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Antioxidant Effect of L-carnitine in Rats Fed Cholesterol Rich Diet

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Abstract: This study was conducted to assess the effects of L-carnitine on antioxidant enzymes in rats fed cholesterol rich diet. A total of 32 healthy male Wistar Albino rats were allocated to four groups. Animals of the first group were fed standard rat pellets, animals of the second group were fed standard rat pellets that contained 7.5 % cholesterol powder, animals of the third group were fed standard rat pellets and water contained 75 mg/l L-carnitine while those of the forth group were fed standard rat pellets that contained 7.5 % cholesterol and water that contained 75 mg/l L-carnitine for 40 days. On the 40 th day of the study, blood samples were taken from all animals and thiobarbituric acid reactive substances (TBARS), glutathione (GSH), superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) levels were determined. The results showed that feeding with high cholesterol diet resulted significantly increase in TBARS level and decreases in GSH, SOD, GPx levels when compared to control group ($p<0.05$). L-carnitine addition to the high cholesterol diet significantly decreased in TBARS level and increased in GSH, SOD levels compared to cholesterol group ($p<0.05$). In conclusion, our results showed L-carnitine may be useful an antioxidant in hypercholesterolemic condition.

Keywords: L-carnitine, Cholesterol, Antioxidants, Lipid Peroxidation, Rat

1. Introduction

Oxidative stress is occurred by the existence of free radicals or radical-producing agents in levels that exceed natural radical-blocking or -scavenging mechanisms [1, 2]. There are many sources of oxidative stress including some disorders such as diabet, hypercholesterolemia, hyperlipidemia, obesity [3, 4, 5, 6].

The antioxidant system consists of low molecular weight antioxidant molecules, such as glutathione and various antioxidant enzymes. Superoxide dismutase is the first line of defense against oxygen-derived free radicals, catalysis the dismutation of superoxide anion into H_2O_2. H_2O_2 can be transformed into H_2O and O_2 by catalase. Glutathione peroxidase reduces lipidic or nonlipidic hydroperoxides as well as H_2O_2 while oxidizing GSH [7, 8]. The process of lipid peroxidation is one of oxidative conversion of polyunsaturated fatty acids to products known as malondialdehyde (MDA) or lipid peroxides [9, 10].

L-carnitine is a natural nutrient related to B vitamins that is essential for the β-oxidation of fatty acids in mitochondria to generate adenosine triphosphate. The protective effects of L-carnitine on the metabolism of tissues in organs (heart, brain and liver) have been studied [11]. L-carnitine has been reported to protect cell against free radical damage and lipid peroxidation [12, 13] Carnitines are essential factors of several enzymes necessary for the transformation of long-chain fatty acids, and act also as scavengers of oxygen free radicals in mammalian tissues [10, 14].

The objective of the present work is to study the influence of L-carnitine on oxidative status (TBARS, GSH, SOD, GPx and CAT) in rats fed cholesterol rich diet.

2. Materials and Methods

The study was conducted on 32 healthy male Wistar Albino rats. The rats were allocated to four groups consist of eight animals each. The mean weights of all groups were similar. All rats were kept in individual cages during the 40 days of experiment and were fed ad libitum as follows: animals of the first group were fed standard rat pellets (Purina®, Optima Besin Maddeleri San. ve Tic. A.Ş., Balıkesir, Turkey), while those of the second group were fed

standard rat pellets that contained 7.5 % cholesterol powder (Sigma-Aldrich, Steinheim, Germany), but the animals of the third group were fed standard rat pellets and water contained 75 mg/l L-carnitine (Solgar Vitamin and Herb, Leonia, NJ) and the animals of the forth group were fed standard rat pellets that contained 7.5 % cholesterol and water that contained 75 mg/l L-carnitine. On the 40 th day of the study, blood samples were taken from all animals. The TBARS, GSH, SOD, GPx and CAT (Cayman Chemical, Ann Arbor, MI, USA) levels were determined in the plasma samples using a commercial sandwich enzyme-linked immunosorbent assay (Bio-Tek Instruments, Inc). The data were analyzed using one-way ANOVA (SPSS 17). Differences among the groups were determined by Duncan's multiple range tests. Differences were considered significant at $p<0.05$.

3. Results

The levels of TBARS, GSH, SOD, GPx and CAT obtained from all groups were shown in Table 1. Feeding with high cholesterol diet resulted significantly increase in TBARS level and decreases in GSH, SOD, GPx levels when compared to control group (Table 1, $p<0.05$). L-carnitine addition to the high cholesterol diet significantly decreased in TBARS level and increased in GSH, SOD levels compared to cholesterol group (Table 1, $p<0.05$). The levels of these enzymes in L-carnitine group were not different than that of control group levels. It was not found any difference in CAT levels of cholesterol group and L-carnitine+cholesterol group compared to control group.

