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"CLINICAL STUDY OF CENTCHROMAN FOR ITS CONTRACEPTIVE BENEFITS"

Obstetrics & Gynaecology

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ABSTRACT

Background: Centchroman is a new type of contraceptive that works by preventing the fertilized egg from implanting, effectively preventing pregnancy. The objective of the study was to know about the acceptability, contraceptive efficacy, and safety mainly on postpartum, post-abortal patients seeking this method of contraception. **Materials and Methods:** A prospective observational study was conducted in the Family Planning Department of a Tertiary Care Centre for 18 months, from July 2020 to December 2021. The study involved monitoring 100 patients who were receiving Centchroman. **Results:** Most of the women (48%) belonged to the age bracket of 19-24 years. The average age of the women was 25.40±3.2 years. The most common acceptors were primipara (47%) followed by second para (37%) and third para was only 10%. About 48% had undergone either abortion or medical termination of pregnancy, or were in the postpartum period. Maximum (99%) patients used Centchroman for 1 month. The discontinuation rate was 70%. The major cause for discontinuation was non-compliance with the drug (24 %). The major menstrual complaints were delayed menstrual cycle (17%) and irregular cycle in 7%. Very few side effects were observed in total 10% of patients. 21% of acceptors who had menorrhagia before, had less blood loss when they were started on Centchroman as compared to their previous cycles. Of the 100 women, pregnancy occurred in 1 woman. Pearl index calculated for Centchroman was 1. **Conclusion:** Centchroman is a safe non-steroidal, non-hormonal oral, weekly contraceptive used for delaying, spacing, and limiting birth of pregnancies. It does not alter the metabolism of carbohydrate or lipid and is a safe contraceptive that can be used in women where the steroid pills are contraindicated or should be avoided.

KEYWORDS

Centchroman; Nonsteroidal; Contraception; Multipara; Postpartum; Menorrhagia; Pearl index

INTRODUCTION

Since gaining independence in 1947, India has prioritized family planning as a crucial aspect of reproductive health. The Ministry of Health established the first structured family planning program in 1952, which has undergone several transformations over time. [1]Today, the focus of family planning in India has shifted towards maternal and newborn health, rather than population control. Despite the strides made in this area, there is still a significant unmet need for contraception, currently standing at 20.5 percent. [2] Ensuring the timing and spacing of pregnancies is a critical component of reproductive, maternal, neonatal, child, and adolescent health strategies. In 2012, the Indian government pledged to expand family planning services to an additional 48 million people by 2020. [3] The emphasis is on the use of safe and reversible methods of contraception. The government recognizes the importance of women's reproductive health, and there is now a concerted effort to improve access to oral contraceptive methods for women. The expansion of family planning services will provide women with more options, enabling them to make informed decisions about their reproductive health. [4]

Contraception is a crucial aspect of family planning, and oral contraception is one of the most widely used methods for preventing or delaying pregnancy. This method involves taking birth control pills orally, which contain synthetic hormones that prevent ovulation. The first type of oral contraceptive, the combined oral contraceptive pill, was introduced in 1960 and has since undergone various improvements and modifications. In addition to the combined pill, newer methods such as progestin-only pills, Centchroman (Ormeloxifene) and emergency contraceptive pills have become popular. These newer methods offer a wider range of options for women to choose from, based on their individual needs and preferences. When taken consistently and correctly, oral contraceptives are highly effective, with a failure rate of less than 1% when used correctly. However, there are certain factors that can affect the effectiveness of this method, such as missing doses or taking medications that interfere with the pill's effectiveness. Therefore, it is important to discuss the use of oral contraceptives with a healthcare provider to determine the best option and ensure proper usage. Overall, oral contraception remains a reliable and convenient method for preventing unintended pregnancies.[5]

Combined Oral Contraceptives (COCs) and Progestin-Only Pills (POPs), also known as minipills, are effective birth control options. COCs contain both progestin and estrogen, while POPs contain progestin only, making them safe for breastfeeding women. In 1967, the Central Drug Research Institute (CDRI) in Lucknow developed the first non-steroidal once-a-week pill, Centchroman (Ormeloxifene). This pill was clinically launched in 1991 and has been a reliable contraceptive option ever since.[5]

Ormeloxifene, also known as Centchroman, is a contraceptive pill that is safe and non-hormonal. It is taken once a week and functions as a selective estrogen receptor modulator (SERM). This unique pill has both weak estrogenic and potent anti-estrogenic properties, making it effective at spacing out pregnancies. Ormeloxifene selectively suppresses estrogen receptors in the reproductive organs while stimulating those in other organs such as the bones. By inhibiting the fertilized ovum from implantation, it prevents pregnancy. Importantly, it does not affect carbohydrate or lipid metabolism, coagulation factors, or blood pressure, making it a safe option for women who cannot take steroidal pills. [6, 7] This study based on this novel contraceptive was done to know about the acceptability, contraceptive efficacy, and safety mainly on postpartum, post-abortal patients seeking this method of contraception.

