Study on functional mechanism of functional nutritional food supplement to human body

Received for publication, May, 2, 2018
Accepted, June, 23, 2018

XIJUN SUN
Department of Pshycail Education, Huaiyin Institute of Technology, Huaian, Jiangsu, 223003, China
*Address for correspondence to: xijsunhy@yeah.net

Abstract
In this paper, by analyzing the mechanism of the supplementation of L-carnitine contained in functional nutritious food to human body, the possibility of improving the ability of human exercise by supplementing L-carnitine was discussed, providing a theoretical basis for future researches on the functional mechanism of functional nutritious food supplement. The results showed that L-carnitine supplementation can help improve energy supply during exercise, inhibit lactate production, slow down the occurrence of fatigue movement, promote the recovery of sports fatigue, and improve athletic ability to a certain extent.

Keywords: body movement, exercise capacity, Heart rate, L-carnitine, mechanism of action

1. Introduction
Functional nutrition food can be divided into three categories according to sport event categories: speed strength class, endurance class, recovery class after exercise. Each type of ingredients contained in food has its own supplement mechanism on the human body after exercise. Among them, L-carnitine is the main component of the endurance class functional nutritional food. It is a kind of amino acids which can promote fat to convert into energy (HUANG & al [5]) and a necessary cofactor for fat metabolism (STEPHENS & al [10]), which can be mostly found in red meat, without toxic and side effect. In 1982, the Italian team used L-carnitine when participating in the Spanish World Cup and won the championship relying on their perfect technology and abundant energy. Since then L-carnitine began to be widely used in the sports world. At present, whether L-carnitine can have a huge impact on the athlete's exercise performance remains controversial. Atalay et al. (ATALAY & al [1]) investigated the effects of supplementation of L-carnitine at different doses on the production of nitric oxide (NO) and oxidative stress after exhaustive exercise and found that L-carnitine had a strong antioxidant effect at the dose of 3 g and could reduce the amount of nitric oxide through increasing the content of glutathione and nitrite. Sung et al. (SUNG & al [12]) emphatically studied the antioxidative effect of L-carnitine in exercise and its application. They found through detecting active oxygen cluster (ROS) that L-carnitine as an antioxidant was capable of enhancing physical function and
assisting oxidative stress. Koozehchian et al. (KOOZECHIAN & al. [6]) studied the effects of L-carnitine supplementation on specific exercise induced oxidative stress markers in 35 men, and concluded that the intake of L-carnitine (2 g/day) increased the total antioxidant capacity and weakened the production of exercise induced oxidative stress. To explore the effects of L-carnitine supplementation on aerobic metabolic efficiency and blood lipids in sedentary and athletic men, Leelarungrayub et al. (LEELARUNGRAYUB & al. [7]) provided 15 sedentary men and 15 athletic men who were twenty years old. The results showed that levocarnitine had obvious influence on the efficiency of aerobic metabolism and blood lipid in sports men and had insignificant influence on men who were sedentary and lack of exercise. In this study, the action mechanism of L-carnitine supplement to human body after exercise was investigated through experiments, aiming to explore whether it can help improve the athletic ability of human body.

2. Materials and Methods

2.1. Function of L-carnitine

2.1.1. Regulating the percentage of acyl in mitochondria

The stability of energy metabolism of human cells is closely related to the ratio of acyl coenzyme A to coenzyme A in mitochondria. Pyruvate dehydrogenase is an important catalyst in the metabolism cycle of cell energy, and acetyl in mitochondrial matrix can inhibit the activity of pyruvate dehydrogenase. If the percentage of acyl coenzyme A/coenzyme A in mitochondria is not reduced timely, i.e. if acetyl is not timely transferred from mitochondrial matrix, then cell energy metabolism will be greatly affected. Acetyl cannot be expelled from mitochondria independently unless under the assistance of carriers, L-carnitine. It combines with short-chain acyl in mitochondria to form acyl carnitine, and then acyl carnitine is transported out of membrane. In this way, the ratio of acyl coenzyme A to coenzyme A in mitochondria can be reduced. Moreover the acetyl which is transferred from mitochondria is involved in the synthesis of fatty acid. L-carnitine cannot enter mitochondria directly, but can combine with acyl-coenzyme A to form acyl L-carnitine under the catalytic action of L-carnitine acyl transferase I of mitochondrial outer membrane and then passes through mitochondrial membrane under the assistance of acyl L-carnitine translocase in mitochondrial inner membrane. Acyl coenzymem A is generated by fatty acid in cytoplasm under the catalytic action of acyl coenzymem A synthetase which mainly distributes in endoplasmic reticulum. Acyl coenzymem A is generated again under the catalytic action of carnitine acyl transferase II after acyl L-carnitine enters mitochondria. Then L-carnitine is released.

