

Centchroman – A novel drug for D U B.

Sudha Prasad

Maulana Azad Medical College & Associated Lok Nayak Hospital, New Delhi – 110 002.

Summary: Prospective study of 70 cases of DUB diagnosed after following certain exclusion criteria were recruited. Abnormal endometrial pattern was excluded in perimenopausal patients. All the patients were followed-up on tablet Centchroman 30 mg. bi-weekly for 6 months. Eighty percent of patients were relieved of menorrhagia at the end of the treatment. Majority of patients (90%) reverted to their normal cycle by 4th month. The incidence of amenorrhoea and oligomenorrhoea were observed in 4.2% and 5.7% of patients respectively. No abnormal effect was seen on endometrium after the treatment. Side effects were few and were well tolerated by the patients. Centchroman was found to be very effective in controlling the symptoms of D U B.

Introduction

Abnormal uterine bleeding is one of the most common problems which is seen in routine Gynaec practice. It may represent a normal physiological state or it can be a sign of a serious underlying condition. Cause of abnormal uterine bleeding should be ascertained quickly and appropriate therapy instituted.

The treatment of DUB comprises of administration of steroidal hormones, like progesterone or OCs and Danazol. Centchroman is a widely used non-steroidal oral contraceptive. This agent is developed at Central Drug Institute, Lucknow in 1967. It exhibits unique combination of weak estrogenic and potent antiestrogenic activities, so it offers endometrial suppression. Therefore, it protects against endometrial hyperplasia and endometrial carcinoma. It also cures the abnormal uterine bleeding pattern.

This prospective study was conducted to observe the efficacy and safety of this drug.

Materials and methods

A detailed protocol and case record form was developed for the studies. The patients diagnosed of DUB, after removal of IUCD and perimenopausal DUB were included in the study. Patients with uterine size more than eight weeks, adnexal mass or tenderness, active heavy bleeding necessitating emergency treatment, breast or genital tract malignancy, bleeding due to pregnancy complications e.g. vesicular mole/incomplete abortions; women with any evidence of hepatic, renal, cardiac metabolic dysfunction, lactating mothers; active venereal diseases; infertility with menstrual problems,

endometriosis, palpable fibroids and pelvic inflammatory diseases were excluded from the study.

The total duration of the trial was of 6 months for each patient. The scheduled dose of 30 mg Centchroman was given biweekly for 6 months to each patient.

A detailed systemic and gynaecological examination was carried out initially. Subsequently, on every visit, i.e. every month, a detailed inquiry into the menstrual pattern, routine physical examination, pelvic examination and sonography were performed. Routine haematological investigations and endometrial aspiration were done. Whenever indicated, pelvic sonography was repeated. Drugs were provided to each patient for a month after each examination.

A diagnostic curettage was performed in all cases of perimenopausal bleeding. In case of abnormal histopathological findings, the patient was excluded from the trial.

Seventy-six patients were selected as DUB from Gynaecological Out Patient Department. Six patients were excluded from the trial as they were not fulfilling the criteria. Observations were tabulated and discussed.

Observations and discussions

In the present ongoing study a total of 70 patients have completed 6 months follow-up. The criteria for improvement of the condition was change in the menstrual pattern. Sixty percent of patients were of 35-45 years of age group (Table-I). Amount of bleeding from "heavy to normal" was the subjective appreciation by the patient herself. Seventy-eight percent patients were

satisfied by the 13th week of treatment.

Table - I
Demographic Profile of Treated Patients

Age (in yrs)	No.	Percentage
25-35	20	28.5
35-45	42	60.0
46-55	8	11.4

Majority (80%) of patients were relieved of menorrhagia at the end of treatment (Table II). Amount of bleeding could not be assessed as patients used home made napkins or clothes of different sizes.

Table - II
Distribution of patients who responded to menorrhagia in relation with duration of centchroman therapy

Responded patients	Duration of treatment (Weeks wise)		
	Ist	13 th	25 th
No. of patients	15	55	56
Percentage	21.4	78.5	80

Presence of clot in the menstrual loss is a very easily discernible aspect of the symptoms and also is a parameter of severity of the pathology. In this study, 59 patients (84.2%) reported presence of clot (Table-III) Forty six patients (77.9%) were relieved of dysmenorrhoea by the end of the treatment, whereas 10 patients have not responded and so dysmenorrhoea persisted in 17% of patients. Three patients (5%) have shown the indication of increased dysmenorrhoea. Out of these three patients, two had fibroid uterus which was somehow missed. One patient had a pedunculated submucous fibroid of 7 c.m. in size. Others had a subserous fibroid with a long pedicle of 6-8 cm in size. There was torsion of the pedicle and was buried in P.O.D. Third patient had a bulky uterus and adenomyosis which was diagnosed later. All these three patients went through abdominal hysterectomy.

