Comparative Biochemical Study of Insulin like Growth Factor-1(IGF-1) in Sera of Controlled and Uncontrolled Dyslipidemia in Type2 Diabetic Iraqi Patients and Healthy Control.

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Abstract

The objective of the present study is to compare the effect of insulin like growth factor-1 on the lipid profile in sera of diabetic patients with and without dyslipidemia having the same medical treatment and compared with healthy control. The study included three groups. The biochemical parameters which were measured include, fasting blood sugar(FBS), glycated hemoglobin (HbA1c), fasting insulin, insulin like growth factor-1(IGF-1), lipid profile [Total cholesterol (Tc) , triglyceride(TG), high density lipoprotein cholesterol(HDL-c) ,low density lipoprotein-cholesterol (LDL-c)and very low density lipoprotein-cholesterol (VLDL-c)], Atherogenic index of plasma(AIP), insulin resistance(IR). The results revealed a significant increase in FBS,HbA1c,Tc,TG,LDL-c,VLDL-c,AIP, insulin level and HOMA-IR while a significant decrease in IGF-1 and HDL-c in G_2 and G_3 was noticed comparing to G_1. The conclusion could be drown from the present study that low levels of IGF-1 in groups comparing with healthy control, which may be led to the high levels of insulin resistance, while no effect of dyslipidemia on IGF-1.

Key words: Type2 diabetes mellitus DM, IGF-1, IR .

Introduction

Insulin-like growth factor-1(IGF-1) is a small polypeptide (70 amino acid &7500KDa) straight chain synthesized mainly by the liver in response to growth hormone(GH)action[1]. It shares nearly 50% amino acid sequence homology with proinsulin, it composed of an alpha and a beta chain connected by disulfide bonds[2]. IGF-1 is present in circulation in the free form and in the form complexed with protein which bind (IGFBP). Six IGF-binding proteins were identified with various affinity to IGF-1, main binding protein of IGFs is IGFBP-3 and its synthesis is mainly determined by growth hormone[3]. IGF-1 synthesis remains linked to nutrient intake and has retained some insulin-like properties such as stimulation of glucose transport into skeletal muscle cell[3]. Decreased levels of circulating IGF-1 in diabetic patients have been discovered to be associated with insulin resistance [4],which is a pathological state in which insulin action is impaired in target tissues, including liver, skeletal muscle and adipose tissue[5].

IGF-1 levels are strongly determined by changes in growth hormone secretion[6]. Dyslipidemia is increased in the lipid and lipoprotein, it is elevated of plasma cholesterol (Tc), triglyceride (TG), or both, or a low HDL-c level that contributes to the development of atherosclerosis [7]. The abnormal lipid profile observed in type2DM may be related to insulin resistance which has been closely associated with diabetic dyslipidemia and hypertension[8,9].

Aim of the study

The aim of this study is to compare the effect of insulin like growth factor-1 on the lipid profile in sera of Iraqi diabetic patients with and without dyslipidemia having the same medical treatment and compared with healthy control, this may provide an additional factor of glucose homeostasis .

Subjects and methods

The studied groups comprised of (20)subjects [(10)male and (10) female] as healthy control group1(G_1) and G_2 which consist of type2 DM with controlled lipidemia [(11)male and (9)female] and G_3 which consist of type2 DM patient with dyslipidemia [(9) male and (11) female]. All studied groups matched with age range (45-65) years and body mass index (BMI)(25-29 Kg/m^2). Smokers, alcoholics and patient with cardiovascular disease, insulin treatment , kidney disease ,hepatic failure and statins treatment were excluded.

Blood samples were collected from venipuncture each subject in the study after 12 hours fasting. Samples were immediately centrifuge and serum was separated and frozen until assayed, for determination of fasting serum glucose [10]. Total cholesterol[11], high density lipoprotein cholesterol HDL-c[12] and triglyceride TG [13] were determined by using commercial kits (Bio Labo SA-France). LDL-c and VLDL-c were calculated by Freidweld equation[14].

LDL-c=Total cholesterol-(HDL-c+VLDL-c)

VLDL-c(mg/dL)=(TG(mg/dL/5)

Fasting serum insulin [15] was determined by using ELISA kit (DRG-GERMANY). Insulin like growth factor-1 (IGF-1) was determined by radioimmunoassay using commercial kits (Beckman Coulter)-Germany. The bound radioactivity is directly proportional to IGF-1 concentration in the sample (IMMUNOTECH s.r.o –Radiova ,I). Insulin resistance was assayed by calculating the homeostasis model assessment for insulin resistance (HOMA-IR) which is estimated using the following formula .

HOMA-IR= [(Fasting glucose x Fasting insulin)/405] [16].

Atherogenic index of plasma (AIP) calculated from the formula (AIP=Log(TG/HDL-c)) [17]. The results were expressed as mean ± SEM and P≥0.05 was considered significant. Unpaired student t-test was used to examine the differences of mean.

