e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(5); 1207-1215

Original Research Article

Role of Centchroman (Ormeloxifene) in Dysfunctional Uterine Bleeding

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Received: 25-03-2024 / Revised: 23-04-2024 / Accepted: 26-05-2024
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Conflict of interest: Nil

Abstract:

Background: Dysfunctional uterine bleeding (DUB), also known as anovulatory bleeding, is a common gynecological condition characterized by abnormal vaginal bleeding that deviates from a woman's regular menstrual cycle. Centchroman is commonly used contraceptive to treat DUB. The aim of the present study is to evaluate efficacy and safety of Centchroman in patients of dysfunctional uterine bleeding.

Materials and Methods: The present study was conducted in patients of dysfunctional uterine bleeding, in Nehru Hospital, affiliated to the Department of Obstetrics and Gynaecology, B.R.D. Medical College, Gorakhpur. 90 female patients of DUB were recruited for this study based on the inclusion and exclusion criteria after taking informed consent. Centchroman 30-mg bi-weekly was given for a period of 3-6 months and patients were kept under regular follow up during and after completion of therapy.

Result: Centchroman (Ormeloxifene) in doses of 30mg bi-weekly for a period of 3-6 months is found to be effective in controlling menorrhagia as we found cure rate of menorrhagia to be 85.5%. The present study found that maximum prevalence of DUB was observed in the age group between 35-44 years (60%) and only 5.6% cases were between 20-24 years. Maximum numbers of patients belonged to the parity 4-5 (53%). History of tubectomy was present in 42.2% cases. 90% of patients with menstrual disturbances complained of excessive bleeding during menses with regular or irregular cycles. (Menometrorrhagia - 36.7% followed by Menorrhagia 27.8% & Polymenorrhagia in 25.5% cases).

Conclusion: The present study concludes that Centchroman (Ormeloxifene) used for DUB in dose of 30mg bi-weekly is very cost effective, devoid of any side effects, very effective in controlling DUB, so it should be used in more patients.

Keywords: Dysfunctional Uterine Bleeding (DUB), Abnormal Uterine Bleeding, Centchroman, Contraceptives.

Introduction

Dysfunctional uterine bleeding (DUB) is defined as abnormal uterine bleeding that result from an ovarian endocrinopathy. Both ovulatory and anovulatory cycles may be linked to it. A comprehensive history and physical examination are necessary for the diagnosis of DUB in order to exclude out organic illnesses. [1] Dysfunctional uterine bleeding is the term used to cover all forms of vaginal bleeding for which no organic cause is found. There is some disturbance at Hypothalamo-Pituitary-Ovarian axis. Diagnosis is made by exclusion.

Excessive menstrual loss can cause considerable embarrassment and inconvenience. About 28% of female population have excessive menstruation and plan their main social and work commitments according to their menstrual cycles. Over the years menorrhagia has become increasingly frequent complaint because the women of today experience about ten times more menstrual cycles than their ancestors did. This is associated with a decline in lactational amenorrhea with the introduction of reliable contraception. In addition, women are increasingly unwilling to accept menstrual difficulties. There has been a rise in expectations, and increasingly intolerance of the inconvenience of menorrhagia. These factors have led to an increase demand on the health services. Aetiology is probably hormonal and that the hypertrophy and hyperplasia of endometrium are induced by a high titer of estrogen in the circulating blood.

Treatment of D.U.B. is both Medical and Surgical. Hysterectomy, the traditional surgical treatment for menorrhagia is only suitable for perimenopausal women who have no further wish to conceive. The operation is associated with slight morbidity specially if done in younger age group, therefore considered as over treatment when performed for

functional menorrhagia. Concerns about invasiveness of hysterectomy have led to the development of minimal invasive approaches including endometrial resection and ablation. Again these approaches are unsuitable for women, who wish to continue their reproductive and menstrual function. There continues to be a need, therefore, for effective medical therapy for menorrhagia. The medical treatment of DUB mainly comprises of hormones like progesterone, combined oral contraceptives, danazol and Gn-Rh analogues. Certain non-hormonal agents like antiprostaglandins and antifibrinolytics are also used with variable results.

