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COMPARATIVE STUDY OF SAFETY AND BENEFITS OF ORAL HORMONAL AND NON-HORMONAL CONTRACEPTIVES

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ABSTRACT
Aims: To compare the safety and benefits of different oral hormonal and non-hormonal contraceptives preparations. **Material and Methods:** A prospective observational study was carried out for duration of twelve months at LLRM medical college and associated hospital, Meerut,UP. The cases were selected from the patients attending post partum programme centre and outdoor department of obstetrics and gynaecology, who were taking oral hormonal or non-hormonal contraceptives preparations. Women were 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:** The present study was conducted on 109 cases, among them 84 cases used hormonal oral contraceptives pills (OCPs) and 25 used non-hormonal OCPs. Out of 84 women, 53 cases used hormonal OCPs for contraception and 31 used for other gynaecological problems. Among hormonal OCPs users for contraception, the most common ADR reported was weight gain (32.07%) followed by nausea/vomiting (26.41%), menstrual irregularities (16.98%), While among non-hormonal OCPs users the most common ADR reported was menstrual irregularity (68%). OCPs caused significant improvement in patients of dysfunctional uterine bleeding (DUB) and dysmenorrhoea. No failure rate was observed. **Conclusion:** Oral contraceptives are effective in management of some important gynaecological problems and prevention of pregnancy and are quite safe regarding adverse effect but menstrual irregularities are the major limiting factor for its use as contraceptive.

KEYWORDS: Adverse drug reactions, Hormonal, Non- Hormonal, Oral contraceptives pills, Menstrual irregularities.

INTRODUCTION
The oral contraceptive (OCs) commonly known as pill is a widely accepted and most effective method of fertility control. High efficacy (with proper use), ease of use, non-contraceptive benefits among the reason, women and their sexual partner may choose it over other form of contraception. Over 100 million women worldwide are currently using hormonal contraceptives. With these drugs, fertility can be suppressed at will, for as long as desired, with almost 100% confidence and complete return of fertility on discontinuation. The efficacy, convenience, low cost and overall safety of oral contraceptives (OCs) has allowed women to decide whether and when they want to become pregnant and to plan their activities.[1]

Shortly after the introduction of oral contraceptives, reports of adverse effects associated with their use began to appear. Many of the side effects were found to be dose dependent and this led to the development of current low-dose preparations.[2] Some women discontinue their use because of bothersome side effects such as acne, hirsutism and weight gain. Oral contraceptives adversely affect thrombolysis, carbohydrate metabolism, and lipid profiles.[3-6]

The most serious risks associated with pill use include blood clots and venous thromboembolism, cerebral stroke and heart attacks.[7-8]

On the other hand, to continue OCs until premenopausal age and over could have a protective effect against cancer of ovary, endometrium and colorectum.[9-10]

OCPs are primarily used for the prevention of pregnancy but also a variety of non-contraceptive benefits, ranging from regulation and reduction of both menstrual bleeding and dysmenorrhea to treatment of premenstrual

syndrome, menstrual migraines, acne and hirsutism, endometriosis and polycystic ovarian syndrome. Long-term benefits include reduced rates of endometrial, ovarian and colorectal cancer.[11-12]

In any case, also mild or moderate adverse effects of OCs may impair the woman's quality of life. Besides, even small increases in frequency of adverse effects in OCs-users have a general critical health impact because of their widespread use, which is currently expanding to potential risk groups.[13]

Two types of preparations are used for oral contraception: (1) combinations of estrogens and progestins and (2) continuous progestin therapy without concomitant administration of estrogens. The combination agents are further divided into monophasic forms (constant dosage of both components during the cycle) and biphasic or triphasic forms (dosage of one or both components is changed once or twice during the cycle).[14]

Before patients begin a drug regimen of any type, it is imperative that they are fully informed about the risks and benefits. As seen above, oral contraceptives can have both positive and negative effects. OCs have positive effects by decreasing risks for certain types of cancer, reducing the pain and symptoms associated with menstrual cycles and by treating health problems such as polycystic ovarian syndrome and endometriosis. On the other hand, oral contraceptives can also increase the risk for certain cancers, cause an elevation in blood clotting, and increase cardiovascular problems. In an effort to see how well informed oral contraceptive users are of these risk and benefits, this study was conducted.

MATERIALS AND METHODS

A prospective observational study was carried out for duration of twelve months at LLRM Medical college and associated hospital, Meerut, UP. Study was 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 oral hormonal or non-hormonal contraceptives preparations. Women from 17-35 years of age, otherwise healthy and not suffering from chronic ailments, e.g. hypertension, diabetes, and tuberculosis were included in the study for the effect of hormonal OCPs used for contraceptive purpose, while women of all age groups were included in the study that used non-hormonal contraceptives and hormonal contraceptive for non contraceptive purpose. Women were asked not to use any other method of contraception during the study.

