Effect of Low-Dose Oral Contraceptive Pills on Blood Glucose Level

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Synthetic steroids commonly used as oral contraceptive (OC) have been reported to alter glucose metabolism and insulin sensitivity. These alterations in glucose metabolism induced by OC seem, in part, to be related to dose and type of OC. For example, daily high dose of OC (50-150 mcg ethinyl estradiol, >1 mg progestin) has been associated with decreased glucose tolerance as evidenced by increased blood glucose and plasma insulin levels after oral glucose load, whereas low-dose monophasic or triphasic OC has been associated with lesser hyperinsulinaemia. Several studies have shown that low-dose oral contraceptive pills has almost no effect on glucose metabolism. Therefore, women who uses low-dose OC can continue using it safely for long duration. This case-control study was carried our in the Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period from July, 2005 to May, 2007. The study population consisted of 50 control and 50 cases. The mean (± SD) age were 30.78 ± 6.95 and 31.08 ± 5.82 years, weight 52.98 ± 5.73 and 52.84 ± 6.39kg, and parity 2.76 ± 1.33 and 2.86 ± 1.50 in control and case groups respectively. Comparison of blood glucose level at fasting state did not show my significant difference between control and case groups. Comparison of blood glucose level 2 hours after 75 g glucose load did not show any significant difference between control and case groups. Use of low-dose OCP containing 30 mcg EE plus 150 mcg LNG for at least 1 year did not alter fasting blood glucose level and there was also no statistically significant change in blood glucose level 2 hours after 75 g glucose load in these women.

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Key words: Oral contraceptive pill, Blood glucose

Introduction

During the past three decades, oral contraceptives have been changed substantially. These changes have occurred in the type and dose of both the oestrogen and progestogen components.[1] Since that time, major shifts have occurred in the understanding of the safety of the method of birth control.[2] A number of side-effects are encountered by the users, e.g. nausea, vomiting, dizziness, metabolic disorders, hypertension, diabetes, thromboembolism etc.

Synthetic steroids commonly used as oral contraceptive (OC) have been reported to alter glucose metabolism and insulin sensitivity.[2-5] These alterations in glucose

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metabolism induced by OC seem, in part, to be related to dose and type of OC.[6,7] For example, daily high dose of OC (50-150 mcg ethinyl estradiol, >1 mg progestin) has been associated with decreased glucose tolerance as evidenced by increased blood glucose and plasma insulin levels after oral glucose load,[3,4] whereas low-dose monophasic or triphasic OC has been associated with lesser hyperinsulinaemia.[8]

Studies of the individual steroid components suggest that the ethinyl estradiol in OC has little effect on circulating glucose or insulin levels, but the progestogen content of OC alters glucose tolerance in resting women.[7] In addition, alterations in glucose tolerance were observed depending on type of progestogen used in OC.[1,5] Studies on laboratory rodents have shown that estradiol treatment improve glucose tolerance by increasing insulin sensitivity of glucose uptake, whereas progesterone counteracts the influence of estradiol by decreasing insulin sensitivity of glucose uptake.[9]

Several studies have shown that low-dose oral contraceptive pills has almost no effect on glucose metabolism. Therefore, woman who uses low-dose OC can continue using it safely for long duration.

In our country, the contraceptive prevalence is 58 percent and oral contraceptive pills (OCP) continue to be by far the most popular method of contraception with over a quarter of currently married women (26.2% of eligible couple) using the method. There are different types of combined low-dose OCP used by the women, e.g. Shukhi, Femicon, Nordette, Marvelon etc. All these OCPs contain 30 mcg of ethinyl estradiol, but their progesterone component varies.

Persistent hyperglycaemia can have adverse multisystem health effect, so we did this work on women who are regularly taking low-dose oral contraceptive pills. The study was carried out in the Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), to ascertain the changes in blood glucose level after the used of low-dose OCP for more than 1 year duration.

Methods

Type of Study: This was a case-control study.

Place and Period Of Study: The study was carried our in the Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period from July, 2005 to May, 2007.

Study Population: The study population consisted of 50 control and 50 cases.