A better understanding of the precise pathophysiology of dysfunctional uterine bleeding should lead to more rational treatment plan by inducing non-specific endometrial suppression and could provide novel therapeutic strategies in the new millennium for management of this common clinical problem.

Centchroman (Ormeloxifene) is a Selective Estrogen Receptor Modulator (SERM) synthesised after decades of research by Central Drug Research Institute (CDRI) Lucknow in 1967. It is marketed in India in 1992 as "Saheli" and "Choice-7" by Hindustan Latex Ltd., Thiruvananthapuram and as Centron & "Sevista" by Torrent Pharmaceuticals Ltd., Ahmedabad. It is a non-steroidal oral contraceptive agent and included in the National Family Welfare Programme in 1995.

A novel class of medicinal drugs known as selective estrogen receptor modulators (SERM) binds to estrogen receptors with great affinity, mimicking the effects of estrogen in certain cases while acting as an antagonist of estrogen in others. Centchroman is optimally designed SERM as presence of basic amine side chain as pyrrolidine imparts antagonistic character while the presence of benzopyrane group defines its receptor binding ability (RBA) and estrogen agonistic activity.

Centchroman (Ormeloxifene) elicits weak estrogen agonistic and potent antagonistic activities but is devoid of progestational, androgenic and antiandrogenic activities. Since Centchroman has got strong antiestrogenic action it is able to offer endometrial suppression and hypoplasia and provide effective haemostasis. Strong estrogen antagonism is achieved by binding of estrogen receptors, thus offers protection against endometrial hyperplasia and carcinoma endometrium. Centchroman is a well-known drug for its contraceptive properties. It has a well-documented effect on the endometrium, thinning it and inhibiting implantation. Several studies have investigated the efficacy of Centchroman in treating DUB. [2-6]

The aim of the present study was to evaluate efficacy and safety of Centchroman in patients of dysfunctional uterine bleeding.

Material and Methods

The present study was conducted in patients of dysfunctional uterine bleeding, as an outpatient in Nehru Hospital, affiliated to the Department of Obstetrics and Gynaecology, B.R.D. Medical College, Gorakhpur.

Inclusion Criteria: Patients with symptoms of menstrual abnormalities such as menorrhagia, polymenorrhoea, menometrorrhagia without any generalized systemic disorders and pelvic pathology.

Exclusion Criteria:

- Patient with evidence of hepatic, renal, cardiac and metabolic dysfunctions.
- Patient with uterine size > 8 weeks.
- Patient with adenexal mass or tenderness.
- Patient with history of abortion within 3 months
- History of any hormonal therapy within 6 months.
- Patient with breast and genital malignancies.
- Patient with very heavy bleeding necessitating emergency treatment.

A detailed protocol and case record form was developed for the study.

History:

Following points are noteworthy:

- Patient's particulars include name, age, occupation, marital status, parity and history of tubectomy.
- Menstrual history regarding cycle, duration and amount of flow and associated symptoms.
- Use of hormonal contraceptives or IUCD insertion.
- History of chronic liver disease, jaundice, tuberculosis and other systemic disorders.
- History of previous treatment.

Examination:

- Complete general and systemic examination.
- Detailed gynaecological examination includes-per-speculum examination to exclude local disease of vagina and cervix followed by bimanual pelvic examination to find out uterine size, direction, mobility of uterus and any pelvic pathology.

The following investigations were conducted.

Hb%, Total leucocyte count, Differential leucocyte count, Bleeding time, Clotting time, Biochemical, Blood sugar, Liver function test, Lipid profile, Urine examination and

Ultrasonography - To note endometrial thickness, ovarian size and to exclude any pelvic pathology before starting treatment and then after 3 months.

Methodology:

Total of 100 patients were screened from Obstetrics & Gynaecology O.P.D. after detailed history and clinical examination, 10 cases were excluded after investigations. 90 women with the diagnosis of DUB based on clinical and ultrasonography findings were recruited for this study along with normal routine investigations. Scheduled dose of Centchroman was 30-mg bi-weekly for 3-6 months for each patient. Patients were kept in regular monthly follow-up after menses and were enquired about detailed menstrual pattern. Physical and gynaecological examination performed at each visit. Pelvic sonography was repeated whenever indicated.

