Asian Journal of Cardiology Research

4(2): 27-37, 2021; Article no.AJCR.66904

Treatment with Omega-3 and L-Carnitine Improve Cardiac and Renal Complications in Metabolic Syndrome-Induced Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Author EAZ designed the study, performed the statistical analysis, wrote the protocol, managed the analyses of the study, managed the literature searches and wrote the first draft of the manuscript. Authors HAAE and AAAS designed the study, wrote the protocol and reviewed the first draft of the manuscript and author AEMKEM managed the analyses of the study. Author AAZ managed the literature searches. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Dr. Sam Said, Hospital Group Twente, Netherlands.
Reviewers:
(1) Ivonilce Venturi, Brazil.
(2) Ricardo Fernandez, Federal University of Parana (UFPR), Brazil.
Complete Peer review History: http://www.sdiarticle4.com/review-history/66904

Original Research Article

Received 28 January 2021
Accepted 04 April 2021
Published 09 April 2021

ABSTRACT

Background: Frequent consumption of fructose and saturated fatty acids increase risk of metabolic syndrome (MS). Features of MS include insulin resistance, dyslipidemia, visceral obesity, and hypertension. The aim of this study was to investigate the role of Omega-3and L-carnitine in ameliorating features of MS.
Methods: Induction of MS in rats by high-fructose high-fat fed diet was certain after 8 weeks. Animals were divided into four groups: normal control, MS control group given saline, MS groups given Omega-3 (260 mg/kg), and L-carnitine (200 mg/kg) daily for 4 weeks. Blood pressure, heart rate, CK-MB, and lactate dehydrogenase (LDH) were estimated. Also, renal function and

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antioxidant activity were evaluated. In addition, to C-reactive protein (CRP), and fibrinogen determined.
Results: Omega-3and L-carnitine caused decrease in both -induced increase in blood pressure and heart rate. They reduced creatinine, blood urea nitrogen (BUN), uric acid, albumin, and malondialdehyde (MDA) with increased glutathione (GSH), and superoxide dismutase (SOD). Drugs also decreased CRP, and fibrinogen compared with MS control group.
Conclusion: Omega-3and L-carnitine ameliorate cardiac and renal complication of MS via their antioxidant activity

Keywords: Metabolic syndrome; omega-3; l-carnitine; antioxidant activity.

1. INTRODUCTION

The prevalence of metabolic syndrome has increased worldwide mainly due to the obesity epidemic [1]. Although there was no accepted central underlying mechanism for the pathogenesis of the metabolic syndrome, two features; the visceral obesity and impaired insulin in particular stand out as potential etiologies underlying the associated abnormalities of MS [2].

Many authorities also recognize metabolic syndrome as a pro-inflammatory and prothrombotic state, although these features are not included in the formal definition [3].

Fructose feeding induced ventricular dilatation, ventricular hypertrophy, decreased ventricular contractile function, and infiltration of inflammatory cells in heart [4].

Insulin resistance has been proposed as a strong predictor for the development of hypertension [5]. Substituting the starch carbohydrate content in laboratory rodent diet with fructose resulted in elevated blood pressure within a period of 6-8 weeks. The effects of high fructose feeding have been reported to be concentration and time-dependent [6].

Vascular dysfunction due to a fructose-rich diet has been reported in the rat, and it is recognized that vascular dysfunction in metabolic syndrome is associated with increased vasoconstrictor sensitivity and production of vascular superoxide anions [7].

It is evident that this state of chronic inflammation may contribute to the chronic illnesses associated with obesity, namely atherosclerosis, dyslipidemia and insulin resistance [8]. Additionally, CRP is emerging as an independent and strong predictor and mediator of cardiovascular diseases [9].

S´anchez-Lozada et al., [10] reported functional changes including elevated plasma creatinine and albuminuria and morphological changes including fatty infiltration and thickening of glomeruli have been reported after 60 days of fructose feeding in rat [11].

Oxygen-derived free radical reactions have been implicated in the pathogenesis of many human diseases/disorders, including cardiovascular disorders, renal disorders and, diabetes [12].

