

ORAL CONTRACEPTIVE USE AND GLUCOSE METABOLISM

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ABSTRACT

This is a prospective study done at the family planning clinic of Basrah Maternity and Child Hospital from February till September 2002. The objective was to determine the effect of combined oral contraceptive pills on glucose metabolism. The results showed that there is significant elevation in the HbA1C ($P < 0.001$) readings after 3 months of using combined oral contraceptive pills and there is no significant changes in random blood sugar reading after 3 months of combined oral contraceptive pills using. There is highly significant change in HbA1C readings in association with age between 31-34 years, body mass index $> 25 \text{ kg/m}^2$, parity ≥ 5 and low social class.

INTRODUCTION

Systemic contraception, operating through its effect on the endocrine system, was first introduced in 1956 in form of synthetic estrogen and progesterone combined pills^[1], the history of development has been progressive reduction in the dosage to that is now properly the lowest dosage compatible with therapeutic effect that is, to inhibit ovulation^[2]. The combined oral contraceptive pills are available as monophasic preparation^[3], acts by inhibition of ovulation and suppression of leutinizing hormone surge^[2,4], beside its action on cervical mucus^[5], and alteration of endometrium by decreasing glycogen production^[6]. Combined oral contraceptive pills effect carbohydrate metabolism by increase glucose level and suppress the insulin response^[7], those changes are usually reversible and rarely occur with low progestin dose pills^[8]. Combined oral contraceptive pills can be prescribed for women who have had an elevated blood glucose test but are not currently diabetic^[9]. Combined oral contraceptive pills are not recommended for insulin depended diabetes with vascular changes because combined oral contraceptive pills may increase there risk of thrombotic events^[10]. Glycosylated haemoglobin (HbA1C) is usually used as a supplementary to blood glucose estimation to monitor to over all degree of diabetic control achieved, and its known that its formation depend on mean blood glucose level^[11]. Therefore HbA1C has been a successfully used for monitoring diabetic patients assuming a normal red cell survival^[12]. Glycation occurs gradually while the erythrocytes are circulating normally for about 2-3 months, recurring early in their development and remain constant until their death, a reason

why HbA1C has been used for monitoring of diabetic patient as an index of long term control over the previous 6-8 weeks^[13]. In this study, identified the effects of combined oral contraceptive pills on glucose metabolism, through measurement of HbA1C and random blood sugar in relation of different characteristics of the clients.

PATIENTS AND METHODS

A prospective study was carried out in Basrah Maternity and Child Hospital, from February till September 2002. The data were collected from clients attending the family planning clinic. The study including clients who use combined oral contraceptive pills for the first time. Blood samples for HbA1C and random blood sugar were taken. The clients were advised to take their pills regularly for three months, then 2nd blood samples for HbA1C and random blood sugar were taken and analyzed in the hospital's laboratory, the normal value for HbA1C was 3-6%, random blood sugar above 200 mg/dl is diagnostic for diabetes mellitus (D.M), less than 140 mg/dl is normal, between 140-200 mg/dl require Glucose Tolerance Test^[14,15]. The questionnaires were used for the details regarding type of combined oral contraceptive, family history of D.M, and history of gestational D.M, woman's age, parity and socio economic status. The first samples were taken from 97 clients but missing of 33 clients, most of them living in areas far away from hospital. Statistical analysis was done by paired t-test which analyses two reading for some individual.

RESULTS

Prospective study in family planning clinic in Basrah Maternity and Child Hospital.

Investigations were taken for 64 clients (RBS+HbA1C) 2 times 3 months apart before and after using of combined oral contraceptive. Table-1 shows the demographic characteristics of client. Patients age between 17-30 years (54.6%). 44 patients from study group use low dose contraceptive pills (68%). 53% of our patients have Body Mass Index (BMI) ≤ 25

kg/m². 30 patients (47%) lactating their babies. Only 5 patients (7.8%) have family history for D.M. Most of our patients were having children < 5 (67%). No history of gestational diabetes in our clients. No any client was smoker or taking any medication. Our clients were in the primary and secondary levels (26%,34.3%) respectively.

Table 1. *Demographic characteristics of client.*

Characteristics	Subgroup	No.	%
Age	17-30	35	54.6
	31-43	29	45.4
Type of pills	High dose	20	31.2
	Low dose	44	68.8
Body mass index	≤ 25	34	53
	> 25	30	47
Lactation	+ Ve	30	47
	- Ve	34	53
Family history of D.M.	+ Ve	5	7.8
	- Ve	59	92.2
Parity	< 5	43	67
	≥ 5	21	33
Social class (level of education)	Primate	16	25
	Primary	17	26
	Secondary	22	34.3
	High	9	14.7

* - ve: Negative *+ ve: Positive

There is significant change reading of Hb A1 after 3 months (P<0.001) (Table-2). There is no significant change in the random blood sugar reading after 3 months.

Table 2. *Measurement of HbA1C and RBS 3 months apart for all clients (before and after COC use).*

Characteristics	Mean (1)	Mean (2) after 3 months	p-value	Significant or not
HbA1C	3.9±0.52	4.1±0.42	0.001	HS
RBS	88±16.97	88.3±14.00	0.896	NS

* RBS: Random blood sugar

Table-3, shows R.B.S. readings 3 months apart according to selected characteristics, which reveals no significant change with all characteristics.