METHODS AND MATERIALS

A prospective observational study was conducted at a tertiary care hospital's Department of Obstetrics and Gynaecology's Family Planning OPD section. The study lasted for 18 months, from July 2020 to December 2021. A total 100 patients of age between 18 to 40 years with normal menstrual cycles, not taking other contraceptives, oral contraceptive pills were contraindicated, patients coming to family planning OPD for interval contraception, post abortal or post MTP patients, postnatal patients wanting temporary contraception and patients willing to participate in the study were included. Non-probability consecutive sampling technique was used for the proposed study until the required sample size was achieved. Patients in the age group of <20 years and > 40 years, patients having medical disorders of pregnancy like jaundice and other liver disorders, tuberculosis, patients with PCOS and cervical hyperplasia were excluded from the study.

During the course of the study, there was no other nonsteroidal pill available for comparison, therefore the manufacturers' claim was taken as the benchmark. To ensure comprehensive analysis, the patients' detailed histories were reviewed, including their age, parity, educational status, systemic illness, medical termination of pregnancy, nature of last delivery, detailed menstrual history, previous use of contraceptives, the reason for discontinuation, and lactation status. Before undergoing a general, systemic, and gynaecological examination, patients were informed of the potential delay in the onset of menses. During the gynaecological examination, the state, position, mobility of the cervix, uterus size, and any palpable adnexal masses were thoroughly noted. Haemoglobin and urine examinations were also included in the study, to ensure a comprehensive assessment of the patients' health.

After recruiting the patients coming to the family planning OPD, each was given Tablet Centchroman to be taken two times a week for the 1st 3 months followed by once a week to be continued till the patient wanted contraception. Starting from the 4th month, the pill was given once a week on the first pill day and continued irrespective of the menstrual cycle. Additional barrier contraception was advised for the first month for the patients wanting interval contraception. In interval cases, the first pill was given on the first day of first menstrual cycle. In post abortal or post MTP, the pill was given on the day of abortion or MTP. In postpartum patients, was given at 6 weeks. Patients were followed monthly for side effects and for complaints of delayed cycles for more than 15 days. If a tablet was missed, the patient was instructed to take it immediately and then take the next tablet according to the regular schedule. If a dose had been missed for two or more days, the patient was advised to continue with the normal schedule and use a barrier contraceptive until the next period, twice a week for the first three months and weekly thereafter. If the tablet had been missed for more than seven days, the pills were to be started again as if the patient were a new user.

Patients were followed up monthly. Any chief complaint was noted. The patient's menstrual history, including the duration, cycle length, type of bleeding, and vaginal discharge, was recorded. Both breast and vaginal examinations were conducted. After a two-week delay, a urine pregnancy test was administered. If the patient was not pregnant, they were advised to continue taking Centchroman according to the prescribed schedule. However, if the patient was pregnant, the medication was immediately stopped and the option of terminating the pregnancy was presented. During the study period, the effectiveness of the contraceptive drug was measured by the number of pregnancies resulting from method failure. If a pregnancy occurred due to the user not following the prescribed treatment schedule, it was considered a user failure. Any chief complaints such as nausea, vomiting, giddiness, headache, hirsutism, and decreased libido to be noted. Pearl index was calculated using the formula number of accidental pregnancies x 1200/cycles of use. The lower the Pearl index, the higher the effectiveness of the contraceptive.

Statistical Analysis

SPSS for Windows software (version 22.0, SPSS Inc, Chicago) was used to analyze the data. For continuous variables, mean and standard deviation (SD) was calculated, while for categorical variables, frequencies and percentages were calculated.

RESULTS AND OBSERVATIONS

During the study period, 100 women coming to the family planning OPD who had accepted Centchroman as a contraceptive method were studied for the efficacy of the contraceptive. Age range of 19 to 24 years was the most common among women, accounting for 48% of the total sample. The average age of these women was 25.40±3.2 years, indicating a relatively young but diverse population. In total, Centchroman was given to 25 patients who had some co-morbidity in the form of either medical or surgical illnesses, (Table 1).

Table 1: Age and Co-morbidities distribution of acceptors taking Centchroman

Age and Co-morbidities		Frequency	Percentage
Age- group	19-24	48	48.0
	25-29	38	38.0
	30-34	14	14.0
Co-morbidities	Diabetic	10	10.0
	Hypothyroidism	09	9.0
	Asthma	04	4.0
	Hypertension	01	1.0
	Uterine perforation	01	1.0

The maximum no. of patients at the time of acceptance of contraceptive were primipara (47%) followed by second para (37%) and third para was only 10% as depicted in figure 1. There was equal acceptance (47%) of Centchroman by primiparas and multiparas.

