EFFECT OF HORMONAL CONTRACEPTIVES ON SERUM ELECTROLYTES AND BLOOD PRESSURE

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ABSTRACT

Objective: To find out serum electrolytes and blood pressure in Pakistani females, using oral and injectable contraceptives.

Methodology: This descriptive study was conducted at Department of Biochemistry and Molecular Biology, Army Medical College Rawalpindi and various family planning clinics of Rawalpindi and Wah from June 2002 to June 2003. Using convenient sampling technique, ninety women were included in the study. They were divided into three groups: Group A [Oral contraceptive users (n=30)]; group B [Injectable users (n=30)], both using contraceptives for more than 1 year; and Group C [Controls (n=30)], not using any form of contraceptives. Blood pressure was recorded. Fasting blood samples were analyzed for serum electrolytes. One way anova was used at 95% of confidence interval for comparing the data of various groups and $p<0.05$ was taken as significant. Pearson's correlation coefficient was calculated between variables.

Results: Systolic blood pressure shows a significant difference in both groups A and B as compared to control ($p < 0.05$) but diastolic blood pressure was higher in injectable users only ($p < 0.05$) and group A was higher than group C but difference was not significant. Serum potassium was less in group A and B as compared to control but the difference was significant in group B ($p<0.01$) while in group A was non-significant ($p>0.05$). Serum sodium shows higher level in group A and B than control but the difference was statistically not significant

Conclusion: In hormonal contraceptive users there are significant changes in blood pressure and electrolytes except serum sodium.

Key words: Blood pressure, Serum electrolyte, Hormonal contraceptives, Depot medroxyprogesterone acetate (DMPA)

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INTRODUCTION

The use of oral contraceptive pill (OCP) by women the world over is on the increase, nearly 100 million women are using especially in recent years when various governments and organizations are campaigning for its use in order to space pregnancies especially in developing countries like Pakistan where the prevalence of contraceptive use is 5.5% and this use of contraception is more common in urban area (9.8%) than rural area (3.9%)[1, 2]. The most widely used methods of hormonal contraception in Pakistan are oral tablets (combined estrogen and progestins) and injectables (progestins only) which are currently provided by family planning centers[3]. Most of the oral contraceptives contain a combination of estrogen and progestin, the doses of which have been progressively decreased over years. Ethinyl estradiol is the most frequently used estrogen in combined oral contraceptive pills in a dose range from 20-35 µg. The adverse effects associated with oral pills decrease in direct proportion to the reduction of the estrogenic content[4]. Several authors have observed that OCP use may increase the risk of cardiovascular disease. Estrogen is primarily responsible for the rise in the blood pressure, but studies have suggested that progestogens may also contribute to the raised blood pressure by hormone cascades and direct effect on small blood vessels. Estrogens induce the hepatic production of renin substrate, angiotensinogen, with a subsequent increase in angiotensin[5].

Previous studies have shown that women who use oral are six times more likely to develop hypertension than non-users, and the risk increases with higher doses of estrogen and progestin, and with increased length of exposure to the Oral Contraceptives (OCs). Hypertension related to OCs is usually mild to moderate, with

increases of 10 to 20 mm Hg diastolic and 20 to 40 mm Hg systolic. The hypertension is usually reversible within one to three months after OCs are discontinued[6]. In a study of risk factors for CAD in premenopausal women, use of OC was one of the risk factor[7]. A review of 24 years of data suggests that most women taking oral contraceptive experience a small but detectable, increase in both systolic and diastolic blood pressure[8]. Definitive data from long-term studies on the newer low-dose OCs are not yet available, but some show no risk of venous thromboembolism with third generation in young European [9].

Depot medroxyprogesterone acetate (DMPA) is a synthetic steroid similar to progesterone, a hormone normally produced by the ovaries each month as a part of menstrual cycle and used as along acting hormonal contraceptive methods. DMPA is administered in a dose of 150 in 1 ml aqueous suspension. The injection is given every 90 days into the deep gluteal region or deltoid muscle, and one injection inhibits ovulation for at least 14 weeks. It is estimated that 13 million women are currently using DMPA and method is marketed in more than 90 countries worldwide[10]. In controversy exist regarding the adverse and beneficial effects of hormonal contraceptives on blood pressure and serum electrolytes which are associated with increased risk of renal and cardiovascular disease. This study was carried out to compare the effects of injectable hormonal contraceptives and oral contraceptives on blood pressure and electrolytes among Pakistani women within reproductive age.

