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## ORIGINAL ARTICLE

# Effect of L-carnitine on Serum LH, FSH and Testosterone Levels in Adult Male Rats

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**ABSTRACT**

*L-carnitine is an essential nutrient. It has vitamin-like qualities and it is considered essential in helping to transport fatty acids into mitochondria. The benefit effect of L-carnitine is proposed for treatment of obesity as long time periods. L-carnitine presented which have a beneficial impact on fertility. Its androgenic activity may by increasing testosterone level that promotes spermatogenic activity. So, the objective of this study was to determine the effects of supplementation of L-carnitine on serum FSH, LH and testosterone levels in adult male rats. Rats were treated different doses of L-carnitine tartarate daily for 16 days, interperitoneally. The control group was treated saline as vehicle. After 16 days, animals were anesthetized with ether and blood specimens were obtained from heart. Serum FSH, LH and testosterone were measured by radioimmunoassay. The results showed that L-carnitine increased serum FSH, LH and testosterone levels in treated animals, significantly. The present study indicated that L-carnitine could affect on sex hormones and reproduction system and also could be an appropriate candidate for improving male reproductive function.*

***Keywords:*** *L-carnitine, Testosterone, LH, FSH, Rat, Male*

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## INTRODUCTION

Carnitines are widely distributed in nature and their potential health benefits have been popularized. Free carnitine (3-hydroxy-4-N-trymethylaminobutyric acid) was first isolated from bovine muscle by Russian scientists in 1905 and only the L-isomer (L-carnitine, LC) was found bioactive [1]. In 1955, Fritz found that LC could accelerate lipid metabolism and then identified its pivotal role in mitochondrial β-oxidation of long-chain fatty acids for cellular energy production [1, 2]. Moreover, carnitine protects cell membrane and DNA against damage induced by free oxygen radicals. It also prevents protein oxidation and lactate oxidative damage [3].

In fact, LC could be biosynthesized *de novo* by human body. However, LC present in human tissues is mainly of exogenous origin from meat, poultry and fish in dietary [4]. It has long been assumed that carnitine is not an essential component of diet as humans have the ability to synthesize this compound. However, when groups of strict vegetarians were studied, the results showed that their average plasma concentration of carnitine was significantly lower than those of the respective omnivorous controls, which may be attributed to the much less carnitine that strict vegetarians consumed per day [5]. In 1973, Engel reported the first case of carnitine deficiency and treated it with carnitine supplementation [4]. In

1985, carnitine was identified as an essential nutrient of multifunction for the body by the International Nutritional Conference held in Chicago.

Carnitines for medication use are mainly approved to treat carnitine nutritional deficiency induced by hemodialysis in chronic renal failure patients by Food and Drug administration (FDA). However, considering their safety and multifunction, carnitines, including LC and L-acetyl-carnitine (LAC), are widely used in various diseases including male infertility.

Male infertility is a significant problem affecting 7.5% of the male population [6]. Approximately 60% of these cases are idiopathic and related to sperm dysfunctions such as oligo-astheno-teratozoospermia (OAT). By providing readily available energy for use by spermatozoa thus positively affecting sperm motility, maturation and the spermatogenic process [7,8], a key role in sperm metabolism is strongly suggested by the high levels of LC found in epididymal fluid due to an active secretary mechanism [9] and there is also evidence that the initiation of sperm motility is related to an increase of LC in the epididymal lumen and LAC in sperm cells [10-12]. Based on these fundamental roles, numerous clinical trials have attempted to demonstrate a beneficial therapeutic effect of LC and/or LAC when administered to infertile men with various forms of sperm dysfunction.

However, there has been no in-depth systematic overview of efficacy of carnitines in infertile treatment yet. This study was conducted to evaluate the effectiveness of carnitines on serum LH, FSH and testosterone levels in adult male rats.

## MATERIALS AND METHODS

Male Wistar rats initially weighing 200 to 250 g purchased from the Pasteur Institute (Karaj, Iran) were used in the experiments. The animals were housed in groups of 5 per cage with free access to standard laboratory chow in animal house of Islamic Azad University (2013). The diet was purchased from Pars-Dam food service, Tehran, Iran. The animal room was maintained at 22°C ± 2°C with timed lighting on from 7 AM to 19 PM and relative air humidity of 40% to 60%. Eight animals were used for each group of study. Each animal was used once only. The animal protocol was approved by the Ethics Committee of Islamic Azad University, Tehran, Iran and conforms to the guidelines of the Committee for the Purpose of Control and Supervision on Experiments on Animals, Iran, as also international guidelines.

L-carnitine tartarate (Sigma, Germany) dissolved in saline and administered interperitoneally once daily for 16 days. Animals were randomly divided into the following 7 experimental groups. Group I included control animals; group 2 were treated interperitoneally with saline as vehicle; groups 3 to 7 were administered L-carnitine at doses 3.5, 7, 14 and 28 mg/kg body weight, interperitoneally. The volume of administration was 0.5 ml and the treatments were lasted for 16 days.

