The Effect of L-Carnitine as an Adjuvant Supplement on Lipid Profile in Iraqi Diabetic Patients

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Abstract

Diabetes is a complex set of diseases require continuous medical care, to control blood sugar and prevent complications is .The aim of this research is to determine the effect of administration of L carentin to diabetics on the lipid profile. The research was conducted on sixty diabetic patients were selected from endocrinology and diabetes center / Al-Rusafa, within selected criteria. The patients divided into 3 groups (control group of healthy people and two groups of patients with diabetes who were on metformin and glibenclamide, one group took a L carnitine in a dose of 1000 mg twice daily and a group dealing with a placebo for a period of 3 months continuously). The study found that patients who took Lcarnitine, showed a significant reduction ($p < 0.05$) in the triglyceride level, while no significant changes were observed in the level of cholesterol and HDL and LDL. This study concluded that administration of L carentin improved the lipid profile in type-2diabetic patients.

Key word: Diabetes mellitus (DM), Dyslipidemia, l-carnitine (LC).

تأثير مكملات الكارنتين اليساري على صورة شحوم الدم عند مرضى السكري في العراق

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الخلاصة

ان مرض السكري هو مجموعة معقدة من الامراض تحتاج لعناية طبية مستمرة لضبط سكر الدم و منع تعقيدات المرض .الهدف من البحث هو معرفة تأثير اعطاء الكارنتين اليساري لمرضى السكر على صورة شحوم الدم. تم اجراء البحث على ستين مريضا تم اختيارهم من مركز الغدد الصم و السكري/الرصافة,ضمن معيارية محددة في الدراسة.تم تقسيم المرضى الى ٣ مجاميع (مجموعة سيطرة من الاشخاص الاصحاء و مجموعتين من مرضى السكري ممن يتناولون علاج الكلبنكلامياد و الميتفورمين , تناولت مجموعة منهم كارنتين يساري بجرعة ١٠٠٠ ملغم مرتان يوميا و مجموعة تتناول علاج وهمي لمدة ٣ اشهر متواصلة). توصلت الدراسة الى ان المرضى الذين الذين تناولوا كارنتين يساري, لوحظ عندهم تغيرات معنوية ($p<0.05$) في مستوى الدهون الثلاثية بينما حدثت تغيرات غير معنوية في مستوى الكوليسترول و البروتين الدهني العالي و الواطئ الكثافة.هذه الدراسة استنتجت ان اعطاء الكارنتين اليساري يفيد في تنظيم شحوم الدم المضطرب عند مرضى السكري.

الكلمات المفتاحية :مرض السكري ،اضطراب شحوم الدم ،الكارنتين اليساري.

Introduction

Diabetes mellitus (DM) is a global health issue affecting children, adolescents, and adults. According to the World Health Organization, approximately 180 million people worldwide currently have type 2 DM (formerly called adult-onset diabetes); over 95% of people with diabetes have this form [(1)]. World Health Organization (WHO) has recently proposed new diagnostic criteria and classification of diabetes mellitus. A major change in diagnostic criteria is lowering of diagnostic fasting plasma glucose level to less than 7mM/L [(2)]. It is associated with long-term damage, dysfunction, and failure of different organs [(3)], Diabetes is associated with both micro vascular and macro vascular diseases affecting several organs, including muscle, skin, heart, brain, and kidneys [(4)]. The terms type 1 and type 2 are used for classification based on etiology. The terms insulin-dependent and non-insulin dependent are used for pathophysiological staging of diabetes mellitus regardless of the etiology [(5)].

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The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The number of people with diabetes is increasing due to population growth, aging [(6)], urbanization [(7)], and increasing prevalence of obesity and physical inactivity. L-Carnitine is a natural nutrient cofactor required for transport of long-chain fatty acids into the mitochondria, where they undergo beta-oxidation to produce adenosine triphosphate for cellular energy production which is primary fuel source for proper function in many tissues and prevent the toxic accumulation of long-chain fatty acids[(8)].

Role of L- Carnitine in the T2DM

Patients with type 2 diabetes seem to be at elevated risk for carnitine deficiency [(9)] . L-carnitine short-circuit the Randle cycle by sequestering inhibitory acetyl-CoA units as acetyl-Carnitine and concomitantly increasing free CoA levels. Lowering of the mitochondrial acetyl-CoA: CoA ratio would then favor glucose oxidation [(16)], L-carnitine mediated sequestering of toxic
lipid metabolites may have benefited both mitochondrial performance and insulin signaling[(10)], Also L-Carnitine can play a role in the treatment of type 2diabetics by improving insulin resistance that is caused by post-receptors defect, this means that L-Carnitine may be useful for cell membrane repairing and, removal of harmful lipid from the cells may improve or decrease the resistance to insulin action by photoreceptor defect either at the membrane or intracellular level[(11)], Administration of L-Carnitine may shift the metabolic bias of the liver away from esterification and synthesis of triglycerides toward the formation of acetylcarnitines. This could decrease synthesis of triglycerides and VLDL cholesterol and likely increase mitochondrial β-oxidation of fatty acids [(12)] .

Subjects, Materials and Methods

This study was carried out at the Specialized Center of Endocrinology and Diabetes-AL-Risafa Directorate of Health-Baghdad. The study was conducted on 60 Iraqi subjects 41 male and19 female with age range 40-64 years in non- randomized method, all volunteers follow inclusion and exclusion criteria.