Nature has endowed each cell with adequate protective mechanisms against any harmful effects of free radicals. Superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, thiols, and disulfide bonding are buffering systems in every cell [13].

Nutraceuticals provide a rich source of antioxidants to overcome the action of ROS (Reactive oxygen species) as they can reduce free radical formation and scavenge free radicals [14].

Omega-3 polyunsaturated fatty acids (PUFAs) are long chain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) found in plants and marine sources [15]. The best prevention of cardiovascular diseases appears to be achieved by replacing saturated fat with omega-3 unsaturated fatty acids [16]. Similarly, increased intakes of marine omega-3 can result in decreased triglycerides, fibrinogen and platelet aggregation, which are considered to be beneficial for cardiovascular diseases [17].

L- carnitine (L- b- hydroxyl – c - N-trimethylaminobutyric acid) is a small, water soluble, quaternary amine [18]. L-carnitine plays an essential role in transportation of long-chain fatty acids across the inner mitochondrial membrane for beta-oxidation and energy production [19]. Furthermore, it has been theorized that its absence may contribute to

hyperlipidemia, particularly hypertriglyceridaemia [20,21].

The aim of the study was to investigate the role of omega-3 and L-carnitine on MS-induced cardiovascular complications.

2. MATERIALS AND METHODS

2.1 Animals

Twenty-four male Sprague Dawley rats weighting 200 to 230 g were used in the current study. They were purchased from the animal house of the National Research Center Institute (Cairo, Egypt). During the study, the animals were housed under conventional laboratory conditions on a 12 hours light/dark cycle and constant temperature (22 ± 1°C).

2.2 Drugs and Chemicals

Omega-3 oil (EPA 13% and DHA 9%) was purchased from (Montana Pharmaceuticals, Egypt). L-Carnitine was purchased from (Mepaco Co, Egypt). Refined Fructose powder was purchased from El Nasr Pharmaceutical, (Cairo, Egypt). Heart rate and blood pressure was indirectly measured by non-invasive blood pressure monitor (ML 125 NIBP, AD Instruments, Australia) from the tail of conscious rats by the tail-cuff technique. Albumin, creatinine, blood urea nitrogen, uric acid, lactate dehydrogenase (LDH), creatine kinase-MB (CK-MB), C-reactive protein, and fibrinogen kits were purchased from Spectrum Diagnostics, (Obour, Egypt). Glutathione, MDA, and SOD activity were estimated. kits were purchased from (Biodiagnostic, Egypt).

2.3 Experimental Design

MS was induced by feeding rats a high-fat diet consisting of standard rodent chow in addition to 10% saturated fat, 3% NaCl, and fructose 20% solution in drinking water for 12 weeks (Table 1) according to modified method described by Calvo-Ochoa et al. [22] Body weight was determined every week to prove that animals developed obesity.

Diet and fructose solution were freshly prepared every day. Rats were provided with a high-fructose high-fat diet (HFHFD) for 12 weeks. Induction of MS in rats by high-fructose high-fat fed diet was certain after 8 weeks. Rats were randomly allocated into four groups (six rats each) as follows:

Group 1: this group received normal laboratory diet, tap water ad libitum and given saline daily during the time of experiment.
Group 2: this group fed HFHFD for 12 weeks and given saline daily during the time of experiment.
Group 3: this group fed HFHFD for 12 weeks and omega-3 oil (260mg/kg) for the last 4 weeks [23].
Group 4: this group fed HFHFD for 12 weeks and L-carnitine (200 mg/kg) for the last 4 weeks [24].

At the end of treatment, the animals were fasted for 12 hours weighed and blood samples were withdrawn from the retro-orbital plexus under light anesthesia [25]. Plasma was separated by centrifugation at (1,509g, 15 min, 4°C) and divided into small aliquots that were stored for the estimation of the levels of GSH, MDA, and SOD. In addition, the separated plasma was used for the estimation of creatinine, BUN, uric acid, plasmatic albumin, LDH, CK-MB, CRP, and fibrinogen.

