İNSÜLİN'E BAĞIMLI OLMAYAN DİABETES MELLİTUS (NIDDM)'TA PLAZMA SEKS HORMON BAĞLAYAN GLOBULIN (SHBG), DHEA-SO4, ANDROSTENEDIONE AND 17-alpha HIDROXYPROGESTERONE DÜZEYLERİ.

PLASMA LEVELS OF SEX HORMONE BINDING GLOBULIN (SHBG), DHEA-SO4, ANDROSTENEDIONE AND 17-alpha HIDROXYPROGESTERONE IN NIDDM.*

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Özet

İnsülin'e bağımlı olmayan diabetes mellitus (NIDDM)' un plazma androjen düzeylerinin yüksekliği ile birlikte olduğu bilinmektedir. Çalışmamızda 26 NIDDM vakalasında plazma seks hormonu bağlayan globulin (SHBG), dehydroepiandrosterone sulphate (DHEA-SO4), androstenedione (Δ4), total testosterone (T), free testosterone (FT) and 17-alpha hydroxyprogesterone (17α-OHP) düzeylerini 10 sağlıklı kontrol vakası ile karşılaştırdık ve bu hormonların düzeyleri ile plazma glukoz ve glycohemoglobin (Hb A1c).düzeyleri arasındaki ilişkiyi inceledik. NIDDM grubunda, plazma glukoz, Hb A1c and SHBG, DHEA-SO4, Δ 4, T, FT ve 17α-OHP düzeylerini sırası ile ; 13.89 ± 3.70 mmol / L, 11.91 ± 6.16 per cent, 68.04 ± 46.99 nmol / L, 0.31 ± 0.12 nmol / L, 4.85 ± 4.57 nmol / L, 391.42 ± 325.62 nmol / L, 21.13 ± 2.98 pmol / L ve 2.17 ± 0.60 nmol / L bulduk. Kontrol grubunda aynı parametreleri sırasıyla ; 4.93 ± 0.37 mmol / L, 4.59 ± 1.41 per cent, 61.55 ± 17.26 nmol/L, 0.23 ± 0.03 nmol / L, 9.18 ± 1.36 nmol / L, 905.82 ± 146.09 nmol / L, 14.08 ± 3.78 pmol / L ve 1.24 ± 0.66 nmol / L olarak tesbit ettik. NIDDM grbunda glukoz ve Hb A1c düzeyleri, kontrol grubundan daha yüksek olarak bulundu ($p < 0.0001$ ve $p < 0.0005$). Buna karşılık, plazma SHBG, DHEA-SO4, FT ve 17α-OHP düzeyleri heriki grupta aynı idi ($p > 0.5$). Bunun yanısıra, NIDDM grubunda plazma Δ4 ve T düzeyleri kontrol grubundan daha düşüktü ($p < 0.0005$, ve $p < 0.01$). NIDDM grubunda, plazma glukoz ve SHBG düzeyleri arasında negatif korelasyon tesbit ettik ($r = - 0.226$). Benzeri olarak , plazma Hb A1c ve SHBG ($r = - 0.266$), DHEA-SO4 ($r = - 0.192$), Δ4 ($r = - 0.302$), 17α-OHP ($r = - 0.154$), T ($r = - 0.231$), ve FT ($r = - 0.33$) düzeyleri arasında negatif korelasyon tesbit ettik.

