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CARBOHYDRATE METABOLISM AFTER ONE YEAR OF USING A GESTODENE CONTAINING MONOPHASIC ORAL CONTRACEPTIVE

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Abstract: *Aim: To prospectively evaluate the effects of an oral contraceptive containing the progestin gestodene on carbohydrate metabolism in ordinary Turkish women*

Material / Method: Carbohydrate metabolism was prospectively evaluated in 53 normal women prior to and during their use of monophasic oral contraceptive containing the progestin gestodene plus ethinyl estradiol for one year. The women had a two hour oral glucose tolerance test using 75 gram glucose load, measuring serum glucose and insulin level, performed at the beginning of the contraceptive therapy and after one year.

Results: The results demonstrate no significant changes in either of carbohydrate metabolic indices between the two tests.

Conclusion: The progestin containing contraceptive pill can be safely used in consideration of the carbohydrate metabolism.

Key words: *Blood glucose, Carbohydrates, Oral Contraceptives, Insulin.*

INTRODUCTION:

One major concern about oral contraceptive use has been the secondary effects of the steroids on metabolic indices of the user. Studies have previously shown that the progestin component of these drugs can affect carbohydrate metabolism and produce

an elevation of both serum glucose and insulin levels (1). To reduce potentially adverse side effects, new progestin containing contraceptive market has expanded over the passing time. This study was designed to prospectively evaluate the effect of a gestodene-containing oral contraceptive on the carbohydrate metabolism over one year of combined drug use, while measuring both serum glucose and insulin levels during an oral glucose tolerance test.

MATERIAL AND METHOD:

The subjects consisted of 53 volunteers using oral contraceptives. All were more than one year postpartum or had not used oral contraceptives for that length of time. After the study was explained, each woman gave their informed consent. The study was conducted with the approval of the ethical study board of Zeynep Kamil Hospital. Each subject provided a medical history and underwent a thorough physical examination; which included a pelvic examination and pap smear. No significant pathological states were found. Before initiating the use of the contraceptives, the women had a control glucose tolerance test. They were instructed to eat a high - carbohydrate diet for 3 days before the test and then to report to the laborotory between 0800-0900 hours after fasting for more than two hours; their weights were recorded and they were seated for the duration of the test. An antecubital venous blood sample was drawn and they were asked to drink a flavoured solution containing 75 gr of glucose . The blood was placed in tubes for glucose and insulin analysis respectively, allowed to clot, centrifuged and the serum was separated. The samples for glucose analysis were stored at 4°C and the samples for insulin analysis analysis were stored at -20°C.Repeat venous blood samples were drawn after 0.5, 1, 2, and 3 hours .Following completion of the test, each women was given her package of steroid contraceptives and instructed concerning their use. The monophasic oral contraceptive (had 21 active tablets per month and each contained 75mg gestodene and 30mg ethinyl estradiol.The women were seen periodically afterwards to replace pill packs and to answer questions. In the every third month of use each subject served as her own control. In the end of one year, all women returned and the last week of the pill cycle,they had an identical oral glucose tolerance test.

The serum samples were later analyzed in duplicate for their glucose content using a Beckman Glucose Analyzer 2.The inter-assay and intra-assay precision had a standart deviation less than 3.0 and 2.5 mg/dl respectively. An aliquot of the samples were also analyzed in duplicate for its insulin content using radioimmunoassay (I^{125} Insulin-Kits purcharged from diagnostic Products corporation).All samples from the control and three months tests on one subject were analyzed by the Beckman Gamma 5500B Counter,which were later transported to the Beckman Data Capture program and were analyzed by Beckman Immunofit EIA/RIA program ,using a logit-log curve fit. The inter-assay and intra-assay coefficients of variation did not exceed 10% in the 5-200 unit/ml range,according to the precision profiles (2).

The data were analyzed for the means and standart errors of the means. The changes in values between the control and one year test were compared with paired student's t-tests. The propability values were taken from two - tailed tables and only values $p<0.05$ were considered significant.

RESULTS:

The subjects presented with characteristics similar to those in most contraceptive programs, with a mean age 27.4 (± 0.2 years). The group mean weight was 63 ± 5.6 kg. After one year of drug usage it was not significantly different (mean 64.6 ± 5.7 kg).

The glucose results from the two tests are given in Table 1. None of the values changed significantly between the two tests in plasma glucose results.

The statistical studies of the insulin values are provided in Table 2. Although the mean values are elevated at the twelve month test,none of the canges were statistically significant.

DISCUSSION:

Oral contraceptives were approved for use in the USA in 1960(2), and for use in the Turkey in 1965(3) and since then have been a major method of family planning for millions of women. A multitude of studies over the past thirty years have evaluated their efficacy, side-effect and systemic effects in users were steroid-specific and dose dependent(3). For example, venous thrombosis has been found to be mainly an estrogen effect and altered carbohydrate metabolism to be a progestin effect (4). The pharmaceutical industry modifed the drugs to improve their safety. Two major modifications have been the reduction in total steroid dosage the development and use of new steroids. As the new formulation became available they too needed testing to determine whether their contraceptive efficacy, control of cycle bleeding, or prevalence of adverse effects were reduced (5, 6).

The effects of a new contraceptive containing the progestin gestodene on carbohydrate metabolism in women were studied. Gestodene is similar chemically to levonorgestrel , except for having a double bond at the carbon fiftheen position. Gestodene has been shown to bind strogly to both androgen and progestin receptors and to have little affinity for estrogen receptors (7,8).The results showed no statistically significant changes concerning the carbohydrate metabolic status of the subjects after one year use of the pill.

This study showed the safe use and relatively acceptable side- effects of a new contraceptive containing progestin; gestodene on carbohyrate metabolism in normal Turkish women

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	CONTROL					12 MONTH				
Time in hours	Fasting	0.5	1	1.5	2	Fasting	0.5	1	1.5	2
Mean	76.7	125.9	108.5	89.9	68.3	78.9	127.8	120.2	99.1	74.4
SEM	2.3	5.5	7.2	4.9	3.1	2.5	6.3	7.9	4.7	6.0
T	*0.69*	*0.42*	*1.34*	*1.35*	*0.84*					

*VALUES**

**Probability.*

Table 1. Serum glucose values in mg/dl for the control and 12 month oral glucose tolerance test in normal women using a gestodene containing oral contraceptive (n=53)

	CONTROL					12 MONTH				
Time in hours	Fasting	0.5	1	1.5	2	Fasting	0.5	1	1.5	2
Mean	7.4	58.4	57.9	48.7	16.2	8.8	67.2	73.6	56.9	31.7
SEM	0.8	5.9	5.8	6.0	2.9	0.9	6.2	8.7	7.5	8.7
T	1.46	1.39	1.82	1.06	2.05					
Values*										

**Probability*

Table 2. Serum insulin values in munits/ml for the control and 12 month oral glucose tolerance test in normal women using a gestodene containing oral contraceptive (n =53)

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