Lipid Peroxidation, Lipid Profile, Serum Leptin and Glycemic Control in Patients With Ischemic Stroke:Role of Vitamin E Supplementation

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الخلاصة

الاهداف: لتقييم مفردات السيطرة السكرية (مستوى الكلوكوز في مصل الدم في حالة الصيام، مستوى الانسولين ومقاومة الانسولين)، مستوى اللبتين، المالونديلهايد وصورة الدهون (الكوليسترول، الدهون الثلاثية، الكوليسترول في الدهون العالية الكثافة، الدهون الثلاثية، الكوليسترول في الدهون الواطئة الكثافة، الدهون الواطئة الكثافة جداً، مؤشر تصلب الشرايين)، معدل كتلة الجسم في مرضى السكتةالاقفاريه ولفحص تاثيرات فيتامين أي كعلاج مضاف على مستوى هذه المفردات.

الطرق: ضمت هذه الدراسة 62 مريضاً بالسكتة الاقفاريه مع 28 من الاشخاص الاصحاء كمجموعة ضبط. تم تقسيم المرضى عشوائياً الى مجموعتين. المجموعة الاولي (33 مريضاً) ضمت مرضى بالسكتة الاقفاريه تقرر اعطاءهم العلاج التقليدي، المجموعه الثانيه(28 مريضا) ضمت مرضى تقرر اعطاءهم العلاج التقليدي مع فيتامين أي (400 وحدة/يوم) لمدة 30 يوماً. اخذت عينات دم في البداية من مجموعتي المرضى بين 24-48 ساعة من الحادثه وقبل بدء العلاج وكذا من مجموعة الضبط، وتم قياس مستوى الكلوكوز في مصل الدم في حالة الصيام، مستوى الانسولين، اللبتين، الكوليسترول الكلي، الدهون الثلاثية، الكوليسترول في الدهون العالية الكثافه ،المالونديلهايد وتم حساب معدل مقاومة الانسولين، الكوليسترول في الشحوم واطئة الكثافة، الكوليسترول في الدهون الواطئة الكثافه جدا، مؤشر تصلب الشرايين ومعدل كتلة الجسم باستخدام معادلات خاصة. في مجموعتي المرضى اخذت عينة دم ثانيه بعد العلاج وتم قياس وحساب نفس المفردات المذكورة اعلاه.

النتائج: قبل بدء العلاج كان هنالك اختلافاً معنوياً بين مجموعة المرضى الاولى مع مجموعة الضبط فيما يتعلق بمستوى الكلوكوز في مصل الدم في حالة الصيام، مستوى اللبتين، المالونديلهايد، ومؤشر تصلب الشرايين فيما كان هنالك اختلافاً معنوياً بين مجموعة المرضى الثانية ومجموعة الضبط في مستوى الكلوكوز في مصل الدم في حالة الصيام، اللبتين، المالونديلهايد.

بعد العلاج كان هنالك زيادة معنوية في الكوليسترول في الدهون عالية الكثافة مع انخفاض معنوي في مستوى الانسولين، اللبتين والمالونديلهايد ومؤشر تصلب الشرايين لمرضى المجموعة الاولى فيما كان هنالك زيادة معنوية معدل كتلة الجسم مع انخفاض معنوي في مستوى اللبتين، المالونديلهايد الكوليسترول الكلي، الشحوم الثلاثية، الكوليسترول في الدهون واطئة الكثافة، والدهون واطئة الكثافة جداً ومؤشر تصلب الشرايين في مرضى المجموعة الثانية بالمقارنة مع فترة ما قبل العلاج.

بمقارنة التغيرات بين مجموعتي المرضى بعد العلاج كان هنالك انخفاضاً معنوياً في مستوى المالونديلهايد والكوليسترول الكلي في مرضى المجموعة الثانية بالمقارنة مع مرضى المجموعة الاولى.

