Serum Cortisol in Type 1 Diabetic females

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Abstract

Background: Diabetes mellitus is regarded as one of the commonest metabolic disorder all over the world. It can cause various endocrine disorders by affecting the secretion, metabolism, clearance or bioavailability of hormones. **Aim of study:** This study is to answer if type1 diabetes changes cortisol level in female diabetic patients who have different degrees of glycemic control. **Subjects, Materials and Methods:** This study includes (81) female subjects, age ranged from (15 to 37) years. (20) subjects are apparently healthy chosen as control group and (61) patients with type 1 diabetes mellitus were divided into two groups according to their glycemic control : (16) with poor glycemic control (HbA1c>8%) and (45) with acceptable glycemic control (HbA1c<8%) . In this study Cortisol was quantitatively determined in patients and healthy subjects by Enzyme-Linked Immuno sorbent Assay [ELISA] test using commercially available kits. In addition to that, the duration of disease, fasting plasma glucose (FPG) ,Glycated hemoglobin (HbA_{1c}), and body mass index (BMI) were identified in the patients. **RESULTS**: In poor glycemic control group, Cortisol level (267.89±16.60 ng/ml,$p<0.05$) was higher than in acceptable glycemic control group (126.84±4.55 ng/ml,$p>0.05$) and in nondiabetic patients (123±6.13 ng/ml ,$p>0.05$). **CONCLUSIONS** In type 1 female diabetic subjects, adrenal activity is enhanced in patients with poorly controlled patients diabetes and the degree of cortisol secretion is related to the glycemic control

Key words: cortisol; hyperglycaemia; glycemic control ;Type 1 diabetes mellitus

الخلاصة:

خلفية البحث يعتبر داء السكري من أكثر الأمراض شيوعا في العالم والذي يعزى الى عمليات أيضيه غير طبيعيه. يسبب داء السكري خلل في الغدد الصم وذلك عن طريق تأثيره على إفراز وايض والفعالية البيولوجية للهرمونات .الهدف من الدراسة هذة الدراسة كانت اللأجابة فيما اذا كان مرض السكري من النوع الاول يغير تركيز الكورتيزول للمريضات بدرجة سيطرة مختلفة من المرض .**العينات ، المواد وطرائق العمل :** هذه الدراسةِ تَضمّنتْ (81) امرأةً بمدى العُمرِ بين (15-37) سَنَه ، (20)امرأة صحيحة كمجموعةضابطة و(61) مصابة بداء السكري"النوع الاول" ، مجموعه المرضى قسّمت إلى مجموعتين وفقا لدرجةالسيطرة على السكري(16) مصابة ذات سيطرة ضعيفة (خضاب الدم المعسل>8%) (45). مصابة ذات سيطرة جيدة (خضاب الدم المعسل<8%) . في هذه الدراسة تم تعين مستويات هرمون الكورتيزول وكان التقييم بواسطة فحص (ELISA) عن طريق العدد المختبرية التجارية المتوفرة. وقيمت أيضا فترة الإصابة بالمرض ,سكر بلازما الدم الصائم ,خضاب الدم المعسل(HbA_{1c}).,دالة كتلة الجسم (BMI في مصل الدم.**النتائج :** يوجد اختلاف معنوي في مستوى الكورتيزول لمجموعة المصابات ذات السيطرة الضعيفة(267.89±16.60 ng/ml,$p<0.05$) عند مقارنتهم مع مجموعه المصابات ذات السيطرة المقبولة (126.84±4.55 ng/ml,$p>0.05$) ومجموعة الأصحاء.(123±6.13 ng/ml ,$p>0.05$)**.الأستنتاج:**في النساء المصابات بمرض السكري من النوع الأول زيادة فعالية القشرة الكظرية تكون في مجموعة المصابات ذات السيطرة الضعيفة وزيادة درجة إفراز الكورتيزول تكون متعلقة بدرجة السيطرة على المرض