Observation and Results

Table 1 shows distribution of cases screened for inclusion in the study. Total of 100 patients were screened from Obstetrics & Gynaecology O.P.D. after detailed history and clinical examination, 10 cases were excluded after investigations, out of which 6 cases had small myoma, 2 had impalpable ovarian cysts diagnosed only after ultrasonography, one had seedling myoma with small ovarian cyst, one had IUCD in situ which the patient was not knowing and the thread was missing so could be diagnosed only after ultrasonography.

Table 1: Distribution of Cases Studied

No. of cases screened for study	100
No. of cases excluded	10
Myoma	6
Ovarian cyst	2
Myoma with ovarian cyst	1
IUCD in situ	1
No. of cases included in the study	90

Table 2 shows distribution of cases according to their age. Maximum number of patients belonged to age group between 35-44 yrs. (60%). Patients below 30 yrs and above 45 yrs were 15.6% and 11.1% respectively.

Table 2: Age Wise Distribution of the Cases

Age (yrs.)	No. of cases	Percentage
20-24	5	5.6
25-29	9	10
30-34	12	13.3
35-39	36	40
40-44	18	20
>45	10	11.1
Total	90	100

Table 3 shows distribution of cases according to parity. Maximum number of cases 53% belonged to parity between 4-5, 39% were between parity 1-3 and only 8% cases were para > 5.

Table 3: Distribution of Cases According to Parity

Parity	No. of cases	Percentage
1-3	35	39
4-5	48	53
>5	7	8
Total	90	100

Table 4 depicts distribution of patients according to their presenting complaints. 90% of patients complained of excessive bleeding during menses (any form of menorrhagia), out of which menometrorrhagia was commonest seen in 36.7% cases, polymenorrhagia in 25.5% and polymenorrhoea in 10% cases.

Table 4: Distribution of Cases According to Symptoms

Presenting complaints	No. of cases	Percentage
Polymenorrhoea	9	10
Polymenorrhagia	23	25.5
Menorrhagia	25	27.8
Menometrorrhagia	33	36.7
Total	90	100

Table 5 shows distribution of patients according to history of previous treatment taken for DUB. 39% patients received hormonal treatment in the form of progesterone or combined pills while in 30% dilatation and curettage was done. Thermal ablation was done in one patient and rest 42% (n=38) received no previous treatment. In all those cases who took previous treatment only temporary relief was observed by the patients and they again started having menorrhagia.

Table 5: Distribution of Cases According to History of Previous Treatment

Previous treatment	No. of cases	Percentage
Hormones	24	27
D & C	16	18
Both	11	12
Thermal ablation	1	1
No treatment	38	42
Total	90	100

Table 6 shows distribution of cases according to histopathological characteristics of endometrium in 27 patients who had undergone D & C in the past for DUB. Maximum number of patients (52%) belonged to the group having endometrium in proliferative phase with cystic dilatation i.e. picture similar to metropathia haemorrhagica. 4196 cases had proliferative endometrium while 7% had secretory endometrium.

Table 6: Distribution of Cases According to Endometrial Histopathology

Endometrial histology	No. of cases	Percentage
Secretory	2	7
Proliferative	11	41
Proliferative with cystic dilatation	14	52
Total	27	100

Table 7 shows distribution of cases according to history and type of tubectomy. History of tubectomy was present in 38 cases (42.2%). In patients who had undergone tubectomy 73.7% had laparoscopic ligation, 23.7% cases had tubectomy by minilaprotomy and in rest 2.6% tubectomy was done with cesarean section. History of tubectomy is important because increased incidence of menstrual disturbances has been found post sterilization though no definite causal relationship has been established between two.

Table 7: Distribution of Cases According to History of Tubectomy

History of Tubectomy	No. of cases	Type of tubectomy	No. of cases	Percentage
Percentage	38	Laparoscopic Minilap With LSCS	28 9 1	42.2
Absent	52			57.8
Total	90			100

Table 8 (A) shows effect of Centchroman on menstrual pattern. Prolonged cycles were observed in 38 cases (42.2%). In 16 cases (17.8%), cycles were prolonged beyond 45 days and in 24.4% cases cycles remained between 36-45 days. 4.4% cases developed amenorrhoea with Centchroman therapy. Rest of the patients (53.3%) had normal cycles (21-35 days) while none of the patients experienced breakthrough bleeding.