الاستنتاج: السكتة الاقفاريه الحادة قد تكون مصحوبة باختلافات في مؤشرات السيطرة السكرية ، صورة الدهون ، علامات جهد الاكسدة ومستوى اللبتين في مصل الدم. العلاج الاضافي بفيتامين أي في الفترة الاولية تالي الاقفاريه نتج عنه انخفاضاً في جهد الاكسدة وتحسن في مفردات صورة الدهون.

Abstract

Aims: To evaluate parameters of glycemic control (fasting serum glucose "FSG", serum insulin level and insulin resistance), serum leptin, malondialdehyde "MDA" and lipid profile (total cholesterol "TC", triglyceride "TG", low density lipoprotein cholesterol LDL-c, high density lipoprotein cholesterol HDL-c, very low density lipoprotein cholesterol VLDL-c and atherogenic index "AI") and body mass index (BMI) in patients with ischemic stroke and to test the influence of vitamin E supplementation on these parameters, **Methods:** This study included 62 ischemic stroke patients and 28 healthy control subjects. Patients were randomly divided into 2 groups: group I (n=33) involved patients with ischemic stroke who assigned to receive conventional therapy and group 2 (n=28) included patients who received conventional

therapy with oral supplementation of vitamin E (400 IU/d) for 30 days. Fasting blood samples were initially obtained from all patients within 24-48 hours after the accident (before starting treatment) and from the controls and assay of FSG, serum insulin, leptin, MDA, TC, TG, HDL-c and calculation of insulin resistance, BMI, LDL-c,VLDL-c and AI using especial equation were done. For the patients groups, another fasting blood samples were taken after therapy and assessment of the parameters mentioned above were done, **Results:** Before therapy, there was a significant differences between patients in group one (on conventional therapy alone) and the controls with regard FSG, serum leptin, MDA, and AI, while there was a significant difference between patients in group 2 and the controls with regard FSG, serum leptin, MDA.

After therapy, there was a significant increase in HDL-c with significant decrease in serum insulin, leptin , MDA and AI in patients in group one, with significant increase in BMI and significant reduction in serum leptin, MDA, TC, TG, VLDL-c, LDL-c and AI in patients in group 2 compared to pre-therapy stages.

By comparison of the net differences of both groups after therapy, there was a significant reduction in the MDA and TC in patients in group 2 compared to patients in group one, **Conclusion:** Acute ischemic stroke might be associated with disturbances in some parameters of glycemic controls, lipid profile, elements of oxidative stress and serum leptin. Vitamin E supplementation during the early post ischemic period resulted in reduction in oxidative stress and improving some parameters of lipid profile.

Keywords: ischemic stroke, glycemic control, leptin, MDA, lipid profile, vitamin E.

Introduction

Stroke is a global health problem. It is the leading cause of adult disability and the 3rd leading cause of mortality worldwide[1]. Approximately 80% of strokes are ischemic in origin[2]. Ischemic stroke is caused by obstruction of blood flow to the brain, resulting in energy failure that initiate a complex series of metabolic events, ultimately causing neuronal death. One such critical metabolic event is activation of phospholipase A2 (PLA2), resulting in hydrolysis of membrane phospholipids and release of free fatty acids including arachidonic acid. Oxidative metabolism of arachidonic acid generates reactive oxygen species (ROS). Furthermore cardiolipin hydrolysis by mitochondrial PLA_2 disrupts the mitochondrial respiratory chain and increases production of ROS[3]. Focal cerebral ischemia is also associated with a local inflammatory reaction that contributes to the tissue damage[4]. ROS cause oxidative damage that may affect lipids, proteins, nucleic acids and other molecules. Quantification of lipid peroxidation end products is considered to be a measure of whole body oxidative damage. Serum malondialdehyde "MDA", a marker of lipid peroxidation is the most abundant aldehyde generated by the attack of free radicals on poly-unsaturated fatty acids of cell membranes and its measurement provides information of oxidative injury in vivo[5]. Patients with elevated blood glucose levels on admission to the hospitals, whether having known diabetes or not, have poorer recovery and more adverse outcomes after acute ischemic stroke than their non-diabetic counterparts[6]. Leptin receptors exist in many tissues and play a role in metabolism of lipids and carbohydrates as well as reproductive system, immune and inflammatory reactions[7]. There is a clear link between hyperleptinemia and atherosclerosis[8]. Furthermore the relationship between hyperinsulinemia and insulin resistance with atherosclerosis has been confirmed[9,10].

