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COMPARITIVE EFFECTS OF HORMONAL AND NON HORMONAL CONTRACEPTIVES ON FASTING BLOOD SUGAR LEVELS

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ABSTRACT: The objective of the current study was to differentiate contraceptives for their effects on carbohydrate metabolism. This is a cross sectional design that was conducted in different clinical settings of urban population who belong to low socio economic status by convenience sampling method. Females representing fertile age ranging from 26 to 32 and maintained on different types of hormonal and non hormonal contraceptives (OC; Oral contraceptives, DMPA; Depo-medroxy progesterone, NET-EN; Norethisterone, Implant and non hormonal intrauterine contraceptive device (IUCD) are enrolled and invited in 12 hrs fasting to give their blood samples. Fasting blood sugar is analyzed by GOD-PAP method. All the readings were fed on MS- Excel to evaluate mean \pm S.D, Comparative effects were represented by percentile differences between different groups. The present study concluded that all hormonal and non hormonal methods posed no deleterious effects on carbohydrate metabolism. These minimized risks may be due to young age and good monitoring of therapy in clinical practices and could be threatening in the areas where these are consumed as OTC drugs or by aged females, very near to their menopause or having other risk factors.

INTRODUCTION: Hormonal methods of contraception are known to be associated with alterations in carbohydrate metabolism. These alterations may be due to compromised glucose tolerance and increased insulin resistance, which are predisposing factors for NIDDM and CVD (cardiovascular disease). These problems have been raised with progestin-only contraceptives as well as contraceptives containing estrogen ¹. Estrogen alone causes little decrease in fasting levels of glucose and insulin but does not have drastic effects on carbohydrate metabolism.

Some high dose older OCs showed impaired glucose tolerance, but it is uncertain whether these effects were due to the progestin or the estrogen component of those OCs ². Ethinyl estradiol and mestranol are the two estrogens most frequently used in oral contraceptives. When either or have been given alone in doses comparable to those found in OCs, no alterations in glucose or insulin serum concentration have been detected. Carbohydrate alterations after use of these estrogens have been significantly less than reported when OCs were used ³ as estrogen is known for its actions in islet β -cells of pancreas in regulation of insulin secretion and nutrient balance ⁴.

Progesterone increases basal insulin as well as post prandial insulin levels, but this effect rarely alters glucose tolerance. Administration on long term basis of more potent progestins, e.g. norgestrel, may decline glucose tolerance ².

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Medroxyprogesterone has been shown to elevate blood glucose and plasma insulin levels. 300 mg/day dose of Norethisterone for 4 weeks not causing any blood glucose changes. Impairment in CHO metabolism has not shown by Norethindrone. Norgestrel has produced mean treatment values for glucose higher than control values⁴. Furthermore progesterone was also found to be associated with risk of gestational diabetes because of development of insulin resistance. Recent mechanism involves the apoptosis of β - cell of pancreas⁵.

MATERIALS AND METHODS:

Experimental setting: Present study was conducted in family planning clinics of Karachi. Women taking following types of contraceptive were randomly invited and reviewed for their reproductive history. Blood samples of 54 women who responded, met the inclusion/exclusion criteria and willingly agreed to join in the research were collected.

Eligibility criteria:

- Gender: Females

1) Inclusion Criteria:

- Females of fertile age (20-50 yrs).
- Using contraception for at least 1 year.
- Maintained on these drugs and methods just for the indication of contraception.
- Females willingly agreed to join in this research.

2) Exclusion Criteria:

- Females aged less than 20yrs and more than 50 yrs.
- Maintained on contraception for less than 1 yr.
- Maintained on these drugs for indications other than contraception.
- Females not agreed to join in this study.

Grouping:

Subjects were stratified in four groups

1. Women maintained on oral contraceptives.(OC; n=12)
2. Women maintained on injectables. (DMPA; n=14 , NET-EN; n=18)
3. Women maintained on subdermal implants. (IMPLANT; n=4)

4. Women maintained on IUCDs (Cu-T; n=6)

The chemical constitution of the contraceptives used in this research is as follow:

OC: 0.3 mg norgestrol combined with 0.03mg ethinyl estradiol.

DMPA: Depomedroxy progesterone acetate (150mg/ml).

NET-EN: Norethisteroneenatate (200 mg/ml).

Implant: Levonorgesterol (36 mg).

IUCD: non hormonal T –shaped contraceptive device having copper.

Collection of blood sample: 7 ml of fasting blood sample were collected from enrolled subjects by inviting them in 12 hour fasting state for the determination of their fasting blood glucose levels.

Fasting blood glucose analysis: GLUCOSE liquicolor is GOD-PAP method (Enzymatic Colorimetric Test for Glucose Method with Deproteinisation)⁶.

Statistical analysis: All the readings are represented as the means and standard error to the mean (S.E.M.). Since the results analyzed by using one way un-stacked ANOVA were found to be statistically insignificant thus the comparison was done by determining percentile differences among various contraceptive groups.

RESULTS:

Determination of fasting blood sugar: Table 1 reveals the mean concentrations of fasting blood sugar in different contraceptive groups. All the values are expressed in terms of mean \pm S.E.M. The mean fasting blood sugar in Implant, OC and IUCD groups are found to be below normal reference range with the values of 64.75 ± 1.84 , 68.3 ± 1.73 and 68.6 ± 1.96 mg/dl respectively, whereas DMPA and NET-EN shows the concentrations of 72.2 ± 4.80 and 73.38 ± 2.43 mg/dl respectively which lie in the normal reference range.