Furthermore, systolic blood pressure and heart rate of animals were indirectly measured by the tail-cuff technique, where tail of the animals were warmed for 30 min at 28°C to dilate the tail artery in a thermostatically controlled heating cabinet (Ugo Basille, Italy) for better detection of tail artery pulse, the tail was passed through a miniaturized cuff and tail-cuff sensor that was connected to an amplified pulse was recorded during automatic inflation and deflation of the cuff. The average of at least three measurements was taken at each occasion. Heart rate was recorded automatically by a counter triggered by pulse wave.

2.4 Biochemical Assays

Plasma sample were used for estimation of the level of creatinine, BUN, uric acid, albumin, LDH, CK-MB, CRP, and fibrinogen using colorimetric method.

An aliquot of heparinized blood was used for estimating its glutathione contents and the other aliquot was centrifuged for separation of plasma and red blood cells for measurement of lipid peroxide content as MDA nmol /ml plasma. The remaining RBCs pellets were used to assess the SOD activity.

Table 1. Nutritional composition of diets

Nutrient composition	Normal control	HFHFD
Fat (%)	4	14
Carbohydrates (total) (%)	50	50
Fructose (%)	0	20
Maltodextrin 10 (%)	15	15
Protein (%)	22	22

Abbreviation: HFHFD, high-fructose high-fat diet

2.5 Statistical Analysis

Statistical analysis was performed using one-way analysis of variance followed by Tukey's post hoc test using SPSS software v21 (SPSS Inc, Chicago, IL). Data were expressed as mean ± standard deviation (SD) and P values of less than 0.05 were considered as statistically different.

3. RESULTS

During the 8 weeks feeding of HFHFD, normal control rats demonstrated a systolic blood pressure value of 115±1.87 (mm Hg) (Table 2). Maintaining rats on HFHFD for 12 weeks increased systolic blood pressure by 57% compared to normal control (Table 2). Omega-3 oil, and L-carnitine treated groups showed a significant (P<0.05) decrease in systolic blood pressure by 36% and 47% respectively when compared to MS-induced group.

Rats kept on normal laboratory chow exhibited diastolic blood pressure value of 70±7.69 (mm Hg) (Table 2). Metabolic syndrome was associated with an elevation in diastolic blood pressure level by 36% compared to normal control (Table 2). Omega-3 oil, and L-carnitine treated groups showed a significant (P<0.05) decrease in the levels of diastolic blood pressure by 26%, and 32% respectively when compared to MS-induced group.

Maintaining rats on normal laboratory chow exhibited mean blood pressure value of 85±5.25 (mm Hg) (Table 2). Meanwhile MS-induced rats exhibited a significant increase in mean blood pressure by 45% compared to normal control (Table 2). Administration of omega-3 oil, and L-carnitine under the same condition caused a significant (P<0.05) decrease in mean blood pressure compared to the MS-induced rats by 31% and 39% respectively.

Normal control rats demonstrated a heart rate value of 309±13.87 (beat/min) (Table 2). Meanwhile, MS-induced rats exhibited an increase in heart rate by 40% compared to normal control (Table 2). Administration of omega-3 oil, and L-carnitine under the same condition caused a significant (P<0.05) decrease in heart rate compared to the MS-induced rats by 62% and 66% respectively.

Rats kept on normal laboratory chow exhibited total CK-MB value of 101.5±4.32 (U/l) (Table 3). Metabolic syndrome was associated with an elevation in CK-MB level by 210% compared to normal control (Table 3). Omega-3 oil, and L-carnitine treated groups showed a significant (P<0.05) decrease in the levels of CK-MB by 74% and 78% respectively when compared to MS-induced group.

Maintaining rats on normal laboratory chow exhibited LDH value of 115.67±2.31 (U/l) (Table 3). Meanwhile MS-induced rats exhibited a significant increase in LDH level by 132% compared to normal control (Table 3). Administration of Omega-3 oil, and L-carnitine under the same condition caused a significant (P<0.05) decrease in LDH level compared to the MS-induced rats by 71%, and 73% respectively.