Changes in the lipid profile have been suggested as a risk factor for developing ischemic stroke[11]. The favorable vascular effect of antioxidant has been observed in vitro and animal models of atherosclerosis[12,13]. The aim of this study was to assess the glycemic controls (FSG, serum insulin and insulin resistance), serum leptin and lipid profile in patients with ischemic stroke and comparing the effects of conventional therapy with that of conventional therapy plus vitamin E (400IU/d) for one month on these parameters.

Patients and methods

Out of 65 patients with ischemic stroke, only 62 patients completed the follow-up study (49 males / 13 females) . Twenty eight healthy subjects, age and sex matched (23 males / 5 females) were also included as a control for the initial laboratory results.

This study was conducted in Al-Zahrawi Private Hospital in Mosul city from December 2011 to June 2012. Approval to conduct this study was obtained from Ethical Committees of the main health centre in Ninevah, Mosul City and the College of Medicine of the University of Mosul- Iraq.

All patients included in this study were initially diagnosed as having cerebrovascular accident (acute ischemic stroke) on the basis of full physical and neurological examination by neurologist. The diagnosis were then confirmed by either Magnetic Resonance Imaging (MRI) or Computerized Tomography (CT scan) of the brain. Patients with hemorrhagic stroke, intracranial tumor, hypertensive patients, diabetic patients with fasting serum glucose (FSG) > 150mg/dl or those requiring insulin therapy, patients with renal or hepatic diseases, were excluded. So as patients taking antioxidant vitamins during the week preceding the enrollment. For the controls, the criteria for selection were as follows, age > 55 years, healthy subjects, non-smokers, not taking vitamin supplementation.Patients were randomly divided into two groups: group 1 (n=33) involved patients with ischemic stroke who assigned to receive conventional therapy of them 6 were known diabetic on metformin therapy and group 2 (n=28) included patients who received conventional therapy with oral vitamin E capsule supplementation 400IU/d for 30 days of them 5 were diabetic on metformin therapy.

Conventional therapy involved administration of low dose of aspirin or clopidogrel, cinnerzine tablet(25 mg two to three times daily), folic acid 5 mg tablet, citcoline (Somazina- USA) 500-1000mg/d.

Fasting blood samples were initially obtained from all patients within 24-48 hours after accident, before starting treatment and from the controls with assay of serum MDA , FSG, serum insulin level, leptin and lipid profile (TC, TG, HD-c) with calculation of BMI, insulin resistance, LDL-c ,VLDL-c and atherogenic index (AI). For both patients groups another fasting blood samples were taken after treatment with either the conventional therapy or the conventional therapy plus vitamin E and assessment of the same parameters under study were done.

Malondialdehyde "MDA" were measured by the method outlined by Buege and Aust (1978)[14]. Serum glucose was measured by oxidase-perxidase colorimetric method[15], by using a kit supplied from Biocon (Germany). Serum insulin was measured by enzyme-linked immunabsorbent assay (ELISA) technique using a kit from Genway BioTech Inc (USA). Serum leptin was measured using ELISA technique with IBL leptin ELISA kit (Germany). Serum cholesterol (TC), high density lipoprotein cholesterol (HDL-c) and triglyceride (TG) concentration were

measured by enzymatic method using suitable kits supplied by Biolabo Company (France).

Calculation of low density lipoprotein cholesterol (LDL-c) concentration was done by the following equation:

LDL-c= TC-(HDL-c)- TG /2.2 mmol/L (16)

Calculation of serum VLDL-c was done according to the following equation: **VLDL-c= TG/2.2 mmol/l** (16)

Atherogenic index (AI) was calculated using the following equation:

AI= TC /HDL-c (17)

Insulin resistance was calculated using the following equation:

Insulin resistance = fasting serum glucose x serum insulin / 22.5 (18)

Body Mass Index (BMI) was calculated using the following equation:

BMI= Weight (kg) / Height (m^2) (19)

Statistical analysis

The data of the study subjected to statistical analysis were expressed as mean ± Standard Deviation (SD). Statistical comparisons were performed using ANOVA test, paired t-test and unpaired t-test. A P-value < 0.05 was considered to be statistically significant.