Results and discussion

Table(1) showed a significant increase in fasting blood sugar (FBS)in both diabetic groups,G_2(167.45± 7.66 mg/dL)and G_3(201.75±15.14 mg/dL) compared to control group (86.5±2.06 mg/dL), no significant elevation between G_2 and G_3 was observed. Patients with type2 DM characterized by insufficient secretion of insulin as a defect of islet cell function or β-cell mass which cause an increase in blood sugar[18]. Glycated hemoglobin (HbA1c) showed a significant increase in both diabetic groups, G_2 (7.84±0.22%) and G_3 (8.40±0.42%) compared with G_1 (5.74±0.09%). A significant correlation was found between G_1 comparing to G_2 and G_3, while no significant correlation between two diabetic groups was found. It has been reported that the prevalence and overlap between intermediate hyperglycemia was defined by HbA1c(5.7-6.4%), this range was proposed as an indicator of type2 DM.

Table (2) Showed the levels of lipid profile and AIP in all studied groups. No significant elevation was found in Tc, TG, LDL-c,VLDL-c and AIP in G_2 comparing to G_1 which Tc(169.25±6.47mg/dL)comparing to G_1(168.75±4.12mg/dL) and TG(138.85±3.11mg/dL) comparing to G_1(127.3±3.59mg/dL), LDL-c (89.85±6.31mg/dL) comparing to G_1(88.75 ±3.92mg/dL), VLDL-c(27.77±0.91mg/dL) comparing to G_1(26.15±1.21mg/dL) and AIP (0.45 ±0.02) comparing to G_1(0.36±0.02). The results also revealed significant reduction in HDL-c levels in G_2(44.95±1.61mg/dL) comparing to G_1(54.65±1.08mg/dL).

A significant increase in Tc,TG,LDL-c,VLDL-c and AIP in G_3 was found comparing to G_2 and G_1 which Tc was (192.7±12.35mg/dL), TG was (186.75±16.44 mg/dL), LDL-c was (113.45±13.77mg/dL), VLDL-c (36.9±3.32 mg/dL) and AIP was (0.60±0.04). A significant reduction in HDL-c was noticed in G_3 (44.1±1.80)comparing to G_1, while no significant reduction was found between G_2 and G_3. The data in present study showed that dyslipidamic subject had two lipid values outside the normal range of which the most frequent combination was low HDL-c and high LDL-c which is in agreement with Cook et.al study[19] who observed that 54% of DM subjects had two lipid values reduced HDL-c and increased LDL-c as the most frequent combination outside the normal range. The most lipid abnormality in our study reduced HDL-c which is in agreement with Okafo et.al study[20]. Previous study revealed that insulin resistance may be responsible for low HDL-c in patient with type2 DM[21]. The production of HDL-c decreases due to the alteration in hepatic function and increased activity of hepatic lipase which facilitates HDL-c clearance. Dyslipidemia is elevation of plasma cholesterol, triglycerides, or both or a low HDL-c , that contributes to the development of atherosclerosis [22]. Our study revealed that there is a slightly increase in AIP in G_2 who controlled their lipidemia and high increase of AIP in G_3 with dyslipidemia comparing with control (0.45±0.02)(0.6±0.04)respectively comparing with (0.36±0.01) , which is in agreement with Hermans et.al study[23]. The highest value of AIP increased significantly with increased atherogenic risk (0.2-0.5)and in patients with diabetes AIP value was among the highest level[24], therefore, AIP is considered a higher predicted value for atherosclerosis[25]. A study data of AIP value revealed the increasing of AIP value proportion to the cardiovascular (CV) risk, this value increased up to (0.4), the data showed the AIP (0.1-0.24) with medium risk and above (0.24)with high CV risk [26].

Results in table (3) indicate that serum levels of IGF-1(ng/ml) in G_2&G_3 (104±6.77ng/ml) ,(116.9±9.19ng/ml) respectively were significantly decreased, compared with G_1 (236.45 ±8.93 ng/ml).

Serum IGF-1 levels in patients with type2 diabetes depend on the degree of metabolic control, with near normal IGF-1 levels in well controlled diabetics and decreased in poorly controlled diabetics, it has been suggested that lowered serum IGF-1 concentration predict worsening of insulin-mediated glucose uptake in older people[27].Conti et.al[28] reported that insulin has a profound influence on the IGF-1 axis and variation circulating insulin concentration is an important determination of IGF-1 bioactivity, that means the fasting decreases insulin levels which then reduces the concentration of growth hormone (GH)receptors in hepatocytes which in turn causes a reduction in IGF-1. Hasan et.al[29] indicated that IGF-1 can be useful marker in the insulin resistance because low IGF-1 level can help as a better identification of subject at risk type diabetes and cardiovascular disease.

The data in table (3) showed a significant reduction of IGF-1 in G_2 and G_3 comparing to G_1. No significant reduction was observed between two diabetics groups G_2&G_3. Also the results presented in table-3 indicated that fasting insulin and HOMA-IR values were significantly higher in G_2&G_3 than healthy control subjects. Insulin levels for G_2&G_3 was (15.79±1.45ng/ml)(17.46±1.09ng/ml)respectively compared with G_1(2.32±1.11ng/ml). No significant elevation between G_2&G_3 was noticed. Homeostasis insulin resistance (HOMA-IR) was significantly increased in G_2&G_3(6.67±0.70)(8.58±0.79) respectively compared with G_1(2.7±0.28). No significant elevation between G_2&G_3 was noticed.