Normal control rats demonstrated a CRP value of 2.77±0.13 (mg/l) (Table 3). Maintaining rats on HFHFD for 12 weeks increased CRP level by 432% compared to normal control (Table 3). Omega-3 oil, and L-carnitine, treated groups showed a significant (P<0.05) decrease in the levels of CRP by 80% and 84% respectively when compared to MS-induced group.

Rats kept on normal laboratory chow exhibited creatinine value of 0.55±0.02 (mg/dl) (Table 4). Metabolic syndrome was associated with an elevation in creatinine level by 42% compared to normal control (Table 4). Omega-3 oil, and L-carnitine treated groups showed a significant (P<0.05) decrease in the levels of creatinine by 42% and 60% respectively when compared to MS-induced group.

Table 2. Effect of omega-3 oil, and L-carnitine on blood pressure and heart rate in MS-induced rats

Treatment \ Parameters		Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)	Mean blood pressure (mm Hg)	Heart rate (beat/min)
Normal control		115±1.87	70±7.69	85±5.25	309±13.87
MS-induced	Control	180±7.35#	95±5.47#	123±6.23#	433±9.81#
	+ Omega-3 (260 mg/kg)	115±2.16*	70±6.89*	85±4.79*	164±2.73#*
	+ L-Carnitine (200 mg/kg)	95±7.08#*	65±5.48*	75±3.74*	145±2.06#*

Abbreviations: ANOVA, analysis of variance; MS, metabolic syndrome. Results are expressed as mean ± SD (n = 6). The statistical comparison of difference between the control and the treated groups were carried out using one-way ANOVA. Relative organ weight = (organ weight/body weight) × 100

**Statistically significant from the MS-induced rats treated with HFHFD only at P < 0.05.*

#Statistically significant from the control values at P < 0.05

Table 3. Effect of omega-3 oil, and L-carnitine on pathophysiological cardiovascular parameters in MS-induced rats

Treatment \ Parameters		CK-MB (U/l)	Lactate dehydrogenase; LDH (U/l)	C reactive protein; CRP (mg/l)
Normal control		101.5±4.32	115.67±2.31	2.77±0.13
MS-induced	Control	315.07±15.15#	268.83±6.24#	14.73±1.64#
	+ Omega-3 (260 mg/kg)	81.67±4.08#*	77.83±3.97#*	2.92±0.22*
	+ L-Carnitine (200 mg/kg)	70.17±3.31#*	71.67±2.16#*	2.38±0.23*

Abbreviations: ANOVA, analysis of variance; CK-MB, Creatine kinase-MB; LDH, Lactate dehydrogenase, CRP; C-reactive protein; MS, metabolic syndrome. Results are expressed as mean ± SD (n = 6). The statistical comparison of difference between the control and the treated groups were carried out using one-way ANOVA.

**Statistically significant from the MS-induced rats treated with HFHFD only at P < 0.05.*

#Statistically significant from the control values at P < 0.05.

Table 4. Effect of omega-3 oil, and L-carnitine on kidney function in MS-induced rats

Treatment \ Parameters		Creatinine (mg/dl)	Uric acid (mg/dl)	BUN (mg/dl)	plasmatic Albumin (g/dl)
Normal control		0.55±0.02	1.13±0.06	17.97±2.44	3.58±0.23
MS-induced	Control	0.78±0.03#	4.97±0.11#	20.32±3.6	3.05±0.14
	+ Omega-3 (260 mg/kg)	0.45±0.02#*	1.73±0.19#*	14.67±1.86#*	3.75±0.39*
	+ L-Carnitine (200mg/kg)	0.31±0.01#*	1.87±0.12#*	11.38±1.91#*	3.77±0.22*

Abbreviations: ANOVA, analysis of variance; BUN; blood urea nitrogen; MS, metabolic syndrome. Results are expressed as mean ± SD (n = 6). The statistical comparison of difference between the control and the treated groups were carried out using one-way ANOVA.