The inclusion and exclusion criteria for volunteers

The inclusion criteria for healthy subjects to be free from other chronic disease or drugs, while diabetic patients to be poor controlled type 2DM for at least 5years and more, on metformin and glibenclamide therapy, and had lipid profile disorder, while this study exclude the pregnant, breast feeding or on contraceptive and postmenopausal women, also those with liver disease , kidney disease, epileptic disease, thyroid disease, smokers, and alcohol drinkers also must have no infection or on anti-biotic or any other drug has interaction with L-Carnitine. The volunteers are divided into three groups as follows:

Group (1): Includes 20 apparently healthy subjects (16 male and 4 females) as control.

Group (2): include 20 diabetic patients 10 male and 10 female; this group was taken L-Carnitine (1000 mg) tablets two times daily for three months.

Group (3): Includes 20 diabetic patients (15male and 5 female) were treated with placebo for three months.

Blood samples were taken from all individuals included in this study, at base line time and every 30 days of the study period, blood was collected by venipuncture technique in order to measure serum lipid profile.

Statistical analysis was performed by using unpaired student T- test between healthy individuals and diabetic patient's (weather placebo group or on L-Carnitine group), and paired student T- test between zero time , after 1st, 2nd and 3rd month in all groups involved in this study.

Results

Table(1) shows the effect of L-Carnitine on the lipid profile, involving total cholesterol (TC), triglyceride (TG) ,high density lipoprotein (HDL)and low density lipoprotein(LDL) .The comparison between control group with diabetics groups showed a significant difference in the TC,TG and LDL while HDL non- significantly affected. Concerning the TC, the outcome of trial showed non- significant changes observed in the treated group as well as placebo during study period ,meanwhile the data expressed a significant reduction of serum TG from 1st month in comparison with baseline value, at (p <0.05) and highly significant at the 2nd month and 3rd month respectively. For high density lipoprotein (HDL) the table shows non- significant also low density lipoprotein (LDL) showed non-significant changes at the 3 month of the study period weather in treated group or placebo.

Table (1) The effect of treatment with L-Carnitine on lipid profile in T2DM patient (n=20).

Parameter groups	Regime	Total Cholesterol mg/dl	Triglyceride mg/dl	HDL mg/dl	LDL mg/dl
Control	**baseline**	183.5±33.1*	154.7±41.1*	40.90±5.95	85.7±13.5[a]
Placebo	**Baseline**	208.9±30.8[b]	173.6 ±49.7[b]	39.90±8.23	127.4±27.1[b]
	1month	206.69±32.5	176.7±51.7	38.9± 5.38	127.3±26.1
	2month	208.4±39	177.6 ±49.2	39.98±7.58	126.5 ±25.6
	3month	207.37± 21.2	173.2±35.6	40.01±5.25	124.9±17.2
Treatment with L-Carnitine	**Baseline**	201.8±24.1[b]	174.6±38.9[b]	40.05± 6.6	120.1±22.6[b]
	1month	202.1 25.9	164.3±30.9*	39.9 ±5.29	122.1±23.7
	2month	201.7±22.4	158± 28.1 *	40.01±5.12	121.2±20.5
	3month	200.7 ± 27.4	147.9±26.6*	40.1 ±4.96	120.2±21.2

a,b,c represent statistically significant change **(**p <0.05) for comparison between healthy group and diabetics (on placebo or on L-Carnitine**).**

* represent significant change (p value<0.05) for patients comparison between pre and post treatment values of treated groups.

N= number of individuals**.**

Discussion

The current study demonstrated a non-significant decline in Total cholesterol, the serum HDL-C (high density lipoprotein cholesterol) and LDL-C (low density lipoprotein cholesterol) levels in the treated group after one, two and three months of treatment in comparison with zero time readings, and this may be due to a fact that L-Carnitine don't have direct potent effect on the cholesterol synthesis pathway, or the period of trial not sufficient to observe such a change this observation was consistent with that obtained by Gonzalez-Ortiz(2008) [(12)] , Golbidi (2011)[(13)] and Roberto(2012)[(15)], however, these findings disagree with other studies who observed positive effects of L-Carnitine supplementation on total cholesterol[(14,16,17)], while Irat et al. (2003) suggested that the beneficial effects of L-Carnitine treatment partially improve vascular reactivity and antioxidant property beyond its reduction of plasma lipids and it may have an important therapeutic approach in the treatment of diabetic vascular complications [(18)] also it consider a good adjuvant therapy beside cholesterol-lowering drugs (statin) for its mechanism that reverse the myopathy which is possible side effect of cholesterol lowering drugs and potentiated statin effect [(19)] also the LC may has an qualitative effect on HDL rather than increase level of the former through improve the integrity that carries important antioxidant enzymes(paroxanase and platelet activating factor acetyl hydrolase) which serves to protect from oxidation and increase half-life of HDL[(20)] while another study shown LC caused a significant twofold increase in α-tocopherol(vitamin E) content in oxidized LDL and caused a reduction in the level of conjugated dienes, lipid hydro peroxide, malondialdehyde, and dityrosine [(21)]. The present study found a successful improvement and significant decline in Triglyceride level in the treated group in comparison with base line readings, and this may be due to the L-Carnitine effects on FFA metabolism, glucose hemostasis, improvement in insulin sensitivity, down-regulated enzymes essential in glycolipid biosynthesis and were up-regulated Enzymes involved in fatty acid catabolism [(22)] or its role in increase FA consumption through increase physical activity. This outcome of the present study disagrees with other studies which find no such difference in TG level after taking L-Carnitine [(22-24)].while other studies agree with this study outcome [(25)] .

Conclusion

The present study was conclude that administration of L-Carnitine as adjuvant supplement at a dose (1000mg) twice daily for 3 successive months had a benefit effect on the triglyceride level in the T2DM with dyslipidemia meanwhile non-significant changes were observed on the levels of TC,HDL,LDL .

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