INTRODUCTION

Diabetes mellitus is regarded as one of the commonest metabolic disorder all over the world. It can cause various endocrine disorders by affecting the secretion, metabolism, clearance or bioavailability of hormone [(1)]. Cortisol the major natural glucocorticoid, secreted from the adrenal cortex, that affects the metabolism of glucose, protein and fats, as well as regulates the immune system. Due to its direct impact on these very important systems cortisol is referred to as an "active" glucocorticoids [(2)]. Several studies showed alteration of serum cortisol in diabetic patients . In (1993) Steven A. South *et al*, in their study about alterations in luteinizing hormone secretory activity in women with Insulin-dependent diabetes mellitus and secondary amenorrhea, he observed, among the hormones he investigated, that cortisol is elevated in those patients [(3)]. Other study in (1998) demonstrated also increases of serum cortisol in type 2 diabetic patients [(4)] . Recently, some studies speculated that hypercortisolism can result in visceral obesity, dyslipidemia, insulin resistance, and diabetes mellitus
Thus, alterations of serum cortisol have been found in diabetic patients [(5)(6)] .

SUBJECTS, MATERIALS AND METHODS

***Patients* and Controls**:Sixty one females with type 1 diabetes mellitus on insulin therapy were selected according to convenient non-Random one and carried out by consecutive pooling of Diabetic patients attending the National Diabetes Center (AL- Mustansiria University) during the period from November 2009 to February 2010, with ages ranged from 14-37 years. The sample for the assay were taken early in the morning from (8-9:30) am, while the patients were fasting and relaxed for healthy subjects and female patients with type1 diabetes .A careful history was obtained from patients including age, duration of DM, family history of type 1 diabetes mellitus, weight and height. All patients were clinically examined .pregnant ladies were not enrolled .evaluation of each patient is done by Detecting the body mass index (BMI), Hemoglobin A_{1c} blood test, and serum cortisol. After HbA1c measurement, the patients' sera and plasma were divided into two groups according to glycemic control poor and acceptable glycemic control groups .Twenty apparently normal(age and body mass index) matched were included in the study as control groups. They were not complaining from any endocrine disorder or using drugs.

Sample Collection: Blood samples were collected by vein puncture using 10 ml disposable syringes. Blood was divided into 2 parts: **First part** : contains (2ml) blood that was put in EDTA tube, mixed gently and used for HbA1c measurements. **Second part**: the rest was centrifuged at(3000 rpm) for 15 min after allowing the blood to clot at room temperature. The sera were aliquoted and frozen at -20 ^{o}C until the assay day.

Assays

Serum cortisol was measured in duplicate using a competitive immune assay (DRG Instruments GmbH, Germany) [(7)] . HbA1c was measured using HPLC method (Bio-Rad, France) . Fasting plasma Glucose was determined by measuring the amount of H2O2 produced in the reaction catalyzed by glucose oxidase. BMI uses a mathematical formula based on a person's height and weight. BMI equals weight in Kilograms divided by height in square meter ($BMI=Kg/m^2$) [(8)]

Statistical analysis:

All the statistical analysis was done by using Pentium-4 computer through the SPSS program (statistical packages for social sciences version-11) and Excel 2003.ANOVA table with the result of multiple comparison test (LSD).student t-test for independent samples was used to test the difference in mean between two groups .P value equal and less than 0.05 was used as the level of significance

RESULTS AND DISCUSSION

The clinical characteristics and biochemical parameters of adrenal cortex function from the whole diabetic group and from the control group are summarized in Table 1. Age, BMI, FPG and HbA1c were comparable between the all diabetic patients and control subjects. The mean age for poorly controlled diabetic group was (24.25±1.29) years and diabetic patients with acceptable glycemic control were (26.53±0.91) years which was comparable to that of healthy control mean (25.30±1.41) years .The patients and the control were age matched ($P > 0.05$). There are no significant differences in BMI when comparing diabetics with non diabetic counterparts as shown in table (1). The same table revealed that mean FPG for poorly controlled diabetics was (315.88±1.29) and for those with acceptable control (198.16±9.3), while the FPG for non diabetic subjects was found to be (97.20±1.78). The difference was highly statistically significant ($P < 0.0001$). Result were in agreement with Sultanpur *et al* (2010) who stated that higher levels of HbA1c are found in people with persistently elevated plasma glucose as in diabetes mellitus[9] . Glycated hemoglobin was found to be higher in diabetic patients compared with the healthy subjects and significantly elevated in poorly control diabetic patients than acceptable control diabetic patients and healthy subjects ($P < 0.05$) as shown in table (1).