Dyslipidemia and insulin resistance are both considered to be risk factors for metabolic syndrome, insulin resistance are associated with low IGF-1 level, depression of HDL-c concomitant with elevation of LDL-c, increasing risk of obesity and type2 diabetes[30]. Low IGF-1 level was found in diabetic patients which have been discovered to be associated with insulin resistance[4]. The action of IGF-1 is directly on the balance between GH and insulin to the control of glucose homeostasis [31].

Conclusions

The results of the present study indicate that there is no effect of dyslipidemia on IGF-1 level which there are no significant redaction found between controlled and uncontrolled dyslipidemia diabetic patients.

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Table (1): Descriptive parameters of the studied groups.

Groups / parameters	G_1 Mean ± SEM	G_2 Mean ± SEM	G_3 Mean ± SEM	G_1&G_2 T. test	G_1&G_3 T. test	G_2&G_3 T. test
Subject.NO	Male (10) Female (10)	Male(11) Female (9)	Male (9) Female (11)			
FBS(mg/dL)	86.5±2.06	167.45±7.66	201.75±15.14	S	S	NS
HbA1c (%)	5.74±0.09	7.84±0.22	8.40±0.42	S	S	NS

Table (2): Levels of lipid profile and AIP in all studied groups.

Groups / parameters	G_1 Mean ± SEM	G_2 Mean ± SEM	G_3 Mean ± SEM	G_1&G_2 T. test	G_1&G_3 T. test	G_2&G_3 T. test
Tc (mg/dL)	168.75±4.12	169.25±6.47	192.7±12.35	NS	S	S
TG (mg/dL)	127.3±3.59	138.85±3.11	186.75±16.44	NS	S	S
HDL-c (mg/dL)	54.65±1.08	44.95±1.61	44.1±1.80	S	S	NS
LDL-c (mg/dL)	88.75±3.92	89.85±6.31	113.45±13.77	NS	S	S
VLDL-c (mg/dL)	26.15±1.21	27.77±0.91	36.9±3.32	NS	S	S
AIP	0.36±0.02	0.45±0.02	0.60±0.04	NS	S	S

Table (3): Levels of IGF-1 , insulin , HOMA-IR in all studied groups.

Groups / parameters	G_1 Mean ± SEM	G_2 Mean±SEM	G_3 Mean±SEM	G_1&G_2 T. test	G_1&G_3 T. test	G_2&G_3 T. Test
IGF-1 (ng/ml)	236.45±8.93	104.4 ±6.77	116.9±9.19	S	S	NS
Insulin Level (ng/ml)	2.32±1.11	15.79±1.45	17.46±1.09	S	S	NS
HOMA-IR	2.7±0.28	6.67±0.70	8.58±0.75	S	S	NS

دراسة مقارنة المتغيرات الكيموحيوية لعامل النمو شبيه الانسولين-1 في امصال المسيطرين وغير المسيطرين على الدهون في مرضى النوع الثاني للسكري العراقيين مع الاصحاء.

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الخلاصة

تهدف الدراسة الحالية الى مقارنة تاثير عامل النمو شبيه الانسولين-1 على صورة الدهون في امصال مرضى مرض السكري المسيطرين وغير المسيطرين على ارتفاع الدهون بالدم الذين لهم المعالجة الطبية نفسها ومقارنتهم مع الاصحاء . وتضمنت المتغيرات الكيموحيوية التي تم قياسها, سكر الدم الصيامي, الهيموكلوبين المسكر, الانسولين الصيامي ,عامل النمو شبيه الانسولين-1, صورة الدهون (الكولسترول الكلي,الدهون الثلاثية, اللايبوبروتينات عالية الكثافة, اللايبوبروتينات واطئة الكثافة, اللايبوبروتينات واطئة الكثافة جدا), ومؤشر البلازما المعصد, مقاومة الانسولين. كشفت النتائج عن زيادة معنوية في (السكر الصيامي ,الهيموغلوبين المسكر ,الكولسترول الكلي ,الدهون الثلاثية ,اللايبوبروتينات واطئة الكثافة ,اللايبوبروتينات واطئة الكثافه جدا ,مؤشر البلازما المعصد, مستوى الانسولين و HOMA-IR), بينما لوحظ نقصان معنوي في عامل النمو شبيه الانسولين-1 والكوليسترول عالي الكثافة في المجموعة 2 والمجموعة 3 مقارنة مع المجموعة 1. المحصلة التي استنتجت من هذه الدراسة ان انخفاض عامل النمو شبيه الانسولين -1 في المجموعتين بالمقارنة مع مجموعة الاصحاء التي قد تؤدي الى مستويات عالية من مقاومة الانسولين بينما لايوجد تاثير لارتفاع دهون في الدم على عامل النمو شبيه الانسولين-1.

الكلمات المفتاحية: داء السكري النوع الثاني، عامل النمو شبيه الانسولين-1 ، مقاومة النسولين .