The Effect of Leptin Hormone Levels In Type(II) Diabetic Nephropathy Patients

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Abstract

Type 2 diabetes Nephropathy complication is one of the most commonest metabolic disorders that becomes an advanced serum level of hormone altered. The objective is to study the effect of leptin levels in Type 2 diabetes nephropathy (D.N) complication and healthy subject.

This study was done in National Diabetes Center (NDC), AL-Mustansriya University;ona total (64) individuals whase age were ranged from(45-60) years,of which (38) patients of type 2 diabetes nephropathy, and (26) healthy(controls).

The collected data ,information concerning the individuals used in the present study were: age, sex , body mass index (BMI) and blood samples to estimate serum leptin levels , fasting plasma glugcose (FPG) , glycated hemoglobin (HbA1c), serum creatinine, blood urea , and micral tests (urinary to microalbumine to creatinine ratio).

The mean FPG, HbA1c and Micral tests of type 2 diabetes nephropathy (D.N) showed statistical significant with healthy control ;on the other hard the data shows significant increases in leptin level in type 2 diabetes nephropathy (D.N) (urinary microalbumin to creatnin ratio ranged 30-300 mg/g) compared with healthy control.

No significant correlation was present between serum leptin and both serum creatinine and blood urea ,so there wasn't any correlation between BMI and serum leptin levels .In conclusion the results showed that serum leptin level was elevated in type 2 diabetes nephropathy(D.N) because impaired increase with progression of renal disease in diabetic nephropathy.

Introduction

Type 2 diabetes mellitus: called non insulin depended diabetes mellitus (NIDDM) accounts for 90% of the population with diabetes in this type. There are varying degrees of insulin resistance or insulin secretary defects (1). Complication of diabetes occurs after many years of uncontrolled hyperglycemia (2).The consequences of diabetes are nephropathic disease ,which lead to chronic renal failure (CRF)(3). Diabetic Nephropathy (D.N) is a progressive kidney disease caused by angiopathy of capillaries in the kidney glomeruli .It is characterized by nephrotic syndrome and long standing diabetes mellitus and is a primary cause for dialysis in many western countries(4). In diabetic nephropathy measurement microalbuminuria test results may aid clinicians in the detection of patient at risk of developing kidney damage (5,6) .

Leptin is a 16KD protein hormone of 167 amino acids which plays a key role in regulation food intake and energy expenditure , including the regulation of appetite and increase of metabolism (7,8). Human kidney plays a substantial role in leptin removal from plasma by taking up and degrading the peptide . Renal leptin net balance and urinary leptin execretion were detected by Lineweaver-Burk analysis . This analysis indicated that renal leptin uptake followed saturation kinetics with an apparent Michaelis-Menten constant of 10.9 ng/ml . Renal leptin uptake could be 80% of all leptin removal from plasma , generally leptin was undetectable in urine(9) about 20-30% of patients with type1 or type2 diabetes develop evidence of nephropathy, and such patients currently starting of dialysis (10). Furthermore, Hyperglycemia also activate protein kinase c, may contribute to renal diseases and vascular complications of diabetes (9), and also familiar or genetic factor plays a role in diabetic

nephropathy (3) .In addition previously described direct and indirect effects of leptin on the kidney include natriuretic effects ,an increase in sympathetic nervous activity , and stimulation of reactive oxygen species . These findings collectively suggest that the kidney is a target organ for leptin and that this hormone might play an important role in renal pathophysiology (11).

Materials and Method

This study was carried out in National Diabetes Center (NDC), AL- Mustansiriya University; on a total (64) individuals ,(30 females and 34 males) aged (45-60) years .Thirty eight patients Type 2 diabetes nephropathic (urinary microalbumin to creatinine ratio was range 30-300 mg/g) , (26) healthy controls . Data collection about age , sex and body mass index(BMI). Blood samples from the individuals were taken for laboratory investigation: which included , Fasting Plasma Glucose (FPG) , Glycated Hemoglobin (HbA1c) , blood urea , serum creatinine and determination leptin level in serum ; (DGR instruments GmbH , Germany ,ELISA KIT)(12), and Micral tests ; supplied by Bayer Healthy Care, V.S.A(13). Analysis of data was carried out by using SPSS(statistical package for social sciences).

Results and Discussion

A total of 64 individuals(38 patients and 26 control) were examined successfully without any healthy problems .

Diabetes is the most common cause of renal failure, and there is an account for more than 40 percent of new cases who have development of kidney problems in people with diabetes (14). Leptin hormone ,which is secreted from adipocytes has a role in the regulation of appetite and energy expenditure.This protein is produced by adipocrine , pancreas and other organs by activating the transmembranc receptor and is cleared from plasma mainly by the kidney (15).The results showed that the serum leptin levels in the Type 2 diabetes nephropathy (urinary microalbumin to creatinin ratio 30-300 mg/g) significantly were higher $p < 0.05$ (Table-1) compared with healthy controls and this result agrees with Chan- Wb *et al.*(17)and Fruehwared-Schultes *et al.*(16) ,they found significant elevated levels of serum leptin in Type 2 diabetes nephropathy (D.N) compared with non diabetic controls .The human kidney plays a substantial role in leptin removal from the plasma by absorping and degrading the peptide (18). Increasing albumin level in urin (microalbuminuria) is considered as key characteristics of diabetic nephropathy (16).Table(2) showed that there was a significant positive correlation of FPG , HbA1c $p<0.05$ in Type 2 diabetes nephropathy (D.N) compared with healthy control subjects, serum leptin level did not correlate with FPG and HbA1c ($r =0.343$, $r=0.315$) respectively (table-3),these results agreed with Fu-Me chung *et al.* (19) .