**Statistically significant from the MS-induced rats treated with HFHFD only at P < 0.05.*

#Statistically significant from the control values at P < 0.05.

Maintaining rats on normal laboratory chow exhibited uric acid value of 1.13±0.06 (mg/dl) (Table 4). Meanwhile MS-induced rats exhibited a significant increase in uric acid level by 340% compared to normal control (Table 4). Administration of omega-3 oil, and L-carnitine under the same condition caused a significant (P<0.05) decrease in uric acid level compared to the MS-induced rats by 65% and 62% respectively.

Normal control rats demonstrated a BUN value of 17.97±2.44 (mg/dl) (Table 4). Maintaining rats on HFHFD for 12 weeks increased BUN level by 13% compared to normal control (Table 4). Omega-3 oil, and L-carnitine treated groups showed a significant (P<0.05) decrease in the levels of BUN by 28% and 44%, % respectively when compared to MS-induced group.

Rats kept on normal laboratory chow exhibited plasmatic albumin value of 3.58±0.23 (g/dl) (Table 4). Metabolic syndrome was associated with reduction in albumin level by 15% compared to normal control (Table 4). Omega-3 oil, and L-carnitine treated groups showed a significant (P<0.05) increase in the levels of plasmatic albumin by 23% and 24% respectively when compared to MS-induced group.

Normal control rats demonstrated a blood fibrinogen value of 227.33 ± 1.63 (mg/dl) (Table 5). MS-induced rats demonstrated an increase in the blood fibrinogen level by 62% compared to normal control (Table 5). Omega-3 oil, and L-carnitine treated groups showed a significant (P<0.05) decrease in the levels of fibrinogen by 42%, and 40% respectively when compared to MS-induced group.

Normal control rats demonstrated MDA value of 1.59±0.07 (nmol/ml) (Table 6). Maintaining rats on HFHFD for 12 weeks increased MDA by 214% compared to normal control (Table 6). Omega-3 oil, and L-carnitine treated groups showed a significant (P<0.05) decrease in MDA by 75% and 73% respectively when compared to MS-induced group.

Rats kept on normal laboratory chow exhibited glutathione value of 9.813±0.63 (mg/dl) (Table 6). Metabolic syndrome was associated with a lowered glutathione level by 31% compared to normal control (Table 6). Omega-3 oil, and L-carnitine treated groups showed a significant (P<0.05) increase in the levels of glutathione by 403%, and 360% respectively when compared to MS-induced group.

Maintaining rats on normal laboratory chow exhibited SOD value of 11.57±0.51 (u/l) (Table 6). Meanwhile MS-induced rats exhibited a significant decrease in SOD by 32% compared to normal control (Table 6). Administration of omega-3 oil, and L-carnitine under the same condition caused a significant (P<0.05) increase in SOD level compared to the MS-induced rats by 317% and 337% respectively.

4. DISCUSSION

In the present study, 8 weeks of feeding rats with HFHFD resulted in metabolic syndrome manifested by elevated oxidative stress, blood pressure and heart rate. HFHFD-fed rats also showed an increase in fibrinogen and CRP associated with changes in kidney function such as hyperuricaemia.

During insulin resistance, there is an imbalance in glucose metabolism that generates chronic hyperglycemia, which in turn triggers oxidative stress and causes an inflammatory response that leads to cell damage [26].

It has been suggested that hyperinsulinemia is associated with alterations of myocardial metabolism leading to increased myocardial free fatty acids oxidation resulting in lipotoxicity and predisposition to cardiac hypertrophy and

Table 5. Effect of omega-3 oil, and L-carnitine on fibrinogen in MS-induced rats

Parameters / Treatment		Fibrinogen (mg/dl)
Normal control		**227.33±1.63**
MS-induced	**Control**	**369.17±7.83#**
	+ Omega-3 (260 mg/kg)	**212.33±6.37#***
	+ L-Carnitine (200 mg/kg)	**222.33±3.61***

Abbreviations: ANOVA, analysis of variance; MS, metabolic syndrome. Results are expressed as mean ± SD (n = 6). The statistical comparison of difference between the control and the treated groups were carried out using one-way ANOVA.

