|| ISSN(online): 2589-8698 || ISSN(print): 2589-868X ||
International Journal of Medical and Biomedical Studies
Available Online at www.ijmbs.info
NLM (National Library of Medicine ID: 101738825)
Index Copernicus Value 2020: 79.44
Original research article Volume 6, Issue 05; May: 2022; Page No. 30-34

A Study of Ormeloxifene in Treatment of Menorrhagia in Dysfunctional Uterine Bleeding in Reproductive age Group

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Article Info: Received 14 April 2022; Accepted 21 May 2022
doi: https://doi.org/10.32553/ijmbs.v6i5.2544
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Conflict of interest: No conflict of interest.

Abstract

Introduction: Menorrhagia is abnormal vaginal bleeding from genital tract .[1,2,3] Average menstrual blood loss is between 30-40 ml per cycle. It affects 10-30% of women at some stage in their life. The dysfunctional uterine bleeding is largely unknown but occurs in both ovulatory and anovulatory menstrual cycles . 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.

Aim and Objective: To evaluate the study of ormeloxifene in treatment of menorrhagia in dysfunctional uterine bleeding in reproductive age group.

Material and Methods: This was a Hospital based prospective randomize control study started from November 2020 to October 2021 at Department of Obstetrics and Gynecology, S.P.Medical College & AGH, Bikaner, Rajasthan, India. The study included Sample size of 40 Patients whose 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 hemoglobinlevel, thyroid stimulating hormone, coagulation profile, PAP smear, pelvic ultrasound to measure endometrial thickness and rule out any pelvic pathology and endometrial sampling.

Result: The study included Sample size of 40 Patients whose detailed history and clinical examination was done. 83.33% cases in pre-treatment group and 19.4% patients in post-treatment group showed dysmenorrhoea. Mean age of patients was 30.2±7.92 years and majority of cases belonged to 18-30 year. In present study, majority of patients belong to urban area and Majority of patients belong to Hindu religion.

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.

Key words: Ormeloxifene, Menorrhagia, Dysfunctional Uterine Bleeding.

Introduction

Menorrhagia is abnormal vaginal bleeding from genital tract .[1,2,3] Average menstrual blood loss is between 30-40 ml per cycle. It can cause hemorrhagic shock, anemia, iron deficiency and decrease quality of life.[4] It affects 10-30% of women at some stage in their life. [1,5]

The patho-physiology of dysfunctional uterine bleeding is largely unknown but occurs in both ovulatory and anovulatory menstrual cycles .[3]In 80-90% of dysfunctional uterine bleeding results from dysfunction of HPO axis which leads to anovulation and as anovulatory cycle produce no progesterone to stabilize cyclic withdrawal of estrogen prepared endometrium, bleeding episode become irregular and amenorrhoea, metrorrhagia and menorrhagia are common. In other 10-20% women with dysfunctional uterine bleeding, ovulation occurs cyclically and menorrhagia is thought to originate from defects in control mechanism of menstruation. 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.[6]

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. Nonsteroidal anti-inflammatory drugs and tranexaemic acid offer a simple therapy which has to be taken during menses, with reductions of 25-35% and 50% respectively in the Menstrual Blood Loss (MBL).

Ormiloxifene(also known as centchroman) is one of the selective estrogens receptor modulators (SERM).[7] It is a non-steroidal , non hormonal, oral contraceptive which is taken once in a week . In India, Ormeloxifene has been available as a birth control product since the early 1990s. which binds with high affinity of estrogen receptors and mimics the effect of estrogen in some tissue. However, Ormeloxifene acts as estrogen antagonist in uterus (endometrium), breast tissues which lead to endometrial atrophy hence this decreases menstrual blood loss.[8]

This study aimed to analysis ormeloxifene in treatment of menorrhagia in dysfunctional uterine bleeding in reproductive age group.

Material and method

This was a Hospital based prospective randomize control study started from November 2020 to October 2021 at Department of Obstetrics and Gynecology, S.P.Medical College & AGH, Bikaner, Rajasthan, India. The study included Sample size of 40 Patients whose detailed history and clinical examination was done. Group A was given ormeloxifene tablets 60mg twice a week for 12 weeks followed by ormeloxifene tablets 60 mg once a week for next 12 weeks. 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 hemoglobinlevel, thyroid stimulating hormone, coagulation profile, PAP smear, pelvic ultrasound to measure endometrial thickness and rule out any pelvic pathology and endometrial sampling., who went through inclusion and exclusion criteria are included in this study.

Inclusion criteria:- Women in reproductive age group attending outpatient department (OPD) with subjective symptoms of excessive MBL irrespective of bilateral tubal ligation.

Exclusion criteria:-1. Any organic pelvic pathologyor pregnancy

2. Acute heavy bleeding.

3. Haemoynamically unstable patients

4. Recent history or clinical evidence of jaundice, renal disease

5. Chronic cervicitis or cervical hyperplasia.

Result

In our study Mean age of patients was 30.2±7.92 years and majority of cases belonged to 18-30 year. In present study, majority of patients belong to urban area and Majority of patients belong to Hindu religion.

The mean duration of bleeding in our group was 6.8±3.32 in months.