All the women were instructed to start the hormonal OCPs during the 1st cycle from the 5th day of menstruation and continued daily at bed time for 21 days without miss and then to restart again from the 5th day of next menstrual cycle. The women were also instructed, that if one pill is missed, two tablets should be taken the next day as soon as they remember and other at scheduled time. For hormonal contraceptives used for menorrhagia or dysfunctional uterine bleeding (DUB), they were instructed to start with 1 tab TDS till bleeding stops, then gradually decreases the dose and continue for 1 tab daily for 21 days. A second course was started 1 tab daily from 5th day of next menstrual cycle for 21 days. The treatment continued for 3 to 6 months.

For non-hormonal contraceptives users 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 blood sugar were done. Health related quality of life was done by HIQ scoring system.

Statistical analyses were performed by using SPSS 16 & represented in simple frequency & percentage. Categorical variables were analyzed using chi square test and quantitative variables before and after therapy were analyzed using paired t- test.

RESULTS

In the present study 120 women were selected but only 109 cases could be evaluated, 11 were drop out cases, 4 because of severe vomiting and 7 were not turn up for follow up. Out of 109 cases, 84 cases used hormonal oral contraceptives pills (OCPs) and 25 used non-hormonal OCPs. Out of 84 women, 53 cases used hormonal OCPs for contraception and 31 used for other gynaecological problems i.e. dysmenorrhoea, menorrhagia, DUB, HRT.

Among hormonal OCPs users for contraception, the most common ADR reported was weight gain (32.07%) followed by nausea/vomiting (26.41%), menstrual irregularities (16.98%), mood changes and headache (15.09%), skin changes and breast discomfort (9.43%) and raised blood pressure (7.54%). While among non-hormonal OCPs users the most common ADR reported was menstrual irregularity (68%) (Table 1). According to

this women used non-hormonal OCPs showed significant increased percentage ($p < 0.05$) of menstrual irregularities in comparison to women used hormonal pills.

Hormonal and non- hormonal OCPs when used for contraceptive purpose, causes no significant biochemical changes in Hb%, clotting time (CT), bleeding time (BT) and blood sugar level pre and post therapy (Table 2). When hormonal OCPs used for non- contraceptive purpose causes significant increase in Hb% ($p < 0.01$) while no significant changes in clotting time (CT), bleeding time (BT) and blood sugar level were seen.

OCPs caused significant improvement in patients of dysfunctional uterine bleeding (DUB) and dysmenorrhoea. No failure rate was observed.

Health related quality of life (HIQ scores) assessment showed percent improvement was statistically significant ($p < 0.01$) as compared to base line score for hormonal and non hormonal OCPs but quality of life is better in females using hormonal OCPs (Table 3).

Table 1: Comparision of adverse effects of hormonal OCPs with Non- hormonal OCPs used for contraception.

Adverse effects	Hormonal (n=53)		Non-Hormonal (n=25)	
	No. of cases	Percentage	No. of cases	Percentage
Nausea/ Vomiting	14	26.41	–	–
Weight gain	17	32.07	–	–
Skin changes	5	9.43	–	–
Mood changes	8	15.09	–	–
Breast discomfort	5	9.43	–	–
Headache	8	15.09	–	–
Raised BP	2	7.54	–	–
Menstrual Irregularities	9	16.98	17	68*

$P < 0.05$ in comparision to hormonal OCPs.

Table 2: Comparision of biochemical changes, pre and post therapy of hormonal with Non-hormonal OCPs when used for contraception.

Parameters	Hormonal		Non-Hormonal	
	Pre-therapy	Post-therapy	Pre-therapy	Post-therapy
Hb%	10.8 ± 0.21	11.2 ± 1.3	10.04 ± 0.46	10.82 ± 0.52
BT	3min 10 sec ± 1.8	3min 25 sec ± 1.5	3 min 5 sec ± 0.15	3 min 20 sec ± 1.8
CT	4min 01 sec ± 1.1	4min 48 sec ± 1.3	4 min 10 sec ± 0.21	4 min 28 sec ± 0.24
Blood sugar	89.2 ± 2.3	89.8 ± 2.1	92.30 ± 1.8	92.47 ± 2.1

$P < 0.05$.

Table 3: Comparision of assessment of health related quality of life (HIQ scores) in women using hormonal and non- hormonal contraceptives.

	Hormonal OCP (n=53)		Non Hormonal OCP (n=25)	
	Score ±SEM	% Mean improvement	Score ±SEM	% Mean improvement
Before therapy	131 ± 2.48	45.04 ± 1.86	130 ± 2.56	35.39 ± 2.12
After therapy	72 ± 1.96		84 ± 1.81	

$P < 0.01$.

Table 4: Changes in menstrual cycle pattern in patients of dysfunctional uterine bleeding using hormonal contraceptives.