Table 2 reveals the comparisons of the mean serum concentrations of fasting blood sugar (FBS) in different contraceptive groups. All the values are

expressed in terms of percentile differences of mean.

IUCD group shows the difference of 5.7 % high, 6.44 % low, 5.02 % low and 0.49 % high FBS as compared to Implant, NET-EN, DMPA and OC groups respectively.

Implant group shows the difference of 11.7 % low, 10.44 % low and 5.23 % low FBS levels as

compared to NET-EN, DMPA and OC groups respectively.

NET-EN group shows the difference of 1.49 % and 7.41 % high FBS concentrations as compared to DMPA and OC groups respectively.

DMPA group shows the difference of 5.81 % high FBS levels as compared to OC group.

TABLE 1: EFFECTS OF CONTRACEPTIVES ON FASTING BLOOD SUGAR

Parameter	Reference ranges (mg/dl)	Method of contraception / Number of subjects in each group				
		IUCD	IMPLANT	NET-EN	DMPA	OC
		6	4	18	14	12
FBS	70-115	68.6±1.96	64.75±1.84	73.38±2.43	72.2±4.80	68.3±1.73

TABLE 2: PERCENTILE DIFFERENCES OF FBS OF DIFFERENT CONTRACEPTIVE GROUPS

Contraceptives Compared	FBS (%)
IUCD – IMPLANT	5.7
IUCD –NET-EN	-6.44
IUCD-DMPA	-5.02
IUCD-OC	0.49
IMPLANT-NET-EN	-11.7
IMPLANT – DMPA	-10.44
IMPLANT-OC	-5.23
NET-EN – DMPA	1.49
NET-EN –OC	7.41
DMPA-OC	5.81

DISCUSSION: When the currently used hormonal contraceptives were reviewed, it is noted that these contraceptives posed minimized effect on carbohydrate metabolism in females without diabetes. Strong statements are difficult to make due to lack of enough studies that compared different types of contraceptives ⁷.

Conventionally, high dose estrogen preparations were known to affect metabolic parameters that include glucose intolerance, disrupted insulin secretion and increase in lipid parameters, but with new low dose preparations this effect is declined suggesting dose-dependent effect of estrogen. ⁸

The OCs have usually been shown to have adverse effects on carbohydrate metabolism that comprises of increase in both blood glucose and insulin in females maintained on it and these changes have been produced by 19-norproggestins through their action on insulin receptor level and not by estrogen component of OCs. Norgestrel, ethynodiol diacetate, and norethindrone disturb carbohydrate metabolism, but norgestrel causes the most marked

Changes ⁹. In continuation with the Spellacy, the results of the present study showed that though within the normal reference ranges, progesterone containing injectable contraceptives showed highest mean fasting blood glucose levels among different groups but still remained very close to lower limit of reference range but in contrast to Spellacy ⁹. OC containing norgestrel did not showed increased FBS.

Previous studies on high-dose oral contraceptives actually stated impaired glucose tolerance as proved by increases in fasting blood glucose and insulin levels and responses to glucose challenge. These effects have declined as hormone dosages have been lowered, and current low-dose combination contraceptives may even improve insulin sensitivity ⁸. However Diab reported increase in fasting blood sugar in females maintained on OCs and DMPA when compared to Norplant on long term use. This study concluded that in diabetics, Norplant caused minimal metabolic alterations followed by OCs whereas DMPA has unfavorable outcome ¹⁰.

The results of the present study coincide with Diab to some extent as implant and OCs both showed low FBS than DMPA and in continuation with Beasley, Estes and co workers, OCs showed below normal FBS which showed its favorable effect on carbohydrate metabolism.

Use of injectable hormonal contraceptives i.e DMPA can cause slight elevation in fasting glucose and insulin levels¹¹. Present study is in continuation with this study since it showed no drastic differences in FBS levels among DMPA and NET-EN. However these injectables in comparison with other contraceptives showed highest FBS levels but still remained in normal reference range. Glucose control has been more difficult in diabetic patients taking OCs. Overt diabetes caused by use of OCs is uncertain but development of significant changes in Carbohydrate metabolism has been shown. Reversibility of these changes after discontinuing OCs has been shown in 80% of patients. Biochemical monitoring of high risk patients is recommended³.

Based on the results of present study it is evident that OCs, implant and IUCD showed below normal levels of fasting blood sugar and hence these contraceptives are more favorable on carbohydrate metabolism than progesterone containing Injectables which showed slightly elevated FBS in comparison to other contraceptives. Thus the use of implant, IUCD and OCs in non diabetic women has minimum risks and can be safely used in this regard but caution should be taken while using progesterone only contraceptives or when there is a presence of family history, other risk factors for diabetes mellitus or diagnosed diabetes mellitus. Further studies should be conducted to eradicate any possible risk specifically in areas where these drugs are taken as an OTC drugs without monitoring.

CONCLUSION: The present study clearly suggests the safe use of hormonal and non

hormonal contraceptives for young healthy women with no other risk factors. This study however cannot justify its use in the aged female patients very near to their menopause or having certain other risk factors that predispose them to diabetes. Drug utilization reviews are also needed for over the counter use of these contraceptives which is very common in our population.

CONFLICTS OF INTEREST: There is no conflict of interest.

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