Anahtar kelimeler : *Androjenler, SHBG, NIDDM*

Summary

It has been supported that non-insulin dependent diabetes mellitus (NIDDM) is associated with hyperandrogenemia. We evaluated the plasma levels of sex hormone-binding globulin (SHBG), dehydroepiandrosterone sulphate (DHEA-SO4), androstenedione (Δ4), total testosterone (T), free testosterone (FT) and 17-alpha hydroxyprogesterone (17α-OHP) and compared with plasma levels of glucose and glycohemoglobin (Hb A1c). Twentysix patients with NIDDM and ten healthy control subjects were included in our prospective study. In the NIDDM groups, plasma levels of glucose, Hb A1c and SHBG, DHEA-SO4, Δ4, T, FT and 17α-OHP were 13.89 ± 3.70 mmol / L, 11.91 ± 6.16 per cent, 68.04 ± 46.99 nmol / L, 0.31 ± 0.12 nmol / L, 4.85 ± 4.57 nmol / L, 391.42 ± 325.62 nmol / L, 21.13 ± 2.98 pmol / L and 2.17 ± 0.60 nmol / L, respectively. In the control group, above mentioned parameters were 4.93 ± 0.37 mmol / L, 4.59 ± 1.41 per cent, 61.55 ± 17.26 nmol/L, 0.23 ± 0.03 nmol / L, 9.18 ± 1.36 nmol / L, 905.82 ± 146.09 nmol / L, 14.08 ± 3.78 pmol / L and 1.24 ± 0.66 nmol / L, respectively. In the NIDDM group plasma levels of glucose and Hb A1c were higher than those of control group ($t = 7.56$, $p < 0.0001$ and $t = 3.68$, $p < 0.0005$). However, plasma levels of SHBG, DHEA-SO4, FT and 17α-OHP were similar in both groups ($p > 0.5$). In the NIDDM group, however, plasma levels of Δ4 and T were lower than those of control group ($t = - 3.03$, $p < 0.0005$, $t = 2.50$, $p < 0.01$). In the NIDDM group, a negative correlation was detected between plasma levels of glucose and SHBG ($r = - 0.226$). Similarly, a negative correlation was detected among plasma levels of Hb A1c and SHBG ($r = - 0.266$), DHEA-SO4 ($r = - 0.192$), Δ4 ($r = - 0.302$), 17α-OHP ($r = - 0.154$), T ($r = - 0.231$), and FT ($r = - 0.33$). In summary, we detected a relationship between the glucose levels and SHBG, and glucose levels and androgens in the NIDDM.

Key words : *Androgens, SHBG, Diabetes mellitus.*

Table 1. *Comparison of Plasma Levels of Glucose, Hb A1c and Androgens in the NIDDM Group.*

	NIDDM groups	Control groups	p values
Glucose (mmol / L)	13.89 ± 3.70	4.93 ± 0.37	< 0.0001
Hb A1c (%)	11.91 ± 6.16	4.59 ± 1.41	< 0.0001
SHBG (nmol / L)	68.04 ± 46.99	61.55 ± 17.26	> 0.5
DHEA-SO4 (nmol / L)	0.31 ± 0.12	0.23 ± 0.03	> 0.5
Δ4 (nmol / L)	4.85 ± 4.57	9.18 ± 1.36	< 0.0005
17α-OHP (nmol / L)	2.17 ± 0.60	1.24 ± 0.66	> 0.5
T (nmol / L)	391.42 ± 325.62	905.82 ± 146.09	< 0.01
FT (pmol / L)	21.13 ± 2.98	14.08 ± 3.78	> 0.5

Introduction

Adults with non-insulin dependent diabetes mellitus (NIDDM) have dyslipidemia and an increased risk for cardiovascular disease, some of which could be mediated by altered endogenous sex hormone levels (1,2). Also, the clinical significance of lower androgen levels in the patients with NIDDM is unknown (1). It well know that android obesity nearly associate NIDDM. Androstenedione and total testosteron levels are commonly elevated whereas SHBG is reduced in the patients with android obesity (2,4). Calculation of the ratio of waist to hip girth has been shown to be an important predictor of alternations in the metabolic profile, the incidence of cerebrovascular events, ischaemic heart disease and diabetes mellitus, especially NIDDM (4). It was supported that NIDDM which is associated with hyperandrogenemia is called as Sendrom X (2). We evaluated the plasma levels of SHBG, DHEA-SO4, Δ4 and 17α-OHP, and compared the results with plasma levels of glucose and glycohemoglobin (Hb A1c) in the patients with NIDDM.

Table 2. *Evaluation of Correlation of All Parameters in the NIDDM Group.*

	Glucose levels	Hb A1c levels
SHBG	r = - 0.226	r = - 0.266
	p < 0.01	p < 0.01
DHEA-SO4	r = 0.180	r = - 0.192
	p > 0.5	p < 0.01
Δ4	r = - 0.052	r = - 0.302
	p > 0.5	p < 0.01
17α-OHP	r = 0.013	r = - 0.154
	p > 0.5	p < 0.01
T	r = 0.218	r = - 0.231
	p > 0.5	p < 0.01
FT	r = 0.073	r = - 0.33
	p > 0.5	p < 0.01