Results

The age and sex characteristics of both the patients and the controls were given in tables 1 and 2.

There was a significant difference between patients in group 1 (before conventional therapy) and the controls with regard FSG, serum leptin, MDA and AI, with insignificant differences in other parameters under study (Table 3).

There was a significant differences between patients with in group 2 (before conventional therapy plus vitamin E therapy) and the controls with regard FSG, serum leptin, and MDA, with insignificant differences with regard BMI , serum insulin, insulin resistance, TC, TG, VLDL-c, LDL-c and HDL-c and AI(Table 4)

After therapy, patients in group one, showed a significant increase in HDL-c, with significant reduction in serum insulin, leptin , MDA and AI (Table 5), while there was a significant increase in BMI, with a significant reduction in serum leptin, MDA, TC, TG, VLDL-c, LDL-c and AI in group two patients (Table 6), in comparison to pre-therapy stage.

By comparison of the net differences of both groups after therapy there was a significant reduction in MDA and TC in group 2 in comparison with group 1 (Table 7).

Table 1. The age characteristics of both patients groups and the controls.

Group	Age (years)				p-value
	Min	Max	Mean±SD	95% CI	
Conventional treatment + Vit E	59.00	76.00	67.07±4.28	65.40-68.73	0.4
conventional treatment	58.00	74.00	65.57±4.72	63.90-67.25	
Control	56.00	74.00	65.71±5.08	63.74-67.68	

ANOVA test

Table 2. The Sex characteristics of both patients groups and the controls.

Group	Male No. (%)	Female No. (%)	P-value
Conventional treatment + Vit E	23 (25.8)	5 (5.6)	0.9
conventional treatment	26 (29.2)	7 (7.9)	
Control	23 (25.8)	5 (5.6)	
Total	72 (80.9)	17 (19.1)	

X^2 test

Table 3.Comparison of measured parameters between patients in group 1 (before treatment with conventional therapy alone) and the control group.

	BMI (kg/m^2)				p-value
	Min	Max	Mean ± SD	95% CI	
Before conventional alone	20.02	26.01	23.06±1.44	22.54-23.57	0.5
Control	20.70	25.30	22.87±1.22	22.40-23.35	
	FBS (mg/dl)				
Before conventional alone	93.00	130.00	108.78±9.75	105.32-112.24	0.0001*
Control	75.00	110.00	93.25±10.11	89.32-97.17	
	Insulin (µU/ml)				
Before conventional alone	2.10	19.50	5.29±3.52	4.04-6.54	0.6
Control	2.00	12.10	4.96±2.45	4.01-5.92	
	Insulin resistance				
Before conventional alone	0.59	4.56	1.33±0.79	1.05-1.61	0.1
Control	0.44	2.24	1.10±0.48	0.91-1.29	
	S. leptin (ng/ml)				
Before conventional alone	0.59	4.56	1.33±0.79	1.05-1.61	0.003*
Control	0.44	2.24	1.10±0.48	0.91-1.29	
	MDA (µmol/l)				
Before conventional alone	1.20	2.30	1.84±0.29	1.74-1.94	0.0001*
Control	0.60	1.20	0.94±0.19	0.86-1.01	
	Total cholesterol (mg/dl)				
Before conventional alone	100.00	240.00	176.75±34.68	164.45-189.05	0.1
Control	100.00	220.00	166.14±27.69	155.40-176.88	
	Triglyceride (mg/dl)				
Before conventional alone	75.00	280.00	139.45±48.92	122.10-156.80	0.2
Control	78.00	180.00	127.50±29.04	116.23-138.76	
	VLDL-c (mg/dl)				
Before conventional alone	15.00	56.00	27.89±9.78	24.42-31.36	0.2
Control	15.60	36.00	25.50±5.80	23.24-27.75	
	LDL-c (mg/dl)				
Before conventional alone	30.40	166.00	107.29±32.65	95.71-118.86	0.1
Control	29.00	156.00	94.71±28.85	83.52-105.90	
	HDL-c (mg/dl)				
Before conventional alone	32.00	57.00	41.57±6.57	39.24-43.90	0.08
Control	38.00	58.00	45.92±5.75	43.69-48.15	
	Atherogenic index				
Before conventional alone	2.04	6.86	4.39±1.26	3.94-4.84	0.01*
Control	2.04	5.36	3.69±0.86	3.35-4.02	

