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EVALUATION OF SAFETY PROFILE OF CENTCHROMAN FOR CONTRACEPTIVE PURPOSE

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ABSTRACT

Introduction: Centchroman is an effective oral contraceptive has a good patient acceptability and compliance due to its minimal side effects, low cost and simple dosage schedule. This study was undertaken to study the adverse drug reactions of centchroman used for contraceptive purpose.

Material and Methods: The cases were selected from the patients attending post partum programme centre and outdoor department of Obstetrics and Gynaecology, at LLRM Medical college and associated hospital, Meerut, UP, who were taking non-hormonal oral contraceptives (centchroman) preparations for a period of twelve months. Women of reproductive age groups were included and asked not to use any other method of contraception during the study. Every Woman was asked to report immediately if she develops any problem after taking pills and asked for regular follow up at every month.

Results: During the study period, a total of 25 women receiving centchroman for contraception were evaluated. The most common adverse drug reaction reported was menstrual irregularity. After 6 months of therapy, 40% women presented with this complain. 12% cases presented with other complaints in form of abdominal pain and giddiness.

Conclusion: Non-hormonal oral contraceptives (centchroman) are quite safe regarding adverse effect but menstrual irregularities are the major limiting factor for its use as contraceptive.

Key words: Centchroman, Adverse drug reactions, contraceptive, Menstrual irregularity

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INTRODUCTION

Centchroman (also known as Ormeloxifene) is one of the selective oestrogen receptor modulators (SERMs) a class of medications which acts on the oestrogen receptor. It is best known as a non-hormonal, non-steroidal oral contraceptive with strong anti estrogen and weak estrogenic and anti progestin properties which is taken once per week. In India, centchroman has been available as a birth control product since the early 1990s, and it is currently marketed here under the trade name, Saheli^[1]. The drug is marketed in India since last 20 years as an alternative to steroidal Oral Contraceptive Pills (OCPs) and it is provided free of cost through government sponsored family Welfare

Program. The drug has proved to be a highly effective and safe in various studies and is devoid of side effects of steroidal OCPs^[2]. The weekly schedule is an advantage for women who prefer an oral contraceptive, but they find it difficult or impractical to adhere to a daily schedule which is required by other oral contraceptives. For the first twelve weeks of use, it is advised to take the centchroman pill twice per week. From the thirteenth week on, it is taken once per week^[3]. The standard dose is 30mg weekly, but the 60mg loading doses can reduce the pregnancy rates by 38%. It has a failure rate of about 1-2% with an ideal use, which is slightly less effective than that which is found for the combined oral contraceptive

pills^[4]. At a weekly dose of 30mg it does not alter basal or peak gonadotrophin (FSH/LH) levels and also no effect on the production of estrogen or progesterone. The effects which are seen at these dose levels are slight increase in transport of zygote through oviducts, acceleration of blastocyst formation and suppression of endometrial proliferation and decidualization^[5]. The plausible mechanism of contraception is thus appears to be asynchrony between developing zygote and endometrial maturation leading to prevention of implantation^[6]. Return of fertility on stopping the drug is prompt. Centchroman has also not shown teratogenicity in animals and also no untoward effect of the drug was seen in infants born to mothers with contraceptive failure^[7]. Centchroman is primarily used as a contraceptive but may also be effective for dysfunctional uterine bleeding and advanced breast cancer^[8]. American surveys report annual discontinuation rates among OCs users of 29%^[9] with a much higher percentage among adolescents^[10-11]. Comparable evidence from developing countries is limited, but suggests consistently higher discontinuation rates for OCs^[12-13]. Many authors cite the experience of side effects as a major factor involved in early discontinuation of OCs^[14]. Centchroman is an effective alternative of hormonal OCPs, therefore evaluation of its safety profile among non-hormonal contraceptive users is very important which was the purpose of our study.

MATERIAL AND METHODS

A prospective observational study was carried out for a duration of twelve months at LLRM Medical college and associated hospital, Meerut, UP. Study approved by the Institutional Ethics Committee (IEC) and patient informed consent was taken. The cases were selected from the patients attending post partum programme centre and outdoor department of obstetrics and gynaecology, who were taking centchroman for contraceptive purpose. Women of reproductive age group, otherwise healthy and not suffering from chronic ailments, e.g. hypertension, diabetes, and tuberculosis were included in the study. Women were asked not to use any other method of contraception during the study. The

women were instructed to start with one tablet twice weekly, starting from 1st day of menstruation for first 3 months and then a week irrespective of menstruation. Every woman was asked to report immediately if she develops any problem after taking pills and asked for regular follow up at every month. Detailed clinical history was taken at the initiation of therapy regarding age, parity, last pregnancy, detailed obstetric and gynaecological history, history of hypertension, diabetes, smoking, bleeding disorder, jaundice, headache, migraine, stroke, epilepsy, and drug intake. A thorough general and systemic examination was done at the initiation of therapy and at monthly intervals which included recording of weight, pulse rate, B.P., icterus, anemia, oedema, cyanosis, temperature, liver enlargement, and skin condition etc. and also biochemical tests e.g. Hb percentage (Sahli's method), bleeding time BT (Duke's method), clotting time CT (capillary tube method) and fasting blood sugar were done. Statistical analyses were performed by using SPSS 16 & represented in simple frequency & percentage. Quantitative variables before and after therapy were analyzed using paired t-test.

