

COMPARATIVE STUDY BETWEEN THE OUT COME OF ONLY DILATATION & CURETTAGE AND THE OUTCOME OF ORMELOXIFENE AFTER DILATATION AND CURETTAGE IN DYSFUNCTIONAL UTERINE BLEEDING

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INTRODUCTION: Even a single drop of blood is a boon for anemic women.

Menstruation sets in approximately between the age of 12 and 14 years and persists throughout the reproductive period of life with an average rhythm of 28 days and duration of flow between 4-6 days. A normal menstrual blood loss is 50-80ml and does not exceed 100ml.¹

Menstrual dysfunction is a cause of inconvenience, discomfort and disruption of a healthy lifestyle and affects many millions of women in both the developed and developing world. Abnormal uterine bleeding is one of the most common problem that challenge the Gynecologists. A correct diagnosis is essential because of the consequences of bleeding and the implications of the treatment.

Dysfunctional uterine bleeding (DUB) is one of the most common causes of abnormal uterine bleeding. It is defined as abnormal bleeding that occurs in the absence of pelvic organ disease or a systemic disorder. It is a diagnosis of exclusion and in most instances dysfunctional uterine bleeding is associated with ovulatory dysfunction.² For many years dilatation and curettage (D & C) has been a gold standard for endometrial sampling. Israel³ stated that uterine curettage in DUB was not only the best therapeutic measure to arrest bleeding but also diagnostic. In a study by Mikuta⁴ 50% of the patients were controlled by curettage only.

Winsor⁵ stated that medical management of menorrhagia is a challenging task and wide variations in the available drugs prescribed for this condition show a lack of consensus for medical treatment. Selective estrogen receptor modulators (SERM) are a new category of therapeutic agents that selectively bind with high affinity to estrogen receptors (ER) and mimic the effect of estrogen in some tissues but act as estrogen antagonists in others. Ormeloxifene, one of the SERM, mediates its effects by high affinity interaction with ER, antagonizing the effect of estrogen on uterine and breast tissue and stimulating its effect on vagina, bone, cardiovascular system and central nervous system.⁶ It is therefore, suitable in the treatment of heavy dysfunctional uterine bleeding (DUB).

In spite of the enormous amount of research on DUB both in women and animals, the process is yet not understand and with every fresh addition of theories seems to become more complex and one theory becomes modified or replaced by other. So the aim of this study was to

ORIGINAL ARTICLE

do the comparison between the outcome of only dilatation and curettage and the outcome of Ormeloxifene after dilatation and curettage in DUB.

MATERIAL AND METHODS: The present study was conducted on 50 patients clinically diagnosed as cases of dysfunctional uterine bleeding attending out patients department or admitted in the Department of Obstetrics and Gynaecology at Rajindra Hospital, Patiala. This was an open labeled and comparative study, patient were randomly allocated into two groups. Patient of any age group with a history of excessive/irregular menstrual bleeding for more than three months with normal clinic pelvic examination and lab investigations finding were enrolled in the trial. Apart from the baseline investigations, Ultrasonography was also done to rule out any pathological condition of the uterus. 25 patients were given tablet Ormeloxifene (orally) after dilatation and curettage (Group A) and in 25 patients only dilatation and curettage were done (Group B) and both the groups were followed up for six months. Then comparison was done between the outcomes of only dilatation and curettage and role of Ormeloxifene after dilatation and curettage in dysfunctional uterine bleeding.

TREATMENT SCHEDULE OF ORMELOXIFENE (GROUP A): Patients were administered one tablet of Ormeloxifene (60mg) twice a week (on Sundays and Wednesdays) for first 12 weeks. This was followed by one tablet of 60mg once a week (Sunday/Wednesday) for next 12 weeks. Every patient was followed up at 4, 8, 12 and 24 weeks.

EXCLUSION CRITERIA FOR ORMELOXIFENE:

1. Patient who were not compliant for Ormeloxifene scheduled intake.
2. Women on estrogen, progesterone, testosterone or Danazol.
3. Patients with heavy bleeding necessitating emergency treatment.
4. Women with a known, suspected or with a history of genital tract malignancy.
5. Lactating mothers.
6. Women with pelvic pathology like endometriosis, fibroid and PID.

RESULTS:

1. Both the groups were matched with respect to their age. Maximum no. of patients belonged to the age group of 31-40 year. There was no statistical difference between the age in both the groups.
2. Group A, showed an improvement of 62.5% in no. of bleeding episodes, per month. In group B, there was significant improvement of 51.51% at the end of 12 week but improvement decreased to 48.48%, after 25th week.
3. In group A 85.71% of the patients complaining of heavy flow improved by the end of 25th week. In group B, there was improvement of 60.86%, after 8th week but improvement reduced to 47.82% of patients by the end of 25th week. Statistical analysis showed that there was highly significant improvement in heavy flow in group A patients.