Table 1: Symptoms (Dysmenorrhoea and Irregular Cycle)

Parameter	Pre-treatment		Post-treatment		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	
Dysmenorrhea	34	83.33	7	19.44	
Irregular Cycle	29	74.7	5	12.1	

This table shows distribution of symptoms (dysmenorrhoea and irregular cycle) in our group before starting of treatment and after treatment. 83.33% cases in pre-treatment group and 19.4% patients in post-treatment group showed dysmenorrhoea. Similarly we seen improvement in irregular cycle in post treatment group.

Table 2: Haemoglobin and PBAC

Parameter	Pre-treatment		Post-treatment		P-Value
	Mean	SD	Mean	SD	
Haemoglobin (gm%)	7.29	0.94	9.77	0.89	
PBAC	273.2	42.2	91.5	17.89	

In table 2, we found that mean haemoglobin% in pre-treatment group was 7.29 and after treatment it was 9.77%. The Mean PBAC in pre-treatment group was 273.2 and after treatment it was 91.5.

Table 3: USG Endometrial Thickness

USG Endometrial Thickness	Pretreatment (In mm)		Post-treatment (in mm)	
	No. of Patients	Percentage	No. of Patients	Percentage
4-13	24	60	40	100
14-19	16	40	0	0
Total	40	100	40	100
Mean±SD	12.16±2.92		7.92±1.64	

In table 3, we found that mean endometrial thickness in pre treatment group was 12.16 mm and after treatment it was 7.92mm. There was significant difference seen between both group.

Table 4: Side effects

Side Effects	No. of Patients	Percentage
GI symptoms	3	7.5
Headache	6	15
Amenorrhoea	6	15
Weight gain	0	0
Total	15	37.5

In table 4, we found that 7.5% showed GI symptom, 15% patients showed headache and amenorrhoea. We found that majority 87.5% patients in our group had seen excellent improvement followed by 12.5% patients feel satisfactory result after treatment.

Discussion

Menorrhagia is socially embarrassing, physically incapacitating condition and has great financial drain. In this study, PBAC score was found to be significantly decreased in patients of post-treatment using ormeloxifene drug. Since ormeloxifene drug have anti-proliferative effect on uterus (endometruim) which causes endometrial atrophy and that may resulting in decrease of menstrual blood loss, hence causes decrease in PBAC score. Our results are comparable with the study done in Indian population from Darjeeling and New Delhi by Biswas et al.[9] and Kriplani et al.[10]. 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 al[11] It is a simpler and faster method, not requiring preservation of sanitary products and avoids costly chemical assay.

Dysmenorrhoea is a frequent complaint more reported by most of the patients. In the present study a total of 36 patients reported dysmenorrhoea during initial week and by the end of the study only 6 patients reported improvement which was similar to other studies.[9,10,12,13] We distribution of symptoms (dysmenorrhoea and irregular cycle) in our group before starting of treatment and after treatment. 83.33% cases in pre-treatment group and 19.4% patients in post-treatment group showed dysmenorrhoea. Similarly we seen improvement in irregular cycle in post treatment group. Singh H O et al[14] found that The distribution of frequency of presence of clots during post treatment (18.6%) was found to be lower in compared to pretreatment (70.3%) and the difference was significant ($p =< 0.0001$, paired $t = 12.68$; 95% CI = 0.59-0.43). The distribution of frequency of presence of dysmenorrhea during post treatment (18.6%) was lower in compared to pretreatment (26.2%) and the difference was insignificant ($p = 0.067$, paired $t = 1.87$; 95% CI = 0.15-0.004).

We found that mean haemoglobin% in pre-treatment group was 7.29 and after treatment it was 9.77%. The Mean PBAC in pre-treatment group was 273.2 and after treatment it was 91.5. Singh H O et al[14] found that median pretreatment baseline PBAC score found to be 317.00 with a range of 125-768. The median post treatment PBAC score was 105.00 with a range of 3.0-557. The mean pretreatment Hb concentration found to be 8.89 gm/dl with a range of 6.40-11.20. The mean post treatment Hb concentration was 10.78 gm/dl with a range of 7.20-12.60. The mean increase of 1.89 in Hb concentration was statically significant ($p =< 0.0001$, paired $t = 1.25$; 95% CI = 0.05-1.48). hemoglobin level showed significantly increased in patients of post treatment after using ormeloxifene drug. It is because, ormeloxifene act as antagonist effect on estrogen receptors of uterine endometrium, which decrease the stimulation of receptor activity of uterine and causes their prolonged

depletion on uterus. Therefore, it may decrease the uterine bleeding and may increase the hemoglobin level. Biswas et al.[9] has also reported similar result in Indian population and showed average increase of 1.31 gm/dl in Hb concentration. They observed significant decrease in the presence of clots in patients of post-treatment after using ormeloxifene drug. Presence of clots is an obvious evidence of abnormal excessive menstrual blood flow.[11]

Conclusion

We can say that the treatment of Ormeloxifene in patients with dysfunctional uterine bleeding is significantly increasing the level of hemoglobin by decreasing the clots and PBAC score. These results conferred that the drug has an excellent safety profile and has been found to have very few side effects.

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