Analysis were performed by the of independent two sample student t-test
*significant differences

Table 4.Comparison of measured parameters between patients in group 2 (before treatment with conventional therapy + Vit E) and the control group.

	BMI (kg/m^2)				p-value
	Min	Max	Mean ± SD	95% CI	
Before conventional + Vit E	20.20	26.50	22.91±1.65	22.27-23.55	0.9
Control	20.70	25.30	22.87±1.22	22.40-23.35	
	FBS (mg/dl)				
Before conventional + Vit E	78.00	125.00	106.28±13.02	101.23-111.33	0.0001*
Control	75.00	110.00	93.25±10.11	89.32-97.17	
	Insulin (µU/ml)				
Before conventional + Vit E	2.00	20.10	5.41±3.76	3.95-6.87	0.6
Control	2.00	12.10	4.96±2.45	4.01-5.92	
	Insulin resistance				
Before conventional + Vit E	0.01	4.21	1.31±0.79	1.00-1.62	0.2
Control	0.44	2.24	1.10±0.48	0.91-1.29	
	S. leptin (ng/ml)				
Before conventional + Vit E	1.90	20.50	9.41±4.60	7.62-11.20	0.002*
Control	0.50	10.90	5.93±3.15	4.71-7.16	
	MDA (µmol/l)				
Before conventional + Vit E	1.50	2.30	1.85±0.20	1.77-1.93	0.001*
Control	0.60	1.20	0.94±0.19	0.86-1.01	
	Total cholesterol (mg/dl)				
Before conventional + Vit E	100.00	240.00	175.53±35.02	161.95-189.11	0.2
Control	100.00	220.00	166.14±27.69	155.40-176.88	
	Triglyceride (mg/dl)				
Before conventional + Vit E	75.00	260.00	144.07±46.82	125.91-162.22	0.1
Control	78.00	180.00	127.50±29.04	116.23-138.76	
	VLDL-c (mg/dl)				
Before conventional + Vit E	15.00	52.00	28.81±9.36	25.18-32.44	0.1
Control	15.60	36.00	25.50±5.80	23.24-27.75	
	LDL-c (mg/dl)				
Before conventional + Vit E	32.00	168.00	103.61±32.18	91.13-	0.2
Control	29.00	156.00	94.71±28.85	83.52-105.90	
	HDL-c (mg/dl)				
Before conventional + Vit E	32.00	56.00	43.10±6.84	40.45-45.76	0.1
Control	38.00	58.00	45.92±5.75	43.69-48.15	
	Atherogenic index				
Before conventional + Vit E	2.00	7.50	4.22±1.30	3.71-4.72	0.08
Control	2.04	5.36	3.69±0.86	3.35-4.02	

Analysis were performed by the of independent two sample student t-test
*significant differences

Table 5.Comparison of measured parameters before and after conventional therapy alone.