RESULTS

During the study period, a total of 25 women received centchroman for contraception were evaluated. The most common adverse drug reaction reported was menstrual irregularity. After 6 month of therapy, 10 (40%) women present with this complaint. Out of 10 cases, 2 (8%) have menstrual cycle < 20 days, 4 (16%) have cycle > 45 days and 4 (16%) have developed amenorrhoea of about 2 months. 12% cases presented with other complaints in form of abdominal pain and giddiness. No other ADR was reported by users. (Table 1). Biochemical changes, pre and post therapy showed no significant change in hemoglobin (Hb%), bleeding time (BT), clotting time (CT) and blood sugar level (Table 2). Assessment of health related quality of life (HIQ scores) in women using centchroman showed percent improvement was statistically significant ($p < 0.01$) as compared to base line score (Table 3).

Table 1: Percentage of Women Presenting Adverse Drug Effects of Non-Hormonal OCP (Centchroman) (N=25)

Adverse effects	1 Month		3 Month		6 ≥ Month	
	No. of cases	Percent age	No. of cases	Percent age	No. of cases	Percent age
Nausea/Vomiting						
Weight gain						
Skin changes						
Mood changes						
Breast discomfort						
Headache						
Raised Blood Pressure						
Menstrual Irregularities	2	8	5	20	10	40
Other complaint (Abdominal pain, Giddiness)			2	8	3	12

Table 2: Biochemical changes, pre and post therapy of Centchroman

Biochemical changes	Pre-therapy	Post-therapy
Hb%	10.04 ± 0.46	10.82 ± 0.52
BT	3 min 5 sec ± 0.15	3 min 20 sec ± 1.8
CT	4 min 10 sec ± 0.21	4 min 28 sec ± 0.24
Fasting Blood sugar	92.30 ± 1.8	92.47 ± 2.1

(p < 0.001) paired t-test

Table 3: Assessment of health related quality of life (HIQ scores) in women using Centchroman

HIQ s	Non Hormonal OCP (Centchroman) (n=25)	
	Score ±SEM	% Mean improvement
Before therapy	130 ± 2.56	35.39 ± 2.12
After therapy	84 ± 1.81	

(p < 0.01) paired t-test

DISCUSSION

Centchroman is a safer alternative to Progestogen - Estrogen combination pills. One of the main focus was to have an alternative to steroidal pills available in the market which were not free from side effects. This task was successfully completed by CDRI when the first non-steroidal once a week pill, centchroman was developed by CDRI that reached the general public by the end of the 1980's. The contraceptive effect is readily reversible and subsequent pregnancy and its outcome is normal. It scores over steroidal contraceptive pills because it does not disturb the endocrine system and the normal ovulatory cycle is maintained. Among the females who used non-hormonal OCPs, none has shown any adverse effect observed with hormonal pills viz.-Nausea, vomiting, weight gain, skin

changes, increase in blood pressure, headache and mood changes. Similar findings were reported by Central Drug Research Institute (CDRI) Lucknow, India in 1985, who placed non hormonal OCPs superior to hormonal in comparative study. The incidence of menstrual irregularities was high (p < 0.05) in females who used Centchroman. 47.36% females showed irregular cycles sometimes of > 45 days and sometimes < 20 days, whereas 21.17% developed amenorrhoea. The results of Swarn Nityanand et al (1994) [15] were in line with our study. However the incidence of menstrual irregularities (11.76%) and amenorrhoea (8%) was much lower as compared to our study.

As regard giddiness and abdominal pain which have also been reported with Centchroman, only 8% reported giddiness and 12% abdominal pain in our study whereas the other investigators like Dr.Sonal Das (2004) have reported much higher incidence of giddiness (31.75%) and a lower incidence of abdominal pain i.e. 9.52%.

Irregular bleeding and amenorrhoea are major determinants of quality of life in females taking OCPs as irregular bleeding is very agonising while amenorrhoea always creates doubt of pregnancy. Hence these side effects have adverse psychological impact in female. Considering these factors it can be inferred that with hormonal OCPs the quality of life is much better than with non-hormonal which induces psychological set back.

CONCLUSION

Non-hormonal oral contraceptives (centchroman) are quite safe regarding adverse effect but menstrual irregularities (delayed cycle and amenorrhoea) are the major limiting factor for its use as contraceptive.

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