He found that there was no correlation between leptin level and FPG, HbA1c, which indicate that leptin is not affected by the degree of glycemic control ,while Pistrosh *et al.* (20) found that patients with Type 2 diabetes had high levels of FBG and HbA1c, compared with healthy control .Such increase may be due to insulin resistance in Type 2 diabetic nephropathy patients in which leptin reduces insulin secretion and enhances hematopiesis (21).There was a significant positive correlation of BMI in Type 2 diabetic nephropathy compared with control $p <0.05$ (Table-2) but there wasn't any significant correlation between BMI and leptin level in Type 2 diabetic nephropathy as shown in(table-3) . This correlation may be explained by the presence of additional factor which would increase the impaired degradation by the affected kidney (22) . Hyperliptenimia may play a role in the decreased BMI (anorexia and malnutrition) that usually accompanied chronic renal failure. Furthermore , there were no significant correlation between serum creatinine and blood urea levels with serum leptin levels in Type 2 diabetic nephropathy (19) , but both creatinine and urea levels increase in Type 2 diabetes; this may be due to renal impairment in Type 2 diabetic nephropathy (23) . In conclusion the results showed that serum leptin level was elevated in

type 2 diabetes nephropathy(D.N) because impaired would increase with the progression of renal disease in diabetic nephropathy.

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Table(1) :Serum leptin levels in Type 2 Diabetic Nephropathy and control

	Control	Type 2 (D.N)
Leptin (ng\ml)	10.60+3.17	20.18+4.40

Table(2) :The mean of BMI, FBG, and HbAIc in Type 2 Diabetes Nephropathy (D.N)and controls

	Control n=26	Type 2 (D .N) n=38
BMI (Kg/m)	25.01+3.40	28.99+6.69
FPG (mg/dl)	77.19+2.25	177.62+50.20
HbAIc (%)	4.18+0.12	9.23+2.48

Table(3) :The correlation coefficient (r) between BMI ,FPG, and HbA1c with serum leptin levels (control & diabetic nephropathy)

		Control	Type 2 (D.N)
		Leptin (ng/ml)	Leptin (ng/ml)
BMI	r	0.380	0.392
	P	0.055	0.120
FBG	r	0.259	0.343
	p	0.201	0.101
HbA1c	r	0.256	0.315
	p	0.207	0.164

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تأثير مستوى هرمون اللبتين لدى مرضى السكري النوع الثاني والمصاحب باعتلال الكلى

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الخلاصة

يعد داء السكري النوع الثاني والمصاحب باعتلال الكلى من الامراض الشائعة الذي يعزى الى عمليات ايضية غير طبيعية محدث تغيرات في مستويات معظم الهرمونات.تم درس تاثير مستوى هرمون اللبتين عند مرضى السكري (النوع الثاني) والمصاحب باعتلال الكلى ومدى علاقته بالمعاييرالسكرية الاخرى، اذ اجريت الدراسة على (64) فردا، تراوحت اعمارهم بين(45–60) سنة، (38) مريضا" يعانون من مرض السكري النوع الثاني والمصاحب باعتلال الكلى، و(26) شخصا" من الاصحاء في المركز الوطني السكري– الجامعة المستنصرية. و جمعت المعلومات الخاصة بالعمر، والجنس، ومعدل كتلة الجسم، واخذت العينات لغرض قياس مستوى هرمون اللبتين وقياس الكلوكوز، والهيموغلوبين المتسكر ،واليوريا ، والكرياتنين وكذلك قيس فحص مكرل (نسبة الالبومين الى الكرياتنين في البول) . بينت النتائج وجود قيمة احصائية في فحص السكر الصائم ،والهيموغلوبين المتسكر ،وفحص مكرل عند مرضى السكري

النوع الثاني والمصاحب باعتلال الكلى مقارنة مع مجموعة الاصحاء، وكذلك بينت الدراسة ارتفا ع مستوى اللبتين عند مرضى السكري النوع الثاني المصاحب باعتلال الكلى التي كانت (نسبة الالبومين الى الكرياتنين في البول تتراوح بين 30– 300 ملغم/غم) مقارنة مع الاصحاء كذلك عدم وجود علاقه ترابطيه بين مستوى اللبتين وكل من مستوى الكرياتنين واليوريا في مصل الدم ،ولم يلاحظ وجود علاقة ترابطية بين معدل كتله الجسم ومستوى اللبتين.

نستنتج من هذه الدراسة ان مستوى هرمون اللبتين يرتفع عند مرضى السكري النوع الثاني والمصاحب باعتلال الكلى نتيجه لضعف الكلى تدريجيا على التجزئة والتحليل عند مرضى السكري.