METHODOLOGY

This descriptive study was carried out at Biochemistry Department of Army Medical College Rawalpindi after ethical approval of the college committee. Informed consent was obtained from the subjects and necessary permission was obtained from relevant authorities of the institutions involved. The women were selected from various family planning clinics department of reproductive health from Rawalpindi and Wah. The subjects participated in the study were selected by their record and they were using either tablet Lofemenal (Ethinyl estradiol 0.03mg and Norgestrel 0.3mg) or injectables Depoprovera (Depot Medroxy Progesterone Acetate 150mg/ml after 3 months) and Norigest (Norethisterone enanthate 200mg/ml. Dose: 1 ml deep intramuscular bimonthly) were given to them. The healthy controls were selected from the faculty of international Islamic medical college and Army medical college not using any form of hormonal contraceptives. History and clinical examination was recorded on a separate proforma. Complete menstrual and medical history was taken with details. The history of hormonal contraceptives was taken. Any other complaint like weight gain, ischaemic heart disease and blood pressure was taken. Family history was also asked regarding presence of hypertension, ischemic heart disease etc. Blood pressure (both systolic and diastolic blood pressure) was recorded in sitting position in right arm as mmHg by mercurial sphygmomanometer. Subjects were divided into three groups: Group A: Subjects using oral contraceptives (n=30); Group B: Subjects using injectable contraceptives (n=30); and Group C: Controls, not using any form of hormonal contraceptives (n=30).

A blood sample of 10 ml was taken after 12-14 hours of overnight fast, from antecubital vein in a disposable plastic syringe. Adequate antiseptic measures were adopted for blood collection Serum electrolyte 2 ml blood was taken. For serum electrolyte, ion selective electrode method was used on the same day of collection.

Data was entered in proforma. All the values were expressed as mean ± standard deviation. One way anova was used at 95% of confidence interval for comparing the data of various groups and $p<0.05$ was taken as significant. Pearson's correlation coefficient was calculated between variables.

RESULTS

Table 1 shows the age, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), serum potassium and serum sodium among the three groups. This shows a significant difference in terms of SBP and DBP while it was highly significant for serum potassium. Table 2 shows correlation between age and blood pressure among the three groups.

Table 1: Descriptive statistics between groups

	Oral Contraceptives (Group A) n=30	Injectable contraceptives (Group B) n=30	Control Group (Group C) n=30	p-value
Age (years)	29.77 ± 6.11	31.03 ± 3.0	32.07 ± 20.0	NS
Systolic Blood Pressure (mmHg)	116.83 ± 11.17	118.33 ± 9.85	112.0 ± 7.61	* < 0.02
Diastolic Blood Pressure (mmHg)	76.0 ± 10.53	80.83 ± 10.91	77.0 ± 5.50	* < 0.02
Serum Potassium (mmol/L)	4.06 ± 0.41	3.97 ± 0.34	4.07 ± 0.40	** < 0.01
Serum Sodium (mmol/L)	138.9 ± 1.49	138.63 ± 2.1	133.35 ± 3.42	NS

* $p < 0.05$, ** $p < 0.01$, NS = Not Significant

Table 2: Correlations between age and blood pressure among groups

Group		SBP	DBP
Oral Contraceptives (n=30)	Age	0.10	-0.03
	SBP	-	0.82***
Injectable Contraceptives (n=30)	Age	0.48**	0.59**
	SBP	-	0.85***
Control (n=30)	Age	0.34	0.23
	SBP	-	0.46*

* p < 0.05, ** p < 0.01, *** p < 0.001
Note. SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure

DISCUSSION

For evaluation of the metabolic and risk factor very few studies have been conducted in developing countries like Pakistan. In our study, we found a significant difference of systolic blood pressure in oral contraceptive users as compared to control (p<0.02) while diastolic blood pressure was non-significant. Injectable contraceptives show change that was non-significant. Before starting oral contraceptives, measurement of lipid profile is recommended in women with dyslipidemias and alternative non hormonal contraceptive should be sought out if low density lipoprotein- cholesterol is not below 160 mg/dl. The lowest dose pill containing estrogen and progesterone which can provide good cycle control and produce minimal effect on lipid and carbohydrate metabolism should be prescribed[11, 12].