4. In group A complaint of spotting reduced in 85.71% of patients. In group B, though there was significant improvement in spotting after 12th week but their improvement reduced to only 25% by the end of 25th week.
5. Group A, had significant improvement in complaint of dysmenorrhea also. There was improvement of 87.5% by the end of study. In group B, there was good improvement in dysmenorrhea of 50% after 12th week but improvement deteriorated to 25% after 25th week.
6. Passage of clots in menstrual blood, an obvious evidence of an abnormality associated with DUB. Group A showed an improvement of 77.77% by the end of 25th week. Group B, showed an improvement of only 40% by the end of 25th week.
7. At the start of study, 64-68% of patients were having menstrual flow lasting 6-9 days. In group A 84% of patients had normal menstrual flow for 3-5 days by the end of the study. In group B, only 52% of the patients returned to normalcy by the end of the study.
8. There was improvement in reduction of endometrial thickness in both the groups, but group A patients had significant improvement in this parameter when compared to group B. The mean endometrial thickness reduced to 7.45 ± 1.63 mm in group A and in group B, endometrial thickness reduced to 8.86 ± 1.19 mm by the end of 25th week.
9. Group A patients had statistically highly significant improvement in haemoglobin level when compared to group B. In group A, mean haemoglobin was improved to 10.4 ± 0.88 gm/dl and group B patients showed improvement in haemoglobin levels from 8.74 ± 0.73 gm/dl to 9.73 ± 0.73 gm/dl.
10. In group A, 2 patients reported amenorrhea, 1 patient reported headache, 1 patient reported giddiness and 1 reported weight gain. In group B, 2 patients reported fever and 2 reported pain abdomen after dilatation and curettage, but there was no serious complication reported like perforation of uterus.
11. Dilatation and curettage had more of the diagnostic value. It should be done in all perimenopausal and post menopausal bleeding to rule out endometrial carcinoma and other underlying pathology. In our study, out of 50 patients, 17 patients had proliferative endometrium, 18 had secretory endometrium, 2 patients showed cystic glandular hyperplasia, 3 patients showed endometrial hyperplasia without dysplasia and no opinion was made in 6 patients because of poor sampling.

DISCUSSION: In the present study, out of 50 patients, 24 patients were in the age group of 30-40 and 9 patients were in the age group of 40-50 and 1 patient was above the age group of 50 years. In a study by Sutherland et al⁷ 39% patients were above the age of 50. The difference could be that a significant number of women in India undergo hysterectomy for DUB, fibromyoma and related disorders during perimenopausal age.

The diagnostic and therapeutic value of curettage in treatment of menstrual disorders and post menopausal bleeding has been seldom evaluated in details, although curettage is the most common procedure in the gynecological clinic.⁸

In our study we found that in group A there was a significant decrease in the number of bleeding episodes, heavy flow, Passage of clots and complaint of inter menstrual spotting as

compared to group B, in which though relief of the problem was definitely there but it was of short period, lasting maximum up to 12 weeks. Thereafter its significance deteriorated which is in accordance with other investigators.^{8,9} During episode of profuse bleeding, curettage may help to arrest the hemorrhage, probably by removing the necrotic area of endometrium. So curettage reduces the amount of blood loss at the next menstrual period but has no effect on subsequent blood loss.¹⁰ State of affair was totally different in group A, though improvement in all parameters were slow to start but there was significant improvement by the end of the study, which correlates well with the results of Kripalani et al.¹¹

Dysmenorrhea is a frequent complaint more commonly reported by menarche onset age group. Group A had significant improvement in complaint of dysmenorrhea 87.5% by the end of study as compared to group B, which was in accord with Biswas et al.¹² When we analyze the duration of bleeding per month, we found that it was constantly decreased in group A as compared to group B. 84% of patients had normal menstrual flow by the end of 25th week.

According to Singh and Kamboj¹³ Ormeloxifene has no significant effect on total pituitary – gonadotropin. The drug causes amenorrhoea as its common side effect, which is opposed to abnormal excessive bleeding that characterizes DUB. The drug thus, can normalize the abnormality locally at the level of uterine endometrium without effecting hypothalamo-pituitary-ovarian axis. After analyzing the side effects we found that Ormeloxifene has got an excellent safety profile and been found to have very few side effects limited to gastro intestinal symptoms, weight gain and amenorrhoea, as also noted by other authors.¹²

Our statistical analysis showed significant improvement in endometrial thickness and hemoglobin levels when both groups were compared, which was in accordance with a study done by Dhananjay et al.¹⁴ Israel³ claimed a success rate of 40-60% when curettage was employed as the sole treatment for prolonged dysfunctional uterine bleeding.