Table(1) Clinical characteristics of patients with DM In the three group

Parameter	Healthy subjects		Poor control (HbA1C>8)		acceptable control (HbA1C<8)		P value
	Mean±SEM	range	Mean±SEM	range	Mean±SEM	range	
Age (years)	25.30±1.41	15-37	24.25±1.92	14-37	26.53±0.91	15-37	0.450
BMI (Kg/m2)	23.32±0.44	20.96-27.94	25.36±0.96	18.86-29.75	25.15±0.49	10.81-29.41	0.072
FPG (mg/dL)	97.20±1.78	85.0-110.0	315.88±28.	124.0-488.0	198.16±9.3	98.0-200.0	0.0001*
HbA1c%	5.07±0.16	4.0-5.8	11.04±0.7	8.0-16.9	7.36±0.16	7.01-7.8	0.0001*

*Significant using ANOVA test at 0.05 level of significance.

Cortisol Concentration in the Studied Groups Dividing them According to Glycemic Control

Table (2) showed that mean cortisol is found to be significantly elevated ($p<0.05$) in poorly controlled diabetics when compared with diabetics in whom glycemic control was acceptable, and with healthy subjects. The mean cortisol concentration in patients with acceptable control was found to be insignificantly elevated when compared with healthy subjects . The results of the present study regarding serum cortisol relation to HbA1c are similar to observations of other investigators, Almqvist *et al* (2001) who stated that serum cortisol elevated in diabetic patients with poor glycemic control (HbA1c>8%) in the morning [(10)]. Penhoat and colleagues (1988) demonstrated that insulin enhances the steroidogenic and cAMP response to ACTH, in a series of *in vitro* experiments, based on his study, insulin may also, *in vivo*, enhance adrenocorticotropic action of ACTH, therefore, the stimulation of cortisol secretion by insulin does not seem to be entirely independent of ACTH release, but rather reflects an increased sensitivity of the adrenals to the action of ACTH [(11)]. According to Bujalska *et al*(1997), insulin may also increase plasma cortisol concentration. They demonstrated that adipose stromal cells from omental fat have a large capacity to convert inactive cortisone to active cortisol through the expression of 11ß-HSD1 (11ß-hydroxysteroid dehydrogenase isoform 1). They also proved that *In vitro*, insulin increased the expression and activity of this enzyme [(12)] . This mechanism of converting cortisone to cortisol could be likewise relevant for the *in vivo* increase in cortisol concentrations after insulin administration [(13)]

Table (2) Mean distribution of (cortisol) concentration in the studied groups (dividing them according to glycemic control).

Groups	Serum cortisol (ng/ml)		P value in comparison to	
	Mean±SEM	Range	Acceptable control (HbA1C<8)	Healthy subjects
Poor control (HbA1C>8)	267.89±16.60	210.0-435.9	0.0001*	0.0001*
Acceptable control (HbA1C<8)	126.84±4.55	73.89-168.0		0.636
Healthy subjects	123.06±6.13	70.8-165.3		

*Significant difference using student's t-test for comparing between two independent means at 0.05 level of significance.

CONCLUSION

We concluded that:

1. The levels of serum cortisol is found to be significantly higher in poorly controlled diabetic patients compared with acceptable control group and healthy control groups while the level of serum cortisol is found to be insignificantly higher in acceptable controlled diabetic patients compared with healthy control groups

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