Table 8 (A): Effect of Centchroman on Menstrual Pattern

Menstrual pattern	No. of cases	Percentage
Normal 21-35 days	 48	 53.3
Prolonged 36-45 days > 45 days	22 16	24.4 17.8
Amenorrhoea	4	4.4
Breakthrough. Bleeding	0	0
Total	90	100

Table 8 (B) also shows effect of Centchroman therapy on menstrual pattern. Two parameters, length of cycle and amount of bleeding were assessed. Total 274 cycles were covered with Centchroman therapy during trial. Most of the cycles (85.4%) were found to be of normal duration (21-35 days). 14.6% cycles were prolonged, out of which 7.3% were between 36-45 days and 7.3% were prolonged beyond 45 days. With regard to amount of bleeding, the cycles, which were heavy

initially, became gradually normal after giving Centchroman therapy. Normal flow was observed in 54.4% cycles, moderate flow in 13.8% cycles, heavy flow in 27.4% cycles and scanty flow only in 4.4% cycles.

Table 8 (B): Effect of Centchroman on Menstrual Pattern According to no. of Cycles

Menstrual pattern		No. of Cycles	Percentage
Length of cycle	*Normal 21-35 days	234	85.4
	*Prolonged 36-45 days	20	7.3
	>45 days	20	7.3
	Total	274	100
Amount of Bleeding	*Heavy	75	27.4
	*Moderate	38	13.4
	*Normal	149	54.4
	*Scanty	12	4.4
	Total	274	100

Table 9 shows response of Centchroman therapy in relation with duration of treatment among 90 patients of D.U.B. 57.8% patients showed definite response to Centchroman therapy within 1 month, 80% within 2 months, 88.9% within 4 months. 11.1% patients showed no response to therapy out of which two cases dropped out due to poor response.

Table 9: Response of Treatment versus Duration of Centchroman Therapy

Duration of treatment (Months)	No. of Cases				No. of cases dropped out
	Responded		Not Responded		
	(N)	(%)	(N)	(%)	
1	52	57.8	38	42.2	0
2	72	80	18	20	0
4	80	88.9	9	10	1
6	80	88.9	8	8.9	2
Total 90 cases					

Table 10 shows efficacy of Centchroman in patients of dysfunctional uterine haemorrhage. 85.5% patients achieved complete control of bleeding and were relieved of menorrhagia by the end of treatment. Response to therapy was excellent in 44.4%, good in 41.1%, fair (moderate control of bleeding) in 3.3% cases and 8.996 cases showed no response to Centchroman treatment.

Table 10: Efficacy of Centchroman Treatment

Response of Treatment	No. of cases	Percentage
Excellent	40	44.4
Good	37	41.1
Fair	3	3.3
Poor/None	8	8.9
Drop Out	2	2.2
Total	90	100

Table 11 shows that Centchroman has minimum side effects. Usual side effects which are observed with hormonal therapy like nausea, vomiting, weight gain, breast discomfort and acne are not observed with Centchroman. Ovarian enlargement was observed in 12.2% cases and 4.4% cases developed amenorrhoea. As the drug has virtually no side effect, which can cause discontinuation of the drug by patient, so compliance is very good.

Table 11: Distribution of Cases According to Side Effects

Side effects	No. of cases	Percentage
Nausea/Vomiting	None	0
Weight gain	None	0
Acne	None	0
Breast discomfort	None	0
Ovarian enlargement	11	12.2
Amenorrhoea	4	4.4

Discussion

In the present study, 90 patients of dysfunctional uterine bleeding were treated with Centchroman as an outpatient, at Nehru Hospital, B.R.D. Medical College, Gorakhpur. Centchroman 30-mg bi-weekly was given for a period of 3-6 months and patients were kept under regular follow up during and after completion of therapy.