Table - III
Distribution of patients who responded to dysmenorrhoea

Dysmenorrhoea	No. of patients	Percentage
Improved	46	77.9
Same	10	16.9
Increased	3	5.0

Pathology was confirmed histopathologically.

Majority of patients (90%) reverted to their normal cycle by 4th month of Centchroman. Incidence of amenorrhoea and oligomenorrhoea were observed in 4.2% and 5.7% of patients respectively which was the only limitation of this drug. There was no incidence of breakthrough bleeding.

Patients with Centchroman had also usual side effects mainly abdominal pain & giddiness (Table VI). Ten percent of patients had abdominal pain, giddiness was observed in 54% of patients. All these patients were followed-up and no neurological cause was found. No patient was observed with weight gain, acne or nausea/vomiting.

In spite of all these minor side effects Centchroman was greatly acceptable by the patients.

On sonography and histopathology, endometrial pattern was correlating with endometrial dating. The secretory phase was found in 43 patients (61.4%) whereas decidual pattern were seen in 20 patients (28.5%). It indicates that Centchroman does not interfere with the hypothalamo-pituitary-ovarian axis.

Post-therapy, endometrium did not reveal any pathological pattern. It proves that it does not interfere with ovulation. This is also documented by others (Nigam et al, 1985 ; Singh and Kamboj 1991). Administration of Centchroman in a dose of 1 mg and 2.5 mg/kg on Rhesus monkeys, did not affect the general pattern of plasma LH, FSH, estradiol and progesterone. It indicates again that Centchroman has no effect on hypothalamo-pituitary-ovarian axis (Nigam et al 1985). On administration of Centchroman in a dose of 6.25 mg, 12.5 mg and 25 mg/kg in adult rhesus monkeys for one year shows no significant effect in their total pituitary gonadotrophin content (Singh and Kamboj, 1991). It has been observed by Vaidya et al (1977) that Centchroman at 120 mg/wk. and 60 mg/wk. dose schedule does not seem to inhibit ovulation although it may delay or prolong cycle length. Incidence of functional ovarian enlargement is well documented in 5% cases. In our study, incidence of functional cyst with significant enlargement was observed in only 10% of patients. The largest size of cyst was measured as 7.1 cm in diameter (Table - VIII). Initially

Table - IV

Distribution of patients with uterine pathology observed on sonography

Uterine Pathology	No. of Patients
Subserous Fibroid	1
Submucous Fibroid	1
Adenomyosis	1
	3

Table - V

Effect of centchroman on menstrual pattern

Menstrual pattern	No. of Patients	Percentage
Normal Cycle	63	80
Oligomenorrhoea	4	5.7
Amenorrhoea	3	4.2
Breakthrough bleeding	None	None

Table - VI

Distribution of patients with side effects on centchroman Therapy

Symptoms	No. of patients	Percentage
Abdominal pain	7	10
Giddiness	38	54.2
Weight Gain	None	None
Acne	None	None
Nausea/Vomiting	None	None

Table - VII

Effect of centchroman on Endometrium

Menstrual Phase	Sonographically (No. of patients)	Histopathologically (No. of Patients)	% age
Proliferative	6	6	8.5
Secretory	40	43	61.4
Decidual	23	20	28.5
Hyperplasia	1	1	1.4

Table - VIII

Ovarian Morphology Observed on Sonography

Functional CYSTS (Size in cms)	No. of patients	Percentage
2.5 - 4.5	9	12.8
4.5 - 7.1	7	10
	16	22.8

these patients had pain in abdomen but did not require any treatment as these cysts regressed spontaneously. This was confirmed by repeat sonography post menstrually.

Conclusion

Commonly used drugs like Danazol are expensive and have side effects whereas combined oral contraceptive pills has its own disadvantages on long term use. In the present study of an open trial of 70 patients in DUB, Centchroman was found to be very effective in controlling the uterine bleeding without affecting normal endocrinal and physiological parameters.

References

1. Nigam P.K, Malviya B, Chaudhary S.R, Kamboj V.P. Chandra H., Contaception 32 (3); 283; 1985.
2. Vaidya R, Joshi U, Meherji P, Nayan R, Betrabet S, Joshi L, Seth A and Devi P.K.; Indian J. exp. Biol. (15) 1173, 1977.
3. Singh M M and Kamboj V P, Indian J. of Exp. Biol; 29 (12): 1145- Dec. 1991.

Acknowledgement

I am thankful to **TORRENT** Pharmaceutical Limited for providing the drug (**CENTRON**) for this trial.