2.1.2. Promoting fatty acid β oxidation

In human metabolism, long-chain fatty acids will enter veins from lymphatic vessels in a structure of triglyceride, and then be transported to different tissues for metabolic consumption. But they are often difficult to be consumed completely and may be accumulated to form fat, causing obesity, thrombosis and other symptoms. It can be noted from the introduction of the previous section that L-carnitine plays a key role in the decomposition of fatty acids. L-carnitine transports long-chain fatty acids to mitochondria for
β oxidation as a carrier to assist tricarboxylic acid cycle and the generation of Adenosine Triphosphate (ATP).

2.1.3. Resisting fatigue by inhibiting lactification
An important reason why human body will feel fatigue is the accumulation of lactic acid. Lactic acid is the product of incomplete oxidation of saccharides in human body during short-time strenuous exercise. After rest, the generated lactic acid will be further oxidized to water and CO₂; as a result, feeling of fatigue disappears. L-carnitine has anti-fatigue effect. L-carnitine relieves fatigue by increasing muscle glycogen reserve, reducing muscle glycogen consumption after exercise, control muscle glycogen anaerobic glycolysis through increasing the fatty acid oxidation function, inhibiting lactate production, and accelerating the removal of lactic acid and urea nitrogen.

2.1.4. Other functions
L-carnitine can also affect the metabolism of amino acids, promote the oxidation of branched-chain amino acids (BLANCA & al [3]), accelerate the normal metabolism of branched-chain amino acids by timely delivering branched chain acyl, and eliminate the toxicity generated by acyl accumulation by removing excessive or irrational acyl groups. Moreover it has functions of storing and transferring energy, which is beneficial to the absorption of fat-soluble vitamin and calcium phosphate. Adding L-carnitine into peritoneal dialysis liquid which is used in the treatment of uremia can supplement patients with carnitine and inhibit cell apoptosis induced by the high glucose level of peritoneal dialysis liquid.

2.2. The application of L-carnitine
In the medical field, because L-carnitine is essential for fat oxidation and is considered to be conducive to heart and vascular health and the elimination of fatty liver. L-carnitine can increase blood levels of high-density lipoprotein, helps to clear the body's cholesterol, protect blood vessels and lower blood pressure. The current studies in China focus on its anti-myocardial ischemia, anti-arrhythmia and hypolipidemic effect (XU [14]).

In the food health care field, it is now widely believed that L-carnitine can enhance endurance, promote fatigue recovery and improve athletic performance (PANCHAL & al [9]). Inevitably, L-carnitine is sometimes regarded as a weight loss holy medicine, because it can promote fatty acids into mitochondria for oxidative decomposition. However, the purpose of burning fat cannot be achieved if people take no exercise after taking L-carnitine. L-carnitine is also added to infant formula. Since the self-synthesis capacity of L-carnitine of infants is relatively weak, only 12% that of adults, and L-carnitine is an essential nutrient for body development of infants, it must be additionally supplemented. In 1996, the addition of L-carnitine ingredients to milk drinks, biscuits and solid beverages was approved by the Chinese government. On March 16, 2010, the Ministry of Health of China issued a notice to formally allow L-carnitine to expand its scope and usage amount as a kind of food nutrition enhancer. Now, L-carnitine has entered the diet, health care, medical and many other areas and has become an indispensable nutrient in food and health care products.

2.3. Experimental subjects
A total of 40 students were selected as the experimental subjects in this study, half male and half female, aged 20 ± 1 years old, male height of 178 ± 3 cm, female height of 165 ± 4 cm. All the subjects were in good health, without recent slow, acute disease, nor drinking, taking any drugs. All the subjects signed informed consent and were willing to coordinate with the study.

2.4. Experimental methods

2.4.1. Experimental diet

The male and female subjects were randomly divided into four groups: male L-carnitine group and female L-carnitine group (10 each), male control group and female control group (10 each). The four groups of subjects were given with normal daily diet. After lunch, each subject in the L-carnitine groups were given 2 g of L-carnitine, while the control groups were given placebo (dextrin capsule) at the same dose, for 4 weeks.