	No.of cases	Pre-therapy	Post-therapy
Duration of cycle	14	23.71 ± 1.78	27.57 ± 0.30*
Duration of flow	14	6.85 ± 0.70	3.92 ± 0.24**

*$p < 0.01$.
**$p < 0.001$.

This table shows that hormonal pills causes significant improvement in patients of dysfunctional uterine bleeding.

DISCUSSION

Combined hormonal contraceptives (COCs) are one of the most popular methods of birth control, worldwide.

This reliable form of contraception, having a theoretical failure rate of 0.1% and due to problems with compliance, an actual failure rate of 2–3%, may have several contraindications to use. The majority of women who use the birth control pill experience no side-effects at all; while, some of them experience mild side-effects such as spotting or breakthrough bleeding (BTB), nausea, headache, breast tenderness, weight gain, mood changes, low libido and dermatologic problems.

The incidence of adverse effects was similar whether used for contraception or other gynaecological problems in this study.

Among hormonal OCPs users for contraception, the most common ADR reported was weight gain (32.07%) which not seen with non-hormonal OCPs, Study conducted by Irvine GA (1998)[15] found the same observations. weight gain may be due to oestrogen, which produces oedema and cyclical weight change or to anabolic effect of progestogens causing increase of tissue and fat and increased appetite. The reason for this increase in weight could be due to Na^+ and water retention and androgenic activity of progestational compound in combined pills (Rosenberg, 1998).[16]

Carpenter and Neinstein (1986)[17] reported that low dose preparation fails to demonstrate a significant weight gain with oral contraception. Rosenberg explored weight/OC issue in a study analyzing the daily weight of 128 women during four cycles of triphasic OC use. The mean weight at the end of fourth cycle was the same as baseline. Ruebinoff et el (1995)[18] says that although weight gain is often named as the reason for nonuse or discontinued use of OCs, studies fails to associate use of low dose OCs with significant weight gain.

Next most common ADR reported among hormonal OCPs users was nausea/vomiting (26.41%) also not reported in non-hormonal OC users. This is due to oestrogenic effect. They are found less frequently with the low dose pills and usually pass off during 2-3 months of continued use.

Next important ADR was menstrual irregularities which was more common among non-hormonal OCPs users (68%) as compared to hormonal OCPs users (16.98%). Result observed by Enderkat J. Muller (1997)[19] are similar to our study (10-30%). Menstrual irregularities occurred in the form of break through bleeding, disturbed menstrual cycle and amenorrhoea. break through bleeding is a major continuation problem. Jung-Hoffman and Khul (1990)[20] reported that there is no evidence that onset of bleeding is associated with decreased efficacy. Rosenberg et al (1996) showed that break through bleeding is further increased in women who smoke and use formulation with 20 µg ethinyl estradiol. Endrickat et al (1997) reported that most frequently encountered break through bleeding occurs in first few month of use. The incidence is greatest in the first 3 months ranging from 10-30% in first month to < 10% in the 3rd. Muller et al (1997) reported that break through bleeding are higher with the lowest dose of OCs.

Oligomenorrhoea happens quite frequently with low dose pills because of lack of proliferation of endometrium. Wentz (1998)[21] reported that the incidence of amenorrhoea in the first year of use with low dose OCs is less than 2% and this incidence increases with duration, reaching 5% after several year of use.

Headache was observed in (15.09%) cases used hormonal OCPs. Studies with high dose pills indicated that headache was linked to a risk of stroke. Lidegaard (1995)[22] cocluded that the use of OCPs by migrainers was associated with 4 fold increase of already increased risk of ischemic stroke. Skin changes and breast discomfort was observed in (9.43%) cases used hormonal OCPs. The oestrogen in OCs may produce oedema of the breast leading to heaviness and tenderness. Lamey et al 1990 reported similar results in their study (9%).

Raised blood pressure (BP) was seen in (7.54%) cases. WHO reported that low dose OCs causes modest elevation in BP, particularly in women over 35 year may increase the risk of arterial disease. Kovacs et al (1986) reported that OCPs induced hypertension was observed in approximately 5% of users of higher doses. Nichols et al (1993) reported that there is no increased incidence of clinically significant hypertension with low dose OCPs.

Hormonal and non- hormonal OCPs when used for contraceptive purpose, causes no significant biochemical changes in Hb%, clotting time (CT), bleeding time (BT) and blood sugar level. Both hormonal and non-hormonal pills were effective in prevention of pregnancy and no failure rate was seen during the study period.

CONCLUSIONS

Hormonal OCPs shows more adverse reactions as compared to non- hormonal contraceptives. Non-hormonal pills are quite safe regarding adverse effect but menstrual irregularities are the major limiting factor for its use as contraceptive. Hormonal and non- hormonal OCPs when used for contraceptive purpose, causes no significant biochemical changes. Quality of life is better in females using hormonal OCPs. Significant improvement in patients of dysfunctional uterine bleeding (DUB) and dysmenorrhoea. No failure rate was observed.

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