	BMI			p-value
	Mean ± SD	Mean difference ±SD	95% CI of difference	
Before treatment	23.06±1.44	-0.10±0.45	-0.26-0.05	0.1
After treatment	23.16±1.44			
	FBS (mg/dl)			
Before treatment	108.78±9.75	0.78±7.24	-1.78-3.35	0.5
After treatment	108.00±10.51			
	Insulin (µU/ml)			
Before treatment	5.29±3.52	0.12±0.34	0.00-0.24	0.04*
After treatment	5.16±3.54			
	Insulin resistance			
Before treatment	1.33±0.79	-0.02±0.20	-0.10-0.04	0.4
After treatment	1.36±0.92			
	Leptin (ng/ml)			
Before treatment	8.93±4.45	0.25±0.56	0.05-0.45	0.01*
After treatment	8.68±4.17			
	MDA(µmol/l)			
Before treatment	1.84±0.29	0.46±0.23	0.38-0.55	0.0001*
After treatment	1.37±0.18			
	Cholesterol (mg/dl)			
Before treatment	176.75±34.68	-1.30±19.71	-8.29-5.68	0. 7
After treatment	178.06±30.40			
	Triglyceride (mg/dl)			
Before treatment	139.45±48.92	4.48±26.07	-4.76-13.73	0.3
After treatment	134.96±45.23			
	VLDL-c (mg/dl)			
Before treatment	27.89±9.78	0.89±5.21	-0.95-2.74	0.3
After treatment	26.99±9.04			
	LDL-c (mg/dl)			
Before treatment	107.29±32.65	-0.86±21.46	-8.47-6.74	0.8
After treatment	108.15±28.16			
	HDL-c (mg/dl)			
Before treatment	41.57±6.57	-1.33±2.72	-2.29- -0.36	0.008*
After treatment	42.90±6.23			
	Atherogenic index			
Before treatment	4.39±1.26	0.15±0.59	-0.05-0.36	0.002*
After treatment	4.24±1.01			

Analysis were performed by the paired sample student t-test
*significant differences

Table 6.Comparison of measured parameters before and after conventional treatment + vit E.

	BMI			p-value
	Mean ± SD	Mean difference ±SD	95% CI of difference	
Before treatment	22.91±1.65	0.06±0.11	0.01-0.10	0.009*
After treatment	22.85±1.61			
	FBS (mg/dl)			
Before treatment	106.28±13.02	2.35±7.39	-0.51-5.22	0.1
After treatment	103.92±10.56			
	Insulin (µU/ml)			
Before treatment	5.41±3.76	0.01±0.34	-0.11-0.151	0.7
After treatment	5.39±3.66			
	Insulin resistance			
Before treatment	1.31±0.79	-0.00±0.23	-0.08-0.08	0.9
After treatment	1.31±0.80			
	Leptin (ng/ml)			
Before treatment	9.41±4.60	0.33±0.60	0.10-0.57	0.007*
After treatment	9.07±4.25			
	MDA(µmol/l)			
Before treatment	1.85±0.20	0.76±0.17	0.69-0.82	0.0001*
After treatment	1.09±0.20			
	Cholesterol (mg/dl)			
Before treatment	175.53±35.02	5.17±9.27	1.58-8.77	0.006*
After treatment	170.35±32.60			
	Triglyceride (mg/dl)			
Before treatment	144.07±46.82	6.75±12.75	1.80-11.69	0.009*
After treatment	137.32±39.54			
	VLDL-c (mg/dl)			
Before treatment	28.81±9.36	1.35±2.55	0.36-2.33	0.009*
After treatment	27.46±7.90			
	LDL-c (mg/dl)			
Before treatment	103.61±32.18	4.29±9.25	0.70-7.88	0.02*
After treatment	99.32±29.34			
	HDL-c (mg/dl)			
Before treatment	43.10±6.84	-0.46±2.42	-1.40-0.47	0.3
After treatment	43.57±5.52			
	Atherogenic index			
Before treatment	4.22±1.30	0.21±0.33	0.08-0.34	0.002*
After treatment	4.00±1.09			

Analysis were performed by the paired sample student t-test

*significant differences

Table 7.Comparison of net differences after both lines of therapy.