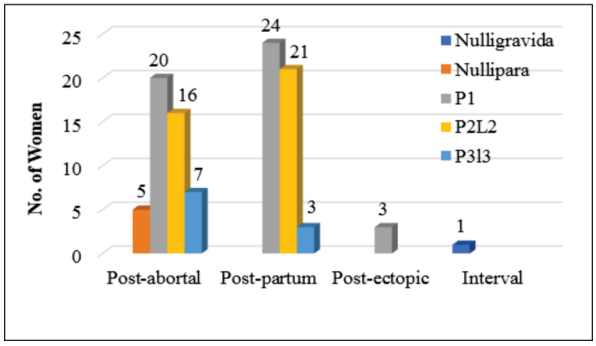

Figure 1: Parity and Obstetric Status at Acceptance

48% of the acceptance was following abortion and postpartum each. 3 cases were post-exploratory laparotomy for ectopic pregnancy and the one patient who was given contraception in the interval period was a nulligravida. 99% patients used Centchroman for 1 month, 85% for 3 months, 62% for 6 months, 45% for 9 months, and 30% for 12 months. The major menstrual complaint was delayed menstrual cycle (17%). 21% of acceptors who had menorrhagia before, had less blood loss when they had started on Centchroman as compared to their previous cycles (Table 2).

Table 2: Timing, duration, menstrual complaints, and benefits in the acceptors of Centchroman

Variables		Frequency	Percentage
Timing of acceptance of contraception	Interval	01	1.0
	Post abortal	48	48.0
	Post ectopic	03	3.0
	Post-partum	48	48.0
Duration of Use (Months)	1 Month	99	99
	3 Months	85	85
	6 Months	62	62
	9 Months	45	45
	12 Months	30	30
Menstrual Complaints	Delayed	17	17.0
	Irregular	07	7.0
	Regular	76	76.0
Benefits	Decreased blood loss	21	21.0
	None	79	79.0

Maximum no. of patients (90%) had no side effects. Side Effects were very few and observed in total 10% of patients as depicted in figure 2. Among the postpartum patients (48%) taking Centchroman, 47% were lactating while on Centchroman. There were no side effects observed on the newborn.

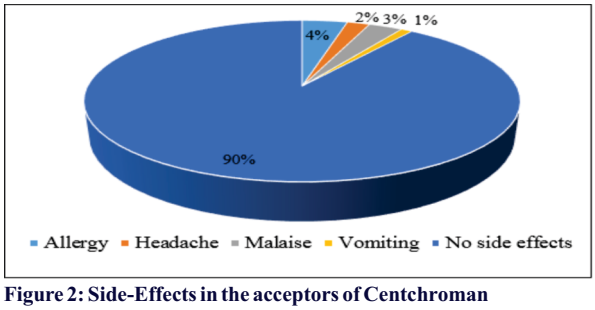

Figure 2: Side-Effects in the acceptors of Centchroman

Out of the 100 patients studied, 1 became pregnant due to user failure where the women had missed the tablets. Using the Pearl Index formula, the Pearl Index was calculated to be 1. The discontinuation rate was 70%. The major cause for discontinuation was non-compliance with the drug (36%), (Table 3).

Table 3: Reason for Discontinuation in the acceptors of Centchroman

Reasons for Discontinuation	Frequency	Percentage
Non-compliant	24	24.0
Drop out	13	13.0
Other method	13	13.0
Lost to Follow-up	12	12.0
Plan pregnancy	04	4.0
Irregular Menses	04	4.0

DISCUSSION

In the present study, the age group amongst acceptors ranged from 19–34 years with maximum number in the age group of 19-24 years (48%). The mean age of patients was 25.40±3.23 years which is comparable with the previous studies. [1, 8, 9] In the present study there was equal acceptance (47%) by primiparas and multiparas. The most common acceptors were primipara (47%) followed by second para (37%) and third para was only 10%. This finding was contrast to the study done by Doke G et al [1] and similar to the study done by Miuli I et al [8] and Nair et al [10]. In the study by Doke G et al [1] there were 74.56% multiparous acceptors. In the study by Nair et al [10] there were maximum number of primiparas (93%) and only 6% multiparas. In the study by Miuli I et al [8] there were 35.8% primiparas and 26.6% multiparas. The number of third para women acceptance was least in our study which is similar to the study by Miuli I et al. [8]

The acceptance of the drug was equal in both the post-abortal and postpartum groups, i.e., 48%. This was similar to the study by Doke et al [1] whereas in the study by Nair et al the acceptance was more in the post-abortal/MTP group (43%) than postpartum (35%). In contrast to this, Miuli I et al study comprised only of post abortal women.