Experimental Plan

The aerobic exercise capacity of the 40 subjects was tested before and after the experiment, and the contents of blood lactate and malondialdehyde (MDA) were measured after exercise. Sweden MONARK power bike was used. The male subjects started bicycling at 60 w, while the female subjects started at 50 w. The power increased 20 w every 3 min until the subjects felt exhausted, i.e. the subjects felt breathless and could no longer maintain the original rhythm after repeated attempts. The heart rhythm of each subject was measured before and after the experiment. The ear blood of each subject was collected before experiment and 1 min, 3 min and 5 min after experiment and put into a blood lactic acid automatic analyzer for measurement of content of blood lactic acid. Moreover the elbow venous blood of each subject was collected and centrifuged at 3000 r/min for 10 min, and the serum was collected for MDA detection.

2.5. Data Statistics

The SPSS statistical software was used for analysis of variance, and differences between the L-carnitine groups and the control groups before and after the experiment were processed using paired T test. Difference was considered as statistically significant if p < 0.05.

3. RESULTS

3.1. Heart rate

Table 1 shows the test results of heart rate of all the subjects. The heart rate of all the subjects increased after exercise, and the differences were significant (p<0.05). It could be noted from Table 1 that the heart rate of the males who took L-carnitine was significantly lower than that of males who did not take L-carnitine before exercise, and the situation was the same among the females. The heart rate became higher in four groups after exercise, because the blood circulation which is responsible for transporting oxygen and CO₂ accelerated as a large amount of oxygen is needed in respiration during strenuous exercise. After exercise, the heart rate of the subjects who did not take L-carnitine was higher than that of the subjects who took L-carnitine in both groups. Moreover the heart rate of males in the L-carnitine group and control group were higher than that of females in the L-carnitine group and control group.
respectively, which might be because of the difference of physical quality between males and females and less exercise of males compared to females.

Table 1. The heart rate of all the subjects before and after exercise (b/min)

<table>
<thead>
<tr>
<th></th>
<th>Male subjects</th>
<th>Female subjects</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>L-carnitine group</td>
<td>Control group</td>
</tr>
<tr>
<td>Before exercise</td>
<td>60.47±9.23</td>
<td>68.64±7.17</td>
</tr>
<tr>
<td>After exercise</td>
<td>147.38±4.45</td>
<td>155.71±5.39</td>
</tr>
</tbody>
</table>

3.2. Blood lactate level

Table 2 shows the blood lactate level of all the subjects before and after exercise. Before and after taking L-carnitine, the level of blood lactic acid changed significantly. The subjects taking either L-carnitine or placebo showed decreased blood lactate level in the 1st min, 3rd min and 5th min after exercise, and the changes of the male and female subjects were the same (p<0.05). The level of blood lactate of the four groups suddenly increased in the first min. It was because that oxygen supply of blood circulation in that period kept at a silent level, which was not enough support aerobic respiration, and the aerobic respiration of cells generated a large number of lactic acid. The level of blood lactate of the four groups became steady after one minute. It was because that the heart rate accelerated, oxygen supply of blood circulation had been able to satisfy the demand, and the generation of lactic acid was basically balanced with the consumption of lactic acid. But the previously generated lactic acid was not completely consumed. The comparison between the L-carnitine and control group suggested that the level of blood lactate of the subjects who took L-carnitine was lower after exercise.

Table 2. The blood lactate level of all the subjects before and after exercise (X±SD, mmol/L)

<table>
<thead>
<tr>
<th></th>
<th>Male subjects</th>
<th>Female subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>L-carnitine group</td>
<td>Control group</td>
</tr>
<tr>
<td>Before exercise</td>
<td>0.61±0.41</td>
<td>1.32±1.36</td>
</tr>
<tr>
<td>1 min after</td>
<td>3.35±1.15</td>
<td>4.01±1.20</td>
</tr>
</tbody>
</table>
3.3. The effective exercise time and MDA changes

The effective exercise time of each subject refers to the period from the moment exercise begins to the moment exercise stops when the subject feels breathless and could no longer maintain the original movement rhythm after repeated attempts. Table 3 demonstrates that the effective exercise time of the males was longer than that of the females, no matter they took L-carnitine or not, which was caused by the difference of physical quality. The effective exercise time of the subjects who took L-carnitine was longer than that of the subjects who did not take L-carnitine in both groups. Malondialdehyde (MDA) has carcinogenicity. It could be noted from the control groups shown in Table 3 that the difference of content of methylene dioxyamphetamine between the males and females was little, indicating that its content was in no correlation with gender. But the content of serum MDA of the L-carnitine groups was lower than that of the control group.