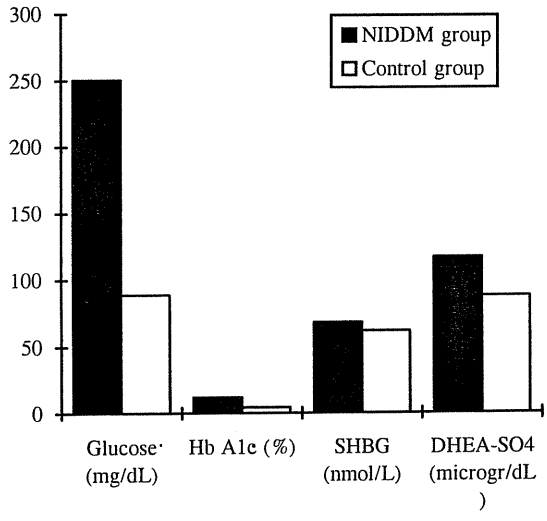
Materials and Methods

Twentysix patients with NIDDM and ten healthy control subjects were included in our prospective study. All of the patients with NIDDM and control subjects were men. In both groups, plasma levels of glucose (Glu-kinase, cat. no : 81795, Sclavo Diagnostics, Italy.) were detected by enzymatic U.V. method, and plasma levels of Hb A1c (Glyc-Affin GHb, code SG-6200, Isolab Inc., USA.) were detected by affinity cromatography method. SHBG, DHEA-SO4, Δ4, T, FT and 17α-OHP were detected by RIA method (DPC, USA.). Student's t-test was used for evaluation the difference among androgen levels, SHBG levels and biochemical parameters. Linear correlation was used for evaluation the relationship among androgen levels, SHBG levels and biochemical parameters. All of the calculations were applied on IBM computer by GB-STAT, Version 3.0 programme (3).

Results

Twentysix patients with NIDDM and ten healthy control subjects were included in the study. In the NIDDM group, plasma levels of glucose, Hb A1c, SHBG, DHEA-SO4, Δ4, T, FT and 17α-OHP were 13.89 ± 3.70 mmol / L, 11.91 ± 6.16 per cent, 68.04 ± 46.99 nmol/L, 0.31 ± 0.12 nmol / L, 4.85 ± 4.57 nmol / L, 391.42 ± 325.62 nmol / L, 21.13 ± 2.98 pmol / L and 2.17 ± 0.60 nmol / L, respectively. In the control group, above mentioned parameters were 4.93 ± 0.37 mmol / L, 4.59 ± 1.41 per cent, 61.55 ± 17.26 nmol/L, 0.23 ± 0.03 nmol / L, 9.18 ± 1.36 nmol / L, 905.82 ± 146.09 nmol / L, 14.08 ± 3.78 pmol / L and 1.24 ± 0.66 nmol / L, respectively. In the NIDDM group plasma levels of glucose and Hb A1c were higher than those of control group ($t = 7.56$, $p < 0.0001$, $t = 3.68$, $p < 0.0005$) (Table-1) (Figure-1). However, plasma levels of SHBG, DHEA-SO4, FT and 17α-OHP was not different in both groups ($p > 0.5$) (Table-1) (Figure-2 and 3). In the NIDDM group, plasma levels of Δ4 and T were lower than those of control group ($t = - 3.03$, $p < 0.0005$, $t = 2.50$, $p < 0.01$) (Table-1) (Figure-2 and 3). In the NIDDM group, a negative correlation was detected between plasma levels of glucose and SHBG ($r = - 0.226$, $p < 0.01$) (Table-2) .Similarly, a negative correlation was detected among plasma levels of Hb A1c and SHBG ($r=-0.266$, $p<0.01$), DHEA-SO4 ($r=-0.192$, $p < 0.01$), Δ4 ($r = - 0.302$, $p<0.01$) and 17 α-OHP ($r = - 0.154$, $p< 0.01$), T ($r=-0.231$, $p<0.01$), and FT ($r=-0.33$, $p<0.01$) (Table-2).