**Statistically significant from the MS-induced rats treated with HFHFD only at P < 0.05.*

#Statistically significant from the control values at P < 0.05.

Table 6. Effect of omega-3 oil, and L-carnitine on oxidative stress parameters in MS-induced rats

Treatment \ Parameters	MDA (nmol/ml)	GSH (mg/dl)	SOD (u/l)
Normal control	1.59±0.07	9.813±0.63	11.57±0.51
MS-induced Control	4.99±0.44#	6.74±0.43#	7.84±0.36#
+ Omega-3 (260 mg/kg)	1.25±0.07#*	33.91±2.42#*	32.73±1.12#*
+ L-Carnitine (200 mg/kg)	1.34±0.05#*	31.05±1.87#*	34.23±2.8#*

Abbreviations: ANOVA, analysis of variance; MDA, Malondialdehyde; GSH, Glutathione reduced; SOD, Superoxide Dismutase; MS, metabolic syndrome. Results are expressed as mean ± SD (n = 6). The statistical comparison of difference between the control and the treated groups were carried out using one-way ANOVA.
*Statistically significant from the MS-induced rats treated with HFHFD only at P < 0.05.
#Statistically significant from the control values at P < 0.05.

dysfunction [27]. The most possible mechanisms for the cardiovascular effect of hyperinsulinemia are that it can cause renal sodium retention, increasing cardiac preload. It also activates the renin-angiotensin system, sympathetic nervous system, promotes oxidative stress, and stimulates cardiac fibroblasts, increases heart rate and cardiac overload [28].

The current data revealed that HFHFD caused oxidative stress as shown by marked decrease in GSH, SOD, and increase in MDA. Several studies have reported that persistent hyperglycemia can cause high production of ROS which may lead to cellular oxidative damage including DNA, lipids, and protein [29].

The results of the present study showed that HFHFD induced kidney dysfunction as indicted by elevation of creatinine, uric acid, BUN, and reduction of albumin levels. Elevated serum uric acid levels are thought to be a potential mechanism linking fructose consumption to MS [30].

The HFHFD in the present work resulted in increase in fibrinogen and CRP level indicting cardiovascular changes. CRP has a role in the modulation of the harmful effect of oxidized LDL on endothelial function, contributing to oxidative stress and the subsequent production of free radicals that may contribute to damage and endothelial dysfunction and to oxidation of the lipoproteins in atherosclerotic lesions [31].

Fibrinogen, an acute-phase reactant like CRP, rises in response to a high cytokine state. Thus, prothrombotic and proinflammatory states may be metabolically interconnected [32].

In the present study, the administration of omega-3 to MS-induced rat provoked a significant increase in GSH, and SOD, and decrease in MDA level. Lalia and Lanza [33] showed that treatment with Omega-3for 13 weeks increased the activity of antioxidant enzymes in a spontaneously hypertensive obese rat model of the metabolic syndrome.

The administration of omega-3 significantly decreased MS-induced increase in CRP level. Similar findings are observed by Kelley et al., [34] who showed that treatment with omega-3 lowered the plasma CRP and inflammatory markers.

In the present study, the administration of omega-3 significantly decreased MS-induced hypertension. Omega-3 fatty acids have been associated with a mild decrease in systolic blood pressure and a decrease in diastolic blood pressure [35]. The suggested mechanisms of antihypertensive effect of omega-3 involve improvement in autonomic function by augmentation of vagal tone, improvement in left ventricular diastolic filling, alterations on the cardiac electrophysiological pathways, increase in urinary sodium, decrease in plasma renin activity, increase in endothelial nitric oxide production, and decrease in arteriosclerosis [35,36,37].

The prostaglandins derived from EPA antagonize the effect of arachidonic acid-derived prostaglandins, thromboxanes, and leukotrienes mediate vasoconstriction, platelet aggregation, and synthesis of inflammatory mediators. Omega-3 appears to suppress the activity of angiotensin-converting enzyme, leading to reduction in angiotensin II production and inhibition of aldosterone secretion [38,39].