In our study patients belonged to the age group 20-50 years as shown in Table 2 and maximum number of patients 60% belonged to age group between 35-44 years and only 11.1% patients were above 45 years. Almost similar results were found by Prasad S. [7] as in their study also 60% patients were between 35-45 years and 11.4% patients were between 45-55 years. In another study (conducted by Torrent. Pharma. Ltd. Ahmedabad) Phase III multicentric trial for treatment of DUB, the results were slightly different as in their study maximum (47.01%) number of patients belonged to 31-40 years and 36.47% belonged to age group between 21-30 years. As it is evident that patients in their study were of lesser age group as compared to our study which may be due to the fact that their study covered 170 patients at three different centres belonging to different zones of India with different socioeconomic conditions whereas our study was smaller with 90 patients only, most of the patients belonging to middle socio-economic status. In our study 61% patients belonged to parity more than three. Patients with parity more than five were 7.8% (Table 3). In other studies parity details were not considered so could not be compared.

In our study 90% patients complained of excessive bleeding during menses with regular or irregular cycles. 36.7% cases had irregular heavy periods (Menometrorrhagia), 27.8% had menorrhagia while polymenorrhagia and polymenorrhoea were present in 25.5% and 10% cases respectively (Table 4). Another study was done in patients of DUB in this institution only by Jina R. et al. [8] in which 81% of patients complained of excessive bleeding during menses, but the distribution of menstrual symptoms was slightly different. Menometrorrhagia was present only in 12% cases, menorrhagia in 33% and maximum percentage (36%) belonged to polymenorrhagia.

In phase III multicentric trial for treatment of DUB (Torrent Pharma Ltd.) out of 170 cases, 131 (77%) cases reported heavy flow during menses out of which 100 cases (58.8%) reported presence of clots. Intermenstrual spotting was reported in 35 cases (20.6%) while dysmenorrhoea was complained by 47(27.6%) cases. Prasad S. [7] reported presence of clots and dysmenorrhoea in 84.3% cases. In our study 38 cases (42.2%) cases took no previous treatment for DUB and received Centchroman as primary treatment (Table 5). In rest of the cases (57.8%) there was history of previous treatment in the form of hormones (39%), D&C (30%) and thermal ablation. (1%), but response to treatment was only temporary.

As we have already mentioned 30% cases of our study had undergone D&C, maximum number of cases 52% had endometrium similar to metropathia haemorrhagica (i.e. proliferative endometrium with cystic dilatation) on histopathological examination. Proliferative endometrium was observed in 41% cases and rest 7.0% cases had secretory endometrium (Table 6). In the study by Prasad S. [7] preliminary diagnostic curettage was performed in all cases of perimenopausal bleeding to exclude any premalignant or malignant lesion in the endometrium. Exact nature of endometrium was not reported, so could not be compared.

History of tubectomy is very important in patients of DUB. In our study, out of 90 patients 38 were ligated (42.2%) as shown in Table 7. This is comparable to Phase IIA clinical trial on DUB (by Torrent Pharma Ltd. Ahmedabad) in which 38.1% cases had history of tubectomy. This difference is not very significant. In rest of the studies no mention was done about history of tubectomy.

Prolongation of menstrual cycles is a well-documented effect of Centchroman therapy. In the present study 42.2% patients experienced prolonged cycles during treatment which became normal afterwards while therapy still continued and most of the patients 85.5% had returned to normal menses by the end of treatment {Table 8 (A) and Table 10.} Nityanand et al. [9] reported normal cycles in 49.85% cases; in remaining 24.38% one, 10.15% two and 15.12% more than two cycles were prolonged. Most cases resumed normal cycles while still on Centchroman. Similarly, Puri et al. [10] observed prolonged cycles in 47.5% cases out of which 22.3% had one, 12.2% two and 13% had more than two cycles prolonged. In rest of the cases (52.5% all cycles remained of normal duration.

Incidence of prolonged cycles reported in these two studies was slightly higher than our study. This may be due to the fact that duration of treatment in our study was only 3-6 months and initial cycles were of short duration while in studies by Nityanand et al. and Puri et al. drug was used for prolonged period with initial cycles of normal duration as drug was used for contraception. In the present study total 274 cycles were covered with Centchroman therapy [Table 8 (B)] during trial, out of which 85.4% cycles were of normal (21-35 days) duration, 7.3% were between 36-45 days and 7.3% were prolonged beyond 45 days. Nityanand et al. [9] studied 648 cases with 9346 months of Centchroman use and covering 8426 menstrual cycles. The drug was used for contraception in doses of 30 mg weekly. 4.21% cycles were of short

(<20 days) duration, 74.12% were of 21-35 days, 12.83% were between 36-45 days and 8.84% cycles were prolonged beyond 45 days. Prolongation of cycles has also been documented in several other studies where drug used for contraception as shown in Table 12.