Table 1. *The effects of L-carnitine on TBARS, GSH, SOD, GPx and CAT levels in rats fed cholesterol rich diet (Mean±SE).*

Group (n=8)	TBARS (µM)	GSH (µM)	SOD (U/ml)	GPx (nmol/min/ml)	CAT (nmol/min/ml)
Group 1	3.61 ± 0.38^{bc}	43.75 ± 3.99^{a}	23.38 ± 3.09^{a}	32.13 ± 3.03^{a}	37.75 ± 5.02^{ab}
Group 2	5.65 ± 0.47^{a}	27.75 ± 2.03^{b}	13.25 ± 1.25^{b}	18.25 ± 2.46^{b}	28.50 ± 2.95^{b}
Group 3	3.14 ± 0.37^{c}	39.88 ± 3.83^{a}	25.38 ± 3.98^{a}	29.13 ± 2.87^{a}	42.63 ± 4.82^{a}
Group 4	4.50 ± 0.34^{b}	38.25 ± 2.85^{a}	21.50 ± 1.09^{a}	24.88 ± 1.92^{ab}	35.38 ± 3.58^{ab}

The difference between mean values with different superscripts in the same column is significant for each parameter, $p<0.05$.
Group 1, control; group 2, cholesterol; group 3, L-carnitine; group 4, L-carnitine+cholesterol.

4. Discussion

It has been shown that animals and humans had an effective process to prevent the free radical induced tissue cell damage. This process is achieved by some antioxidant enzymes and proteins such as SOD, CAT, GPx and GSH [15, 16, 17]. If the balance between ROS production and antioxidant defense is lost, oxidative stress occurs [15, 17]. Our results showed that the plasma TBARS level significantly increased feeding with high cholesterol diet when compared to first group feeding with standard diet (Table 1, $p<0.05$). In respect of antioxidant enzymes activities, we found statically important decreases in plasma GSH, SOD, and GPx levels in rats fed high cholesterol diet compared to first group feeding with standard diet (Table 1, $p<0.05$). These results reflect the oxidative stress and lipid peroxidation resulting from hypercholesterolemia. Under our experimental condition, the increase TBARS and the decrease GSH levels in the hypercholesterolmic group are consistent with the data reported by Sayed-Ahmed et al. [18] and Steinberg [19]. There are some mechanisms suggesting the reduction of antioxidant enzymes in hypercholesterolemia. The increased lipid peroxidation lead to inactivation of the enzymes by crosses linking with MDA; this will cause an increased accumulation of superoxide, H_2O_2 and hydroxyl radicals which could further stimulate lipid peroxidation [15]. On the other hand, decrease of antioxidant enzyme may be due to rapid consumption and exhaustion of storage of this enzyme in fighting free radicals generated during hyperlipidemia [15].

There are several experimental and clinical studies that reported the efficacy of L-carnitine supplementation in cardiovascular diseases and/or atherosclerosis [20, 21, 22, 23]. However, L-carnitine is important component in lipid metabolism for production adenosine triphosphate via β-oxidation and subsequent oxidative phosphorylation [24, 25, 26]. It has been reported that there is a decrease in the concentration of carnitine in blood and tissues in hyperlipidemic condition [27]. In atherosclerotic and hyperlipidemic condition there was a depletion of carnitine, resulting in a decrease in the transport of fatty acid into mitochondria [24]. Thus, Carnitine has also received consideration as a hypolipidemic agent [28]. Further carnitine is reported to exert antioxidant action in experimental animals [14, 28].

In our study, L-carnitine supplementation significantly reduced TBARS level and increased GSH and SOD levels in L-carnitine+cholesterol group compared to cholesterol group (Table 1, $p<0.05$) suggesting that L-carnitine has an antioxidant effect. Although the changes in GPx and CAT levels were not important of L-carnitine+cholesterol group compared to cholesterol group, the levels of these enzymes were close to that of control group. Sayed-Ahmed et al. [18] and Steinberg [19] reported that L-carnitine prevented the increase in MDA and the decrease in GSH induced by a hypercholesterolemic diet. Dayanandan et al. [24] noted elevation in GSH and GPx levels with carnitine supplementation in rats. On the other hand, Rajasekar et al. [28] found significantly increases antioxidant enzyme levels (GSH, SOD, CAT and GPx) of rats treated with L-carnitine compared to untreated rats. In our study, decrease in TBARS level and increase antioxidant enzymes with L-carnitine treatment may be due to enhancement of transport of fatty acids by carnitine into mitochondria for energy production [24]. In addition to its hypolipidemic and hypocholoesterolemic effects, it has reported that carnitine

inhibits the microsomal peroxidation and it has a role in chelating free Fe^{2+} ions and by this way it reduces free radical generation [24, 29, 30].

5. Conclusion

In conclusion, our results showed L-carnitine may be useful an antioxidant in hypercholesterolemic condition. Its beneficial effects may be attributed to its both direct hypolipidemic properties and possible antioxidant mechanisms.

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