In the present study, omega-3 improved hyperuricaemia, and albumin level. The current results are in harmony with the results of Hu et al. [40] who suggested that omega-3 fatty acids significantly reduced the risk of end-stage renal

disease and was associated with a lower risk of proteinuria.

In the present study, omega-3 administration caused a significant reduction in fibrinogen level. The current results are in harmony with the previous study by Larson et al. [41] who showed that omega-3 fatty acids had an antithrombotic effect, particularly a diminution in thromboxane A2, which produces platelet aggregation and vasoconstriction.

The euglycemia caused by L-carnitine resulted into significant increase in GSH, SOD, and decrease in MDA levels. Lee et al. [42] and Rezaei et al. [43] who found that L-carnitine acts as an antioxidant and prevents the accumulation of end products of lipid oxidation during ischemia and reduces the oxidative damage in ageing.

Several mechanisms have been proposed to explain the antioxidant function of L-carnitine. Firstly, the fatty acid transport function of L-carnitine has been favorable for lowering the substrate availability (free fatty acid) for peroxidation [44]. Further, the energy-generating effect of L-carnitine could improve the overall protein and antioxidant enzyme levels in the cells [45].

The administration of L-carnitine significantly decreased CRP level indicating anti-inflammtory mechanisms in alteration of metabolic syndrome. The current results are in harmony with the previous studies [46]. Similarly, Hakeshzadeh et al. [47] reported that 12 weeks of carnitine treatment increased serum free carnitine concentration, whereas plasma fibrinogen and serum CRP were decreased.

The administration of L-carnitine significantly decreased MS-induced hypertension and increased in heart rate. Ruggenenti et al., [48] reported that chronic administration of L-carnitine reduced blood pressure and attenuated the inflammatory process associated with arterial hypertension. L-carnitine might produce a partial inactivation in the renin angiotensin system resulting in a reduction in the production and effects of angiotensin II. Furthermore, the inflammation process, associated with hypertension induced by a long-term blockade of nitric oxide synthesis, is significantly attenuated by administration of L-carnitine [49,50].

Kępka et al. [51] reported that L-carnitine not only had antihypertensive effect but its supplementation also attenuated cardiac fibrosis by increasing prostacyclin production through arachidonic acid pathways.

L-carnitine plays an important role in energy production in the myocardium and has been shown to transport free fatty acids into the mitochondria, thus increasing the preferred substrate for oxidative metabolism in the heart [52,53]. Moreover, Lcarnitine has been shown to prevent fatty acid ester accumulation that occurs during ischemic events, which may lead to fatal ventricular arrhythmias. As myocardial carnitine levels are quickly diminished during an ischemic event, exogenous supplementation with L-carnitine has been shown to replenish depleted myocardial carnitine levels, increase coronary blood flow and improve cardiac metabolic and left ventricular function [46,54].

In the present study, L-carnitine improved MS-induced alteration in kidney function where reduction of hyperuricaemia and albuminuria were observed. Ahmed et al. [55] reported that L-carnitine reduced serum creatinine and BUN, attenuated renal hypertrophy and decreased renal tissue damage. Also, Tashiro et al. [56] showed that L-carnitine administration improved serum albumin.

In the present study, L-carnitine administration caused a significant reduction in fibrinogen level. The current results are in harmony with the previous study by Elgendy and Abbas, [57] who reported that L-carnitine decreased fibrinogen by improving oxidative stress and decreasing the hypercoagulation state in DM. Pignatelli et al., [58] reported that carnitine inhibited platelet aggregation by inhibiting arachidonic acid metabolism, thromboxane A2 formation, and superoxide production in blood platelets.

5. CONCLUSIONS

In conclusion, omega-3 oil and L-carnitine for 4 weeks decreased blood pressure and heart rate. They improve the renal complication induced by MS. These effects could be related to antioxidant activity.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The experimental design was carried out according to the regulation of ethic committee of

faculty of Pharmacy Cairo University (Approval number: PT 1305).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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