliance of the patient is good.

REFERENCES

1. Hallberg, L., Hôgdahl, A. M., Nilsson, L., & Rybo, G. (1966). Menstrual blood loss–a population study: variation at different ages and attempts to define normality. *Acta obstetricia et gynecologica Scandinavica*, *45*(3), 320-351.
2. Cole, S. K., Billewicz, W. Z., & Thomson, A. M. (1971). Sources of variation in menstrual blood loss. *BJOG: An International Journal of Obstetrics & Gynaecology*, *78*(10), 933-939.
3. Gath, D., Osborn, M., Bungay, G., Iles, S., Day, A., Bond, A., & Passingham, C. (1987). Psychiatric disorder and gynaecological symptoms in middle aged women: a community survey. *Br Med J (Clin Res Ed)*, *294*(6566), 213-218.
4. Bravender, T., & Emans, S. J. (1999). Menstrual disorders: dysfunctional uterine bleeding. *Pediatric Clinics of North America*, *46*(3), 545-553.
5. Tejwani, P. L., Srivastava, A., Nerkar, H., Dhar, A., Hari, S., Thulkar, S., ... & Kumar, S. (2011). Centchroman regresses mastalgia: a randomized comparison with danazol. *Indian Journal of Surgery*, *73*(3), 199-205.
6. [6].Ravibabu K et al. A study of efficacy of ormeloxifene in the pharmacological management of Dysfunctional Uterine Bleeding. J Clin Diag Res.2013;7(11):2534-2536.
7. [7].Lal, J. "Clinical pharmacokinetics and interaction of centchroman--a mini review." Contraception. 2010 ;81 (4): 275–80.
8. Higham, J. M., O'brien, P. M. S., & Shaw, R. (1990). Assessment of menstrual blood loss using a pictorial chart. *BJOG: An International Journal of Obstetrics & Gynaecology*, *97*(8), 734-739.
9. Alexandersen, P., Riis, B. J., Stakkestad, J. A., Delmas, P. D., & Christiansen, C. (2001). Efficacy of levormeloxifene in the prevention of postmenopausal bone loss and on the lipid profile compared to low dose hormone replacement therapy. *The Journal of Clinical Endocrinology & Metabolism*, *86*(2), 755-760.
10. Biswas, S. C., Saha, S. K., Bag, T. S., & Ghosh Ray, S. C. (2004). Ormeloxifene: A selective estrogen receptor modulator for treatment of dysfunctional menorrhagia. *J Obstet Gynecol Ind*, *54*(1), 56-59.
11. Kriplani, A., Kulshrestha, V., & Agarwal, N. (2009). Efficacy and safety of ormeloxifene in management of menorrhagia: a pilot study. *Journal of Obstetrics and Gynaecology Research*, *35*(4), 746-752.
12. Rajora, P., & Rajora, V. (2013). Comparative study between the out come of only dilatation & curettage and the outcome of ormeloxifene after dilatation and curettage in dysfunctional uterine bleeding. *Jounal of evolution of medical and dentl sciences*, *2*(6), 510-17.
13. Shravage, J., Mekhala, D., Bellad, M. B., Ganachari, M. S., & Dhumale, H. A. (2011). Ormeloxifene versus medroxyprogesterone acetate (MPA) in the treatment of dysfunctional uterine bleeding: A double-blind randomized controlled trial. *JSAFOG*, *3*(1), 21-24.