Table 3. Changes of the effective exercise time (s) and MDA level after exercise

<table>
<thead>
<tr>
<th></th>
<th>Male subjects</th>
<th>Female subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>L-carnitine</td>
<td>Control group</td>
</tr>
<tr>
<td>Effective</td>
<td>751.31±19.15</td>
<td>701.23±14.27</td>
</tr>
<tr>
<td>exercise time(S)</td>
<td>701.23±14.27</td>
<td>680.64±20.37</td>
</tr>
<tr>
<td>MDA (nmol/ml)</td>
<td>4.36±0.49</td>
<td>4.79±0.58</td>
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</table>

4. Discussion

4.1. Heart rate

In this experiment, the heart rates of the subjects in the L-carnitine groups and the control groups increased obviously after exercise with the increase of the exercise load, but the heart rates of the L-carnitine groups were significantly lower than that of the control groups. It
indicated that that L-carnitine could improve myocardial contractility, slow heart rate in high-intensity exercises, improve the myocardial blood and oxygen supply, and strengthen exercise endurance (BENIWAL & al [2]).

4.2. Blood lactic acid and effective exercise time
In the experiment, the content of blood lactic acid of the L-carnitine groups before and in the 1st min, 3rd min and 5th min after exercise were lower than that of the control groups, suggesting that L-carnitine could reduce the value of blood lactate after exercise. Excessive blood lactic acid during exercise will increase the acidity of blood and tissue fluid and reduce generation of ATP, leading to fatigue. L-carnitine can save glycogen, increase muscle oxidation of fatty acids, eliminate excessive lactic acids (BLANCA & al [4]), accelerate the recovery of exercise-induced fatigue, extending the effective time of exercise. Therefore, supplementing L-carnitine can increase muscle glycogen reserves (NOVAKOVA & al. [8]), save muscle glycogen consumption, and enhance endurance.

4.3. MDA
MDA is incompatible with protein and has potential carcinogenicity. Free radicals induces peroxidation by acting on lipid, and MDA is the final product of oxidation (TSIKAS [13]). MDA can induce the cross linking and polymerization of living macromolecules such as proteins and nucleic acids and moreover has cytotoxicity. Therefore, the level of MDA can reflect the metabolism of free radicals and the intensity of lipid peroxidation of cells. It could be noted from Table 3 that the MDA value of the L-carnitine group was lower than those of the control group. L-carnitine enhanced antioxidant capacity and promoted elimination of free radicals, which was beneficial for the cells to resist free radical damage and maintain the normal redox state, cell integrity and normal physiological functions. Moreover L-carnitine can promote fatty acid beta-oxidation, accelerate the entering of acetyl-CoA into tricarboxylic acid cycle oxidation (SU & al [11]), alleviate oxidative stress-induced cell damage during exercise, and reduce content of MDA. In conclusion, it is effective in enhancing energy metabolism efficiency and relieving fatigue.

4.4. Other studies
Stephens et al (STEPHENS & al [10]) considered that the increase in acetyl carnitine formation during high-intensity exercise, which appears to be more obvious in type I muscle fibers, was directly related to the increase in acetyl-CoA. It suggested that the formation of acetyl-CoA was higher than the utilization speed in TCA cycle (i.e. its condensation speed with oxaloacetate was lower than its formation speed), leading to its subsequent accumulation. As a result, the muscle acetyl carnitine content had no changes at the beginning of the lower-intensity exercise (Figure 1), indicating that the formation speed of acetyl-CoA from pyruvate (and fatty acid oxidation) matched well with the utilization speed in TCA cycle.
5. CONCLUSION

In conclusion, supplementation of L-carnitine can promote the oxidation of glucose through reducing the production of MDA, which is effective in delaying fatigue during exercise. Excessive lactic acid generated during exercise will increase the acidity of blood and tissue fluid and reduce the generation of ATP, leading to fatigue. Supplement of L-carnitine can remove excessive lactic acids, improve exercise capacity, and accelerate recovery of exercise-induced fatigue. Moreover L-carnitine can help fatty acids pass through mitochondrial membrane for energy supply. Proper use of L-carnitine can increase the generation of ATP and improve endurance level, which is very suitable for people participating in endurance exercises. But the experiment and the results had shortcomings and deficiencies. Firstly, the size of samples was small, and all the subjects were from the same place. Therefore the experimental results were not universal and convictive. Secondly, the collected data were not diversified, i.e. the test items were not enough. The detection items roughly displayed the supplement of L-carnitine for human body, but could not reflect the functions of L-carnitine in details. The two points should be considered in the future studies. Firstly, the experimental subjects should include all the social groups and all age groups. Then more indexes should be detected. For example, oxygen consumption and the generation amount of CO₂ at different exercise stages can be detected using a cardiopulmonary function testing instrument, and anaerobic threshold can be calculated using pulmonary ventilation volume curve fitting.

6. CONFLICT OF INTEREST

The author declares no conflict of interest.

References