Selection of subjects: The study subjects were selected from the obstetric and gynaecology outpatient department of Urban Primary Healthcare Project under Dhaka City Corporation, Hzaribagh, Dhaka. Informed written consent was obtained from each of the women included in this study.

*Inclusion criteria***:**

Control -

a) Age less than 40 years
b) Practicing birth control with method other than hormonal one.

Case -

a) Age less than 40 years
b) Taking low-dose oral contraceptive pills (ethinyl estradiol 30 mcg levonorgestrel 150 mcg) for at least 1 year.

Exclusion criteria:

Control and case -

a) Personal history of diabetes mellitus
b) Family history of diabetes mellitus
c) Any medical disease, such as liver disease, cardiac disease

d) Obesity (BMI>24 kg/m^2)
e) History of taking drugs causing hyperglycaemia or hypoglycaemia e.g. Sympathomimetic drugs etc.

Collection of blood sample:
With all aseptic precautions, one sample of 3 ml venous blood was collected from the subject after an 8-10 hours fasting and one sample of 3 ml of venous blood 2 hours after 75g glucose was also taken. After blood collection, these were immediately brought to Department of Biochemistry, BSMMU, and plasma was separated by contrifugation (10 minutes at 3000 rpm at 20^0C). These plasma samples then analyzed for glucose by glucose oxidase method.

Data Collection:
Data from medical history, physical examination and laboratory tests were recorded in a predesigned data collection sheet.

Data Processing and Analysis:
The data were processed by computer based software, Statistical Package for Social Science (SPSS). Statistical tests, such as Chi-square test, paired and unpaired Student's 't' test were used. P value < 0.05 was taken as minimum level of significance.

Results
The mean (± SD) age were 30.78 ± 6.95 and 31.08 ± 5.82 years, weight 52.98 ± 5.73 and 52.84 ± 6.39kg, and parity 2.76 ± 1.33 and 2.86 ± 1.50 in control and case groups respectively (Table I).

Comparison of blood glucose level at fasting state did not show any significant difference between control and case groups (Table II).

Comparison of blood glucose level 2 hours after 75 g glucose load did not show any significant difference between control and case groups (Table III).

All 50 (100%) control and 50 (100%) case subjects had normal blood glucose level at fasting state (Table IV).

Blood glucose level 2 hours after 75 g glucose load was raised in 3 (6%) control and 4 (8%) case subjects (Table V).

Table I: Age, weight and parity of the study subjects

Parameters	Control (n = 50)	Case (n = 50)	t value	p value
Age (years)				
Mean ± SD	30.78 ± 6.95	31.08 ± 5.82	-0.234	>0.50^{ns}
Range	20-40	20-40		
Weight (kg)				
Mean ± SD	52.98 ± 5.73	52.84 ± 6.39	+0.115	>0.50^{ns}
Range	43-68	40-66		
Parity				
Mean ± SD	2.76 ± 1.33	2.86 ± 1.50	-0.353	>0.50^{ns}
Range	1-6	1-7		

Unpaired Student's 't' test, ns = Not significant

Table II. Fasting blood glucose level

Blood glucose level (mmol/L)	Control (n=50)	Case (n=50)	t value	P value (unpaired)
Mean ± SD Range	4.67 ± 0.68 3.5-6.1	4.58 ± 0.59 3.7-5.8	+0.657	>0.50^{ns}

Unpaired Student's 't' test, ns = Not significant

Table III: Blood glucose level 2 hours after 75 g glucose load

Blood glucose level (mmol/L)	Control (n=50)	Case (n=50)	t value	P value (unpaired)
Mean ± SD Range	6.39 ± 0.74 5.0-8.1	6.27 ± 1.02 4.9-10.8	+0.684	>0.10^{ns}

Unpaired Student's 't' test, ns = Not significant

Table IV: Status of fasting blood glucose level

Blood glucose level (mmol/L)	Control (n=50) N. (%)	Case (n=50) No. (%)	P value
Normal (≤ 6.1) Raised (>6.1)	50 (100.0) 0	50 (100.0) 0	