One of the main reported effects of combined OCP is an increased risk of cardiovascular disease (CVD). The progressive change in the composition and dosages in the OCP and more careful selection of women who are to use these products have resulted in a lower risk of CVD associated with their use[13]. The World Health Organization (WHO) study of CVD and steroid hormone contraception conducted in developing and developed countries revealed a higher overall risk of Ischemic stroke among OCP users in developing countries than those in developed countries of Europe. These differences were attributed to the type of OCP used and the frequency with which users reported that their blood pressure had been checked prior to or during OCP. The result of the effect of low dose OCP on lipid shows an increase in weight, systolic and diastolic blood pressure in OCP users compared with non users. This observation is consistent with other studies[14]. It was suggested that blood pressure check the OCP attributable mortality, the impact is however insignificant in women under 35 years. SBP did not show any statistically significant differences among the two groups. However, DBP was statistically significantly different between the groups[15]. Our study showed correlation of blood pressure with age like a previous study which showed that mean blood pressures adjusted for age were significantly higher among oral contraceptive users than they were among non-users (*P* < 0.001 for both systolic and diastolic blood pressures)[16]. There are studies showing impact of hormonal contraceptives on blood pressure consequently leading to heart disease[17]. In a recent study done in Peshawar, with 200 married fertile women of child bearing age group (14-49 years), blood pressure was more in oral contraceptive users and the difference was statistically significant[18]. This study is different from our study that showed different findings and it is only comparing oral contraceptive user as compared to control. Our study also included injectable contraceptives also. A similar study of blood pressure done in Karachi, systolic and diastolic blood pressure was within normal range in control subjects except one subject the blood pressure was 140/90mmHg. In 22 % subjects using oral contraceptives systolic blood pressure was 130-140 whereas diastolic blood pressure was observed over 90 mmHg only in 13% of users. On the contrary injectable contraceptive user systolic blood pressure was higher than 120 mmHg in 13% users whereas diastolic blood pressure >90 mmHg was observed in only 9% subjects[19].

Women who did have blood pressure measurement more chance to risk of heart disease. It might be the combination of oral contraceptive responsible for the metabolic alterations and change in blood pressure, body weight and incidence of other adverse effects[20]. The tolerability of two different preparations i.e., oral contraceptive containing 30g ethinyl estradiol/drosperidone vs. ethinyle estradiol/desogestrel was used by two groups of women and the blood pressure remained unchanged[21]. In an Iraqi study a higher mean blood pressure in women using combined oral contraceptives compared with non-users, this is in agreement with other studies[22]. Other studies fail to support the causal relationship between OC and elevated BP, and suggests that even lower dose of estrogen increase of hypertension and the risk increases with duration of use and with increasing potency of progestin used[23]. The association of combined oral contraceptives (OC) with higher blood pressure (BP) may be attenuated with pills with small-

er doses of oestrogen. The effect of stopping OC on BP of patients with hypertension was not described to date. In a cohort study of patients with hypertension[24], stopping hormonal contraception was recommended to all. The risk of cardiovascular complications is found primarily in women over 35 years of age and in those who smoke. There is more chance of developing hypertension in women using oral contraceptives than non-users. The risk increases with higher doses of estrogen and progestins and also with increased length of exposer to oral contraceptives[25]. It also depends on the dosage and formulation. Our study showed significant correlation of blood pressure with age like a previous study which showed that Mean blood pressures adjusted for age were significantly higher among oral contraceptive users (125/70 mmHg) than they were among non-users (123/68 mmHg, $P < 0.001$ both for systolic and for diastolic blood pressures[25-27]. Our study showed significant correlation of blood pressure with age like a previous study Previous studies have shown that injectable contraceptives have no effect on blood pressure and thromboembolic phenomenon. Some studies have reported that DMPA does not exert any effect on various lipoproteins and lipid components These DMPA-induced alterations in lipid metabolism can cause serious cardiovascular adverse effects in women.

The use of oral contraceptives has been associated with increase serum electrolyte but decrease level of serum electrolyte in injectable users. In a study (n=50), oral contraceptive users and users n=50 taking injectable contraceptives (DMPA or Norigest) the same women served as control before starting drugs. There was a slight increase in serum sodium and chloride but significant decreased in potassium and bicarbonate in OCP users. There was non-significant decrease in serum electrolyte in women taking injectable contraceptives and also there was increase in weight and blood pressure[28]. A study to evaluate oral contraceptive with drospirone on electrolytes and blood pressure done on Thai women (n=90) revealed no significant change after 6 cycles as compared to baseline value showing tolerability of drug formulation and also showed contraceptive efficacy[29].

CONCLUSION

In hormonal contraceptive users there are significant changes in blood pressure and electrolytes except serum sodium. It is suggested that blood pressures should be screened before oral contraceptives are supplied and should be monitored regularly during oral contraceptive use.

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CONTRIBUTORS

SH conceived the idea, did data collection and wrote the manuscript. AKN supervised the study. Both the authors contributed significantly to the final manuscript.