Table 3. *R.BI Sugar readings 3 months apart according to selective characteristics (before and after COC use).*

Characteristics	Subgroup	R.BI sugar ((1 st))	R.BI sugar ((2 nd))	P-Value	Significant or not
Pills	Low dose	86.6±16.72	88.02±15.04	0.597	NS
	High dose	91.1±17.54	88.9±11.73	0.618	NS
Age	17-30 years	86.2± 16.1	90.14±14.37	0.721	NS
	31-43 years	90.1±18.3	85.1±12.9	0.642	NS
BMI	≤ 25 kg/m ²	82.76±15.89	87.88± 15.4	0.104	NS
	> 25 kg/m ²	93.93±1.42	88.77± 12.4	0.115	NS
Family history of D.M	- Ve	87.12±16.53	87.8±13.48	0.525	NS
	+ Ve	98.4±20.6	99.2±16.22	0.668	NS
Parity	≥ 5	86.81±17.2	89.0± 15.0	0.341	NS
	< 5	90.42±16.45	86.71±11.67	0.397	NS
Social class (level of education)	Primate	87±14.17	88.12±14.35	0.771	NS
	Primary	88.47±18.9	89.00±15.5	0.967	NS
	Secondary	84.86±15.04	85±13.87	0.799	NS
	High	96.55±21.49	93.22±11.28	0.679	NS

Table-4, shows HbA1C readings 3 months apart according to selected characteristics, which reveals a significant result regarding using of pills whether high dose or low dose. Highly significant result regarding age subgroup between 31-34 years, and just significant results regarding age group between 17-30 years. Regarding BMI, highly significant result for those who have BMI >25k/m² but only significant result for those who have BMI ≤ 25 Kg/m². There's no difference whether clients

were having or not family history of D.M., both of them have significant results. Regarding parity, clients who have ≥5 children, they have highly significant result while those who have <5 children just significant result. For social class (*level of education*), clients who are in the primate and primary levels have highly significant result, while those who are in the secondary and higher levels just significant result.

Table 4. *HbA1C reading 3 months apart according to selective characteristics (Before and after COC use).*

Characteristics	Subgroup	((1 st)) reading	((2 nd)) reading	P-Value	Significant or not
Pills	Low dose	3.8 ± 0.56	4.1 ± 0.35	0.02	S
	High dose	4.0±0.41	4.2±0.53	0.04	S
Age	17-30 years	3.8± 0.42	4.1±0.54	0.02	S
	31-43 years	4.2±0.17	4.5±0.52	0.004	HS
BMI	≤ 25 kg/m ²	3.8±0.58	4.1± 0.37	0.03	S
	> 25 kg/m ²	4.1±0.43	4.22±0.47	0.001	HS
Family history of D.M	- Ve	3.9±0.53	4.1 ±0.43	0.03	S
	+ Ve	4.1± 0.21	4.1± 0.18	0.04	S
Parity	≥ 5	3.8±0.5	4.1± 0.43	0.004	HS
	< 5	4.02±0.11	4.33± 0.33	0.037	S
Social class (level of education)	Primate	3.8±0.57	4.3 ±0.52	0.004	HS
	Primary	3.8±0.51	4.2± 0.39	0.003	HS
	Secondary	4.0±0.52	4.1± 0.36	0.41	NS
	High	4.0±0.43	3.97± 0.31	0.62	NS

DISCUSSION

There is change in the HbA1C after 3 months of taking combined oral contraceptive pills which is statistically significant ($P=0.001$), but they remain within normal range which is between 3-6% that Hb1C mean after 3 months (4.1) and no any clinical evidence of diabetes, these results are reassuring, therefore the client can continue to take combined oral contraceptive pill until HbA1C reach 7%^[16]. There's highly significant results in regarding to the age between 31-43, for these with BMI > 25kg/m², for clients who have ≥ 5 children and for clients in the low social class, so these clients require follow up while taking combined oral contraceptive pills to detect further changes. Regarding random blood sugar readings which reveal no significant changes and all reading below 140 mg/dl which is also reassuring that there's no need for glucose tolerance test. These results are similar to the results obtained by Simon and Senan, 1990 who reveal significant change in the glucose measurement after 6 months use of combined contraceptive pills with ($P<0.001$)^[17], in contrast to Godstand^[18], who reveal a significant change in glucose metabolism and the magnitude of these changes may depend on the dose progesterone, this could be due to small sample size and restricted types of pills that had been used in the present study. The clients used combined oral contraceptive pills for one year reveal also a significant change associated with the age more than 20 years and restrict the use of pills for older age clients, which is in agreement with study result^[19]. Previous study^[20] 1993 proved that significant changes in glucose tolerance but this change return to the pretreatment level after its stop age, which is reassuring point for further follow up. Regular measurement of blood glucose level in the users of combined oral contraceptive pills and proper follow up to the clients with age between 31-43 years BMI >25, parity ≥ 5 and low social class can decrease the adverse effect in spite in this study it need repeat measurement after stoppage of pills to show if these changes reversible or not.

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