In our study, there were 5% nulliparous and 20% primiparous, 16% had more than 2 living children and 7% had 3 living children in post abortal group. In the study by Miuli I et al [8] there were 37.5% nulliparas and 35.83% primiparas. However, the sample size in the study by Miuli I et al [8] was 120 post abortal women whereas in the current study only 48 post abortal patients had accepted Centchroman. In total 25% of the patients had some systemic illness such as Diabetes, Hypothyroidism, and Bronchial Asthma. One patient had history of preeclampsia but at the time of acceptance she was normotensive. The use of Centchroman was found to be safe in all these patients. According to Nair et al, [10]16 out of the 153 acceptors (10.4%) had associated medical/surgical co-morbidities, where use of Ormeloxifene was not associated with adverse outcome. As compared to the steroidal pills, which are relatively contraindicated in these systemic illnesses, the patients on Centchroman did not develop any inadvertent adverse effects or complications. Therefore, it is safe to use Ormeloxifene in patients with medical/ surgical illnesses where OCP's are contraindicated or relatively unsafe to be given.

The delayed cycles up to 40 days were documented in 17% of acceptors which was similar to the studies by Doke G et al [1], Miuli et al [8]and Ganguli et al [11] which was 15.06 % ,16.66% and 20.9 % respectively. Irregular cycles were observed in 7% of acceptors in our study as compared to Doke G et al [1] (10.9.5%) and Miuli et al,[8] that is10.9% and 4.6% and respectively. As the duration of use advanced, it was observed that there was decreased blood loss, especially in patients with previously heavy cycles. 21% women were relieved of menorrhagia, after accepting Centchroman whereas in the study by Sarbhai V et al [12] and Bhattacharyya TK et al,[13] 88.24 % and 81.67% patients had relief from heavy menstrual bleeding respectively indicating that Centchroman was a better drug for patients with menorrhagia. In the study by Miuli I et al, [8] 22.2% had hypomenorrhea.

In current study, side effects were observed in only 10% of patients. There were 4 cases of allergy (4%), 2 cases of headache, 3 of malaise, and 1 of vomiting which was similar to other studies [1,10] whereas Sarbhai V et al [12] study reported only nausea in 2% cases In other studies, there were no cases of allergy [1, 8,10,12] In contrast the study by Miuli et al [8] showed that vaginal discharge was the most common side effect along with mood disorders, weight gain, loss of libido. The Pearl Index of Centchroman in this study was 1 per HWY which suggests a low failure rate as compared to Ganguli et al,[11] Nair et al [10] and Doke G et al [1] who had pearl indices of 3.125, 1.8 and 2.05 respectively. The study done by Gupta et al had no failure rate. [9]

As the duration of study advanced, 99%, 85%, 62%, 45% and 30% patients followed at 1, 3, 6, 9 and 12 months respectively as compared to the study by Nair et al [10] in which, 100%, 97%, 93%, 84% followed up at 3, 6, 9 and 12 months respectively. In the study conducted by Doke G et al, [1] in which, 100%, 89.04%, 80.82%, 67.12% followed up at 3, 6, 9 and 12 months respectively. However, in the study conducted by Miuli et al, in which, 100%, 98.33%, 91.66% followed up at 3, 6, and 12 months respectively.[8]

In the present study, the rate of discontinuation increased as the duration of use advanced. The major reasons were non-compliance in 24% of the study population. 13% were dropouts due to pandemic who were unable to come for follow-up from far-flung areas and 12% were lost to follow-up. Other reasons were switching to other method of contraceptive (13%), irregular cycles (4%) and other 4% planned for future pregnancy. This finding is similar to Nair et al [10] and Miuli I et al [8] where 4% and 2% patients discontinued due to menstrual irregularity, 2% and 5% respectively want to conceive. 21% patients in the study by Miuli et al [8] discontinued due to psychosocial reasons. Therefore, patient education in the form of advertisements, posters, counselling, and follow-up must be strengthened. Other methods to improve compliance can be done via Radio, television, other tools of public awareness. Patients should be encouraged to take Centchroman in the periphery and primary health centres if they are not able to follow up in the tertiary health centres. Mobile Applications regarding family planning and voice messages for follow up dates or reminders will help the patient and the health facility also to keep a check.

CONCLUSION

Centchroman (Ormeloxifene) is a safe non-steroidal, non-hormonal oral, weekly contraceptive used for delaying, spacing, and limiting birth of pregnancies. It does not alter the metabolism of carbohydrates or lipids and is a safe contraceptive that can be used in women where the steroid pills are contraindicated or should be avoided. It is well tolerated with fewer side effects and can be given to postpartum, post abortal, post ectopic patients and even used as an interval contraceptive without many side- effects. Patients with systemic and/or medical illnesses like diabetes, hypothyroidism, and bronchial asthma had no other associated complications related to the drug. Thus, it can be considered in patients with these systemic/surgical illnesses.

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