Table V: Status of blood glucose level 2 hours after 75 g glucose

Blood glucose level (mmol/L)	Control (n=50) No. (%)	Case (n=50) No. (%)	P value
Normal(≤ 7.8) Raised (>7.8)	47 (94.0) 3 (6.0)	46 (92.0) 4 (8.0)	> 0.50^{ns}

Chi- square test, ns = Not significant

Discussion

The present study was conducted on Bangladeshi women who used oral contraceptive pills (OCPs) for at least 1 year (1-10 years). The main aim of the study was to compare the changes of fasting and 2 hours after 75 g glucose load on blood glucose level between healthy women who did not use oral pills or other hormonal contraceptives and women using low-dose oral pills containing 30 mcg ethinyl-oestradiol (EE) and 150 mcg levonorgestrel (LNG) for at least 1 year.

We did not find any difference in age, weight and parity between control and case groups. The changes in blood glucose levels of the case group was compared with the control group. It was shown that there was no significant change in blood glucose level in fasting state and 2 hours after 75 g glucose load in case group compared to control.

It was found that the subjects of both control and case groups belonged to lower and middle socioeconomic classes. The women from higher socioeconomical class usually did not

attend Urban Primary Helath Care Project (UPHCP) or Bangladesh Association for prevention of Septic Abortion (BAPSA) centre.

It is said that OCPs do not increase the risk of overt diabetes.[10] Estimates on the percentages of oral contraceptive users demonstrated that impaired glucose tolerance very from 4-16 percent to 15-40 percent.[10,11] Oestrogen did not significantly affect carbohydrate metabolism, rather progestin exerted the main effect.[11,12] Changes in glucose tolerance are dose related[10,13] and discontinuing oral contraceptive causes glucose tolerance to return quickly to normal.[13]

In a study of Godsland et al.,[14] to see the metabolic effect of long-term oral contraceptive use in 35-years-old women showed that no potentially adverse interaction existed between user's age and duration of OC use. User's age did not adversely affect oral glucose tolerance, glucose and insulin responses. So, result of studies done at Wynn Institute suggests that 35-year-old women may indeed be able to take current OC formulations as long as they regularly visit a health professional and have their blood glucose and serum lipid levels measured routinely.

A study carried out by Krauss and Burkman[15] to see the metabolic impact of oral contraceptives showed that the changes in carbohydrate metabolism are not as great in women using the lower dose OCs or formulations using the new progestins. Specially, OC use can lead to increased level of plasma insulin, insulin resistance and relative glucose intolerance. A curve analysis of glucose tolerance test remarks this intolerance effects of OCs.

A randomized cross-over comparative study carried out by Kuhl et al.,[16] to see the effect of two low-dose oral contraceptive containing EE and DSG/LNG on glucose tolerance showed that there was a significant increase (13%) in basal glucose level during treatment cycle with both OCs, but no change in glucose tolerance.

Wynn et al.,[1] examined the effect of six different combined oral contraceptive in terms of types and doses on glucose metabolism and observed differences in metabolic effects between combined OCs. Wynn et al.,[1] reported that glucose tolerance deteriorated in all OC groups containting oestrogen progestogens (nortesterone-derivatives) or the gonane norgestrel but was unaltered by OC containing a pregnane progestogen (derived from progesterone). The OCs containing 75 μg or more oestrogen combined with an estrane progestogen caused the greatest deterioration in glucose tolerance associated with impaired insulin secretion. Lowering of the oestrogen dose to 50 mcg without altering the progestogen content of the OCs resulted in less deterioration of glucose tolerance and increased insulin secretion. Those results suggested the importance of the dose of oestrogen and type of progestogen.

The relevant studies conducted in this country and abroad were thoroughly analyzed to draw a conclusion in this study regarding the effect of OCPs on plasma glucose level.

Conclusion

Use of low-dose OCP containing 30 mcg EE plus 150 mcg LNG for at least 1 year did not alter fasting blood glucose level. There was also no statistically significant change in blood glucose level 2 hours after 75 g glucose load in these women.

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