Table 12: Comparison with other studies

Study		No. of cases	Dose	No. of cycles	Cycle Length in days (% cycles)			
					<20	21-35	36-45	>45
Phase III Multi- centric	Puri et al [10] until June 1984	467	30 mg weekly	5242	4.56	71.15	14.22	10.07
	Nityanand et al 1988	648	30 mg weekly	8426	4.21	74.12	12.83	8.84
Extended Phase III	Nityanand et al April1987-Nov.1988	100	30 mg weekly	810	4.10	69.60	16.40	9.90
New extend-ed Phase III	Nityanand et al 1989	125	30 mg weekly	1060	2.5	88.80	3.6	5.09
New regimen Phase III	Nityanand et al [12] 1994	377	30 mg biweekly x 3months fol-lowed by 30mg weekly	3471	2.70	89.30	4.30	3.70
Present study on DUB	2001-2002	90	30 mg biweekly	274	0	85.40	7.30	7.30

Table 12 shows that slightly higher incidence of prolonged cycles was seen in these studies as compared to our study, done for use of Centchroman 30 mg twice weekly for cases of DUB. 'This may be due to the fact that study done for contraception was on patients with normal cycles, few percentages of patients might be lactating with already slightly prolonged cycles whereas in our study most of the patients had short cycles.

Incidence of amenorrhoea after taking Centchroman therapy was found to be in 4.4% cases in the present study [Table 8 (A)]. This is comparable to study conducted by Prasad S. [7] in which amenorrhoea was reported in 4.2% cases post 'therapy. In the study conducted by Torrent Pharma Ltd. (Phase III Multicentric trial for the treatment of DUB) amenorrhoea was observed in 7.06% cases, which is slightly higher.

In our study response of treatment was assessed at each monthly visit during follow up by taking a detailed history about menstrual pattern i.e. length of cycle, amount and duration of blood flow, presence of clots, associated pain and other concomitant illness. 57.8% of the patients showed definite response to therapy with decrease amount of flow during menses, within one month of starting therapy (Table 9).

80% cases responded to therapy within two months and 88.9% cases within 4 months. 8.9% patients showed no response to Centchroman therapy while two cases dropped out during trial at 4th and 5th month of therapy. Both of these cases showed poor response to therapy. Improvement in menstrual blood loss was patient's own subjective appreciation. Though inquiry about menstrual loss was made by asking questions regarding presence of clots and number of napkins used per day made, most of the patients were using homemade napkins, therefore objective assessment could not be made exactly to assess amount of bleeding.

Out of those patients who responded to treatment 85.5% were relieved of menorrhagia at the end of treatment (Table 10) and reverted to their normal cycles with duration of bleeding 3-5 days. In 3.3% cases bleeding were moderately controlled and only 8.9% patients showed no response to therapy.

In the study by Prasad S. [7] 78% patients were responded within 13 weeks and 80% patients were relieved at the end of treatment (25th week) rest had no response. In her study 59 patients (84.2%) reported presence of clots out of which 77.9% (n=46) were relieved of dysmenorrhoea by the end of treatment. Three patients reported with increased dysmenorrhoea. Out of which two had fibroid, one had adenomyosis, the diagnosis was somehow missed initially and all 3 patients had undergone abdominal hysterectomy.

In another study conducted by Torrent Pharma Ltd. Ahmedabad (Phase III multicentric trial for treatment of DUB) improvement in amount of flow (from heavy to normal) was observed in 87.78% cases. 35 cases reported with spotting and by the end of treatment only 4 cases complained of spotting i.c. improvement was seen in 88.57% cases. Dysmenorrhoea was improved in 80.85% cases, out of 100 patients who reported presence of clots initially 68% showed improvement by end of 25th week.