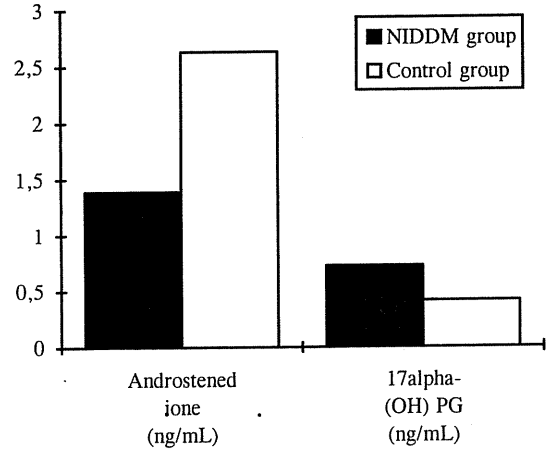
Figure 1. *Comparison of Plasma Levels of Glucose and Hb A1c in the NIDDM and Control Group.*



Discussion

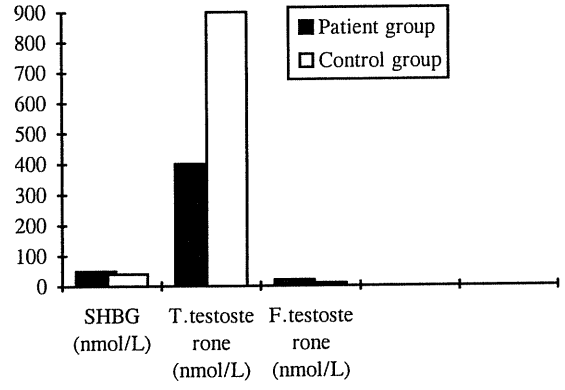
The lower androgen levels can be explained by other variables associated with sex hormone levels, including obesity, fat distribution, cigarette smoking, or alcohol intake (1,2,4). It is possible that more precise estimates of intra-abdominal fat would explain more of the association between diabetes and sex hormone levels. Men with central or upper body obesity (android obesity) often have abnormal carbohydrate tolerance, hyperinsulinemia, insulin resistance, and lower levels of male sex hormones (2,4). According to our opinion, NIDDM should be investigate together with insulin resistance syndromes. Significant associations are seen between excess body fat and hyperandrogenism.

Figure 2. *Comparison of Plasma Levels of DHEA-SO4, Androstenedione and 17 alpha- (OH) PG in the NIDDM and Control Group.*



The topography of fat distribution is correlated with these changes (5,6).In NIDDM group, we detected that plasma levels of Δ4 and T were lower than those of control group. Other androgenic hormone levels were similar in both groups. Physiologically, Δ4 is aromatized to estrogens and testosterone, and this aromatization may occur in the fat tissue. We did not detect obesity parameters in the NIDDM and control subjects. But, this aromatization may elevate in the fat tissue of these patients. Ewans et al (6) have shown body weight and waist to hip girth ratio are inversely correlated with SHBG levels and directly correlated with FT concentrations. Some authors have described a higher production rate from the adrenal cortex and ovaries and increased metabolic clearance of testosterone and dihydrotestosterone.The clearance of testosterone increases as SHBG decreases, as a consequence of an increased fraction of free testosterone (7). SHBG is a circulating globulin produced by the liver which binds in high affinity but low capacity to many of the circulating sex hormones.

Figure 3. *Comparison of plasma Levels Of SHBG, Total Testosterone and Free Testosterone in The NIDDM and Control Group.*



Alterations in SHBG levels have a profound impact on the metabolism and action of bound steroids. The mechanism of decreasing SHBG levels is unclear (4). Upper body obesity is characterized by higher T levels and reduced SHBG levels. Ewans et al (6) have reported that there is a lineer correlation between SHBG levels and increased waist to hip girth ratio. We detected a negative correlation between plasma levels of glucose and SHBG. Similarly, there is an inverse correlation between plasma levels of glycohemoglobin and SHBG. However, we did not detect any correlation between other androgen levels and glucose. We detected a correlation between plasma levels of Hb A1c and androgens. It has been suggested that there is a better correlation between plasma levels of androgen and glycolysed hemoglobin than that of

between plasma levels of androgen and glucose in the patients with NIDDM (4). In summary, we detected a significant relationship between plasma levels of glyco- hemoglobin and androgens in the patients with NIDDM. These results are most probably due to relationship with distribution of fat tissue and aromatization of steroid hormones in this fat tissue. Plasma levels of androgenic hormones is markedly changed in the patients with NIDDM. Future studies are necessary about this matter.

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