	BMI (kg/m^2)				p-value
	Min	Max	Mean ± SD	95% CI	
Traditional treatment + Vit E	-0.30	0.20	-0.06±0.11	-0.10- -0.01	0.04*
Traditional treatment	-0.40	1.90	0.10±0.45	-0.05-0.26	
	FBS (mg/dl)				
Traditional treatment + Vit E	-20.00	15.00	-2.35±7.39	-5.22-0.51	0.4
Traditional treatment	-10.00	15.00	-0.78±7.24	-3.35-1.78	
	S.Insulin (µU/ml)				
Traditional treatment + Vit E	-0.60	1.55	-0.018±0.34	-0.15-0.11	0.2
Traditional treatment	-1.70	0.30	-0.12±0.34	-0.24- -0.00	
	Insulin resistance ()				
Traditional treatment + Vit E	-0.44	0.86	0.00±0.23	-0.08-0.08	0.6
Traditional treatment	-0.33	0.82	0.02±0.20	-0.04-0.10	
	S. leptin (ng/ml)				
Traditional treatment + Vit E	-2.30	0.70	-0.33±0.60	-0.57- -0.10	0.5
Traditional treatment	-2.40	0.70	-0.25±0.56	-0.45- -0.05	
	MDA (µmol/l)				
Traditional treatment + Vit E	-1.30	-0.40	-0.76±0.17	-0.82- -0.69	0.0001*
Traditional treatment	-1.00	0.20	-0.46±0.23	-0.55- -0.38	
	Total cholesterol (mg/dl)				
Traditional treatment + Vit E	-20.00	15.00	-5.17±9.27	-8.77- -1.58	0.09
Traditional treatment	-30.00	80.00	1.30±19.71	-5.68-8.29	
	Triglyceride (mg/dl)				
Traditional treatment + Vit E	-40.00	20.00	-6.75±12.75	-11.69- -1.80	0.6
Traditional treatment	-95.00	85.00	-4.48±26.07	-13.73-4.76	
	VLDL-c (mg/dl)				
Traditional treatment + Vit E	-8.00	4.00	-1.35±2.55	-2.33- -0.36	0.6
Traditional treatment	-19.00	17.00	-0.89±5.21	-2.74-0.95	
	LDL-c (mg/dl)				
Traditional treatment + Vit E	-20.00	15.00	-4.29±9.25	-7.88- -0.70	0.2
Traditional treatment	-45.00	77.00	0.86±21.46	-6.74-8.47	
	HDL-c (mg/dl)				
Traditional treatment + Vit E	-8.00	4.00	0.46±2.42	-0.47-1.40	0.1
Traditional treatment	-5.00	8.00	1.33±2.72	0.36-2.29	
	Atherogenic index				
Traditional treatment + Vit E	-0.93/	0.61	-0.21±0.33	-0.34--0.08	0.6
Traditional treatment	-1.30	1.43	-0.15±0.59	-0.36-0.05	

Analysis were performed by independent two sample student t-test
*significant differences

Discussion

In this study there was a significant differences between patients with ischemic stroke (before therapy) in group one with regard FSG, serum leptin, MDA, HDL-c and AI , and in FSG, serum leptin ,MDA in group two and the controls.

Our findings with regard FSG, were in agreement with Corstjens et al., 2006 [20]. They reported that the prevalence of hyperglycemia in critically ill patients is considerable and there is a pathophysiological link between acute hyperglycemia an complications / mortality, and that underlying mechanisms my differs considerably in various situations of stress and various clinical conditions. Fuentes et al., 2009[21], studied the glycemia in acute stroke patients and concluded that a glucose level ≥155mg/dl at any time within the first 48 hours after stroke onset was associated with poor stroke-related outcomes independently of stroke severity, infarct volume, diabetes or age. Several studies have demonstrated increased insulin responses and elevated glucose levels after oral glucose

stimulation[22,23] or elevated fasting insulin levels in patients with cerebrovascular events[24].

Regarding serum leptin, different studies have confirmed leptin as a strong predictor in cerebrovascular accident (CVA) and have reported that serum leptin level is higher than normal in CVA patients[25,26]. The role of leptin in the atherosclerosis phenomenon is probably one of its significant roles, as follows: first many obese individuals have a hypothalamic resistance to leptin, which leads to an increase in leptin serum level. By causing endothelial dysfunction, oxidative stress, platelet aggregation and inflammatory reactions, hyperleptinmia will lead to atherosclerosis[8].