Efficacy of the drug was assessed at the end of treatment (Table 10). In the present study 44.4% cases showed excellent response to Centchroman with complete control of menorrhagia and had regular cycles when followed post therapy. 41.1% showed good response (bleeding completely controlled with slight irregularity in menstrual cycle which was acceptable to the patients) and 3.3% showed fair response (moderate control of bleeding).

In the study by Torrent Pharma Ltd. Ahmedabad 83.53% cases were evaluated to have excellent to good response. In rest of the cases 8.8% had fair and only 7.6% cases had no response with Centchroman therapy. Thus, we see, the results of this study are almost in accordance with the results of our study.

Centchroman (Ormeloxifene)is virtually free from minor side effects which are commonly observed with hormone therapy like nausea, vomiting, weight gain, acne breast discomfort, metabolic dysfunction etc. In the present study we observed only two side effects- ovarian enlargement and amenorrhoea (Table 11). Ovarian enlargement was observed in 12.2% cases. On ultrasonography it was found to be follicular cyst which disappeared spontaneously within 4-6 weeks after the drug was discontinued. Out of 11 cases, in 9 cases (10%) size of cyst was up to 3-5 cm and only two cases had cyst >5-7 cm diameter. Prasad S. [7] observed mild abdominal pain (10%) giddiness (54.2%) with Centchroman therapy. Significant ovarian enlargement was reported in 10% cases, which is similar to our study. Sonographically ovarian enlargement was documented in 22.8% cases out of which 12.8% cases had cyst size 2.5-4.5 cm and 10% cases had cyst of 4.5-7.1 cm. In all cases cysts regressed spontaneously.

In Phase III multicentric trial for treatment of DUB abdominal pain was observed in 7.06% cases, giddiness in 1% and weight gain in 1% cases.

In another study by Rajan R. [14,15,16] on contraception, 38 subjects were followed by ultrasound between 2 and 4 months of Centchroman use, out of which 10 (26%) exhibited varying degree of ovarian enlargement due to follicular cyst in 6 cases and corpus luteal cyst in 4 cases, ranging from 2.7 to 6.7 cm in size. None of them complained of abdominal pain or pelvic tenderness. The lesser incidence of follicular cyst in our study may be because of the fact that during follow up we could not get ultrasound done in every case. Another side effect, which was observed in our study, was amenorrhoea, in 4.4% cases. All cases that developed amenorrhoea belonged to perimenopausal age group and all patients were satisfied with it. Prasad S. [7] observed amenorrhoea in 4.2% cases which is almost similar to our study, but the age group of these patients was not specified. In Phase III multicentric trial on DUB (Torrent Pharma Ltd.) amenorrhoea was observed in 7% cases.

Conclusion

The present study found that maximum prevalence of DUB was observed in the age group between 35-44 years (60%) and only 5.6% cases were between 20-24 years. Maximum numbers of patients belonged to the parity 4-5 (53%). History of tubectomy was present in 42.2% cases. 90% of patients with menstrual disturbances complained of excessive bleeding during menses with regular or irregular cycles. (Menometrorrhagia - 36.7% followed by Menorrhagia 27.8% & Polymenorrhagia in 25.5% cases). Centchroman may cause prolongation of menstrual cycle (42.2% in the present study) while patients belonging to perimenopausal age group may even develop amenorrhoea as seen in 4.4% cases of our study. Side effects like nausea, vomiting, weight gain, acne, metabolic dysfunctions etc. that are usually observed with hormonal therapy for DUB are not seen with Centchroman (Ormeloxifene), so it is more acceptable to the patients and discontinuation rate is very low. In our study there was no dropout due to side effects. Ovarian enlargement was seen in 12.2% cases in our study, which is also reported in literature. In most cases cyst regressed on discontinuation of therapy. Centchroman in doses of 30mg bi-weekly for a period of 3-6 months is found to be effective in controlling menorrhagia as we found cure rate of menorrhagia to be 85.5%.

Thus, we concluded that Centchroman (Ormeloxifene) used for DUB in dose of 30mg bi-weekly is very cost effective, devoid of any side effects, very effective in controlling DUB, so it should be used in more and more patients.

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