Dilatation and curettage has more of the diagnostic value. It should be done in all peri menopausal and post menopausal bleeding to rule out endometrial carcinoma and other underlying pathology.¹⁵ In our study population secretory/proliferative endometrium was found in most of the cases. Fortunately there was not a single case of carcinoma diagnosed on histopathology

CONCLUSION: Ormeloxifene, a SERM "Selective estrogen receptor modulators" also known as "Designer estrogens" because they are designed to act in specific way at each of the receptor site, is a wonderful drug, effective not only in dysfunctional uterine bleeding but also has positive effect on bone and cardiovascular tissue.¹⁶ There was significant improvement in all parameters of DUB till 12th week in both the study groups, but after that group A patient, kept on showing improvement in their parameters. Group B patients, in which only D & C was done, started showing deterioration as the time passed on. The common distressing problem of dysfunctional uterine bleeding can be better dealt with Ormeloxifene, after diagnosing the underlying pathology and confirming the DUB by diagnostic dilatation and curettage, with additional positive effect on premenopausal and post menopausal patients in treatment of menopausal symptoms, without any side effects.

We are very much convinced with Nelson AL who said that the increased use of effective medical therapies has the potential to reduce the number of surgical procedures, such as endometrial ablation and hysterectomy.¹⁷ In our study groups the number of patient were less. Larger study population is needed so wholesale adoption of this drug in routine practice will not become a gold standard until further research confirms the presence of such an effect .

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ORIGINAL ARTICLE

Table 1: COMPARISON OF AGE IN GROUP A AND GROUP B

Age groups (in years)	Group A		Group B	
	No.	%age	No.	%age
>20	-	-	-	-
20-30	9	36	7	28
31-40	11	44	13	52
41-50	5	20	4	16
51-60	-	-	1	4
Total	22-49		26-50	
Mean	35.12±7.33		35.96±6.48	
't' and p value	0.41		>0.05	
Sig.	NS			

Table 2: COMPARISON OF PARAMETERS OF DUB IN GROUP A AND GROUP B

Duration (in wks)	Bleeding Episodes		Heavy Flow		Spotting		Dysmenorrhoea		Passage of Clot	
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
0	64	66	21	23	7	8	8	8	18	20
4	30	31	9	10	3	2	4	3	7	7
8	29	31	7	9	3	3	3	4	8	9
12	28	32	5	11	2	3	2	4	6	10
25	24	34	3	12	1	6	1	6	4	12
%age of improvement	62.5	48.48	85.71	47.82	85.71	25%	87.5	25	77.77	40

Table 3: Duration of Bleeding per month in Group and Group B

Duration of Bleeding (days)	Group A		Group B	
	Before treatment	After treatment	Before treatment	After treatment
0	-	2	-	-
1	-	-	-	-
2	-	2	-	1
3	3	9	3	5
4	2	4	4	6
5	3	8	2	2
6	8	-	5	7
7	4	-	4	3
8	4	-	4	1
9	1	-	3	-
>10	-	-	-	-
Total	25	25	25	25

Table 4: COMPARISON OF MEAN ENDOMETRIAL THICKNESS

Time	Group	Range (mm)	Mean±SD (mm)	't'	'p'	Sig.
0 wk	A	7.3-16.1	11.26±2.24	0.20	>0.05	NS
	B	7.4-16.80	11.14±2.21			
25 wk	A	3.0-10.1	7.45±1.83	3.20	<0.01	HS
	B	6.8-10.42	8.86±1.19			

Statistical Analysis

Comparison	t	p	Sig.
Group A – Before vs After	8.02	<0.01	HS
Group B – Before vs After	6.80	<0.01	HS

Table 5: COMPARISON OF HAEMOGLOBIN OF GROUP A AND B

Time	Group	Range (mm)	Mean± SD (mm)	't'	'p'	Sig.
0 wk	A	7.85-10.42	8.73±0.76	0.05	>0.05	NS
	B	7.86-10.42	8.74±0.73			
25 wk	A	9.2-12.85	10.48±0.88	3.25	<0.01	HS
	B	9-11.42	9.73±0.73			

ORIGINAL ARTICLE

Table 6: HISTOPATHOLOGICAL REPORT OF 50 PATIENTS

(Group A and Group B after D&C)

Histopathological report	No. of patients
Proliferative endometrium	17
Secretory endometrium	18
Cystic glandular hyperplasia	2
Irregular endometrium	3
Endometrial hyperplasia without dysplasia	4
Carcinoma	-
No opinion made	6
Total	50