Regarding serum MDA levels, and in accordance with our findings, several studies which have been done to evaluate oxidative stress, antioxidant status and markers of inflammation in ischemic stroke patients, have shown enhancement of levels of markers of oxidative stress. Research aimed at evaluating oxidative modified molecules in ischemic stroke patients in the early period of ischemic stroke revealed an increase in the blood, cerebrospinal fluid (CSF) or salivary concentrations of lipid peroxides, protein carbonyl, homocystein, nitric oxide and of malondealdehyde[27,28,29]. There are possible reasons for increased lipid peroxidation in ischemic stroke. First the brain cellular membranes is very rich in polyunsaturated fatty acid side chains which are especially sensitive to free radical attack. Second it has a low content of antioxidant enzymes, while it contain a significant amount of iron despite its iron binding capacity is not very high. Iron ions are known to stimulate free radical generation[27,30].

With regard lipid profile in patients with ischemic stroke, Aggarwal et al., 1995[31], reported that serum TC, LDL-c, and TG were significantly higher in CVA patients on day one and lipid levels reduced significantly on day 7 in respect to day one. Jasim et al., 2010[32], reported a significant decrease in TC, HDL-c, and LDL-c with a significant increase in TG in CVA patients in comparison with healthy controls. Togha et al., 2011[11], conducted that high LDL-c can be considered as a risk factor for both ischemic and hemorrhagic cerebral events. on the other hand Nagaraj et al., 2011[39], reported no significant differences in lipid profile between controls and thrombotic stroke patients.

After therapy with conventional line plus vitamin E, the study reported a significant increase in BMI , with a significant reduction in serum MDA, leptin, TC, TG, VLDL-c, LDL-c and AI in comparison to pre-therapy stage.

Brain damage can be caused by the formation of ROS, which mediate oxidative damage, inflammation and apoptosis[34]. Therefore in addition to standard therapeutic approaches, one alternative strategy for achieving neuroprotection can be the stimulation of an endogenous antioxidant system[35]. There is strong evidence that lipid peroxidation with accumulation of both conjugated dienes and thiobarburate reactive material is consistently found when cerebral ischemia is followed by reperfusion and there is some evidence that this effect is enhanced by poor α-tocopherol and can be mitigated by supplementation with this vitamin[36]. Manzella et al., 2001[37], reported that vitamin E supplementation in a dose of 600IU/d reduced HbAIc, plasma insulin, insulin resistance and oxidative stress indexes. Manning et al., 2004[38] concluded that high dose vitamin E supplementation (800IU/d) for 3 months improves insulin action, decreases plasma insulin and glucose level by decreasing cellular oxidant stress, altering membrane properties and decreasing inflammatory activity.

Regarding lipid profile, most studies with reagent effects of vitamin E on lipid profile came in diabetic patients. Paolisso et al., 1993[39] and in agreement with our findings, reported that vitamin E causes a reduction in TC, TG and LDL-c. Jain et al., 1996[40], reported that vitamin E in a daily dose of 100 IU/d in diabetic patients causes a significant reduction in TG, while other studies did not shows effects of vitamin E

supplementation on lipid profile parameters[41,42].

The only published study with regard serum leptin level and vitamin E supplementation reported by Shen et al., 2010[43]. They concluded that the administration of vitamin E decreases leptin and adiponectin expression in obese rats.

Regarding effects of vitamin E supplementation and BMI only one published study reported by Rashidi et al., 2011[44]. They concluded that vitamin E and zinc supplementation in patients with beta-thalassemia major resulted in a significant increase in BMI without reasonable explanation.

This might be the first study concerning patients with ischemic stroke , before and after either conventional therapy or conventional therapy plus vitamin E 400IU/d for one month, evaluating aspects of glycemic control (FSG, serum insulin and insulin resistance) serum leptin, MDA, lipid profile and BMI.

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