After 16 days, rats were anesthetized by ether, and blood samples were drawn from heart. The animals were removed after blood collection. Serum LH, FSH and testosterone levels were estimated by radioimmunoassay method.

Statistical analyses and representations were performed in Microsoft Excel. All data was analyzed by one-way ANOVA and presented as the mean value ± S.E.M. of eight rats ($n$ = 8). The results were compared to normal control group and those of L-carnitine treated groups were compared to saline group. $p$ values were checked at three levels of significance viz. 0.05, 0.01 and 0.001. $p$ value less than 0.05 was considered "significant" and $p$ less than 0.01 and 0.001 as "highly significant".

## RESULTS AND DISCUSSION

In recent years, many methods of assisted reproduction have been proposed as a possible solution for "male factor" infertility. The present results showed that treatment of L-carnitine increased serum testosterone level in treated rats in comparison to saline control rats, significantly ($p<0.001$) (Fig 1).

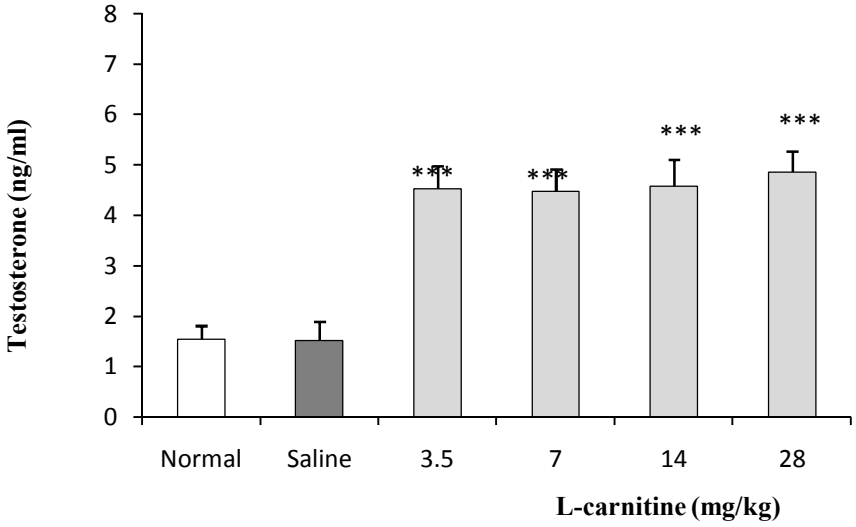


Fig 1- Effect of i. p. L-carnitine treatment at doses 3.5, 7, 14 and 28 mg/kg body weight on serum testosterone level in adult male rats. Each column represents mean ± SEM for 8 rats. Control saline group was administrated with saline as vehicle. ***p<0.001 different from control saline group.

Also, treatment of L-carnitine increased serum LH and FSH levels in treated rats in comparison to saline control rats, significantly (p<0.05, p<0.01, respectively) (Fig 2, 3).

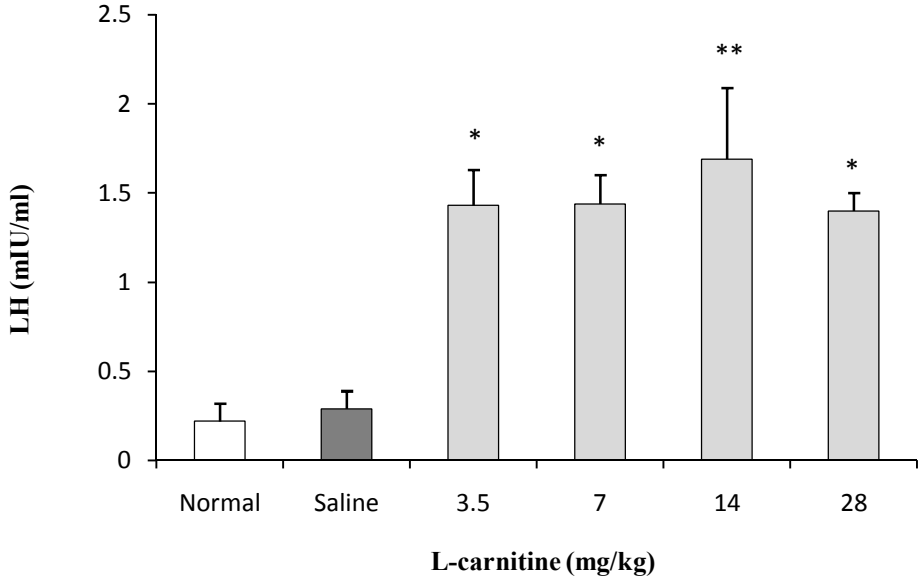


Fig 2- Effect of i. p. L-carnitine treatment at doses 3.5, 7, 14 and 28 mg/kg body weight on serum LH level in adult male rats. Each column represents mean ± SEM for 8 rats. Control saline group was administrated with saline as vehicle. *p<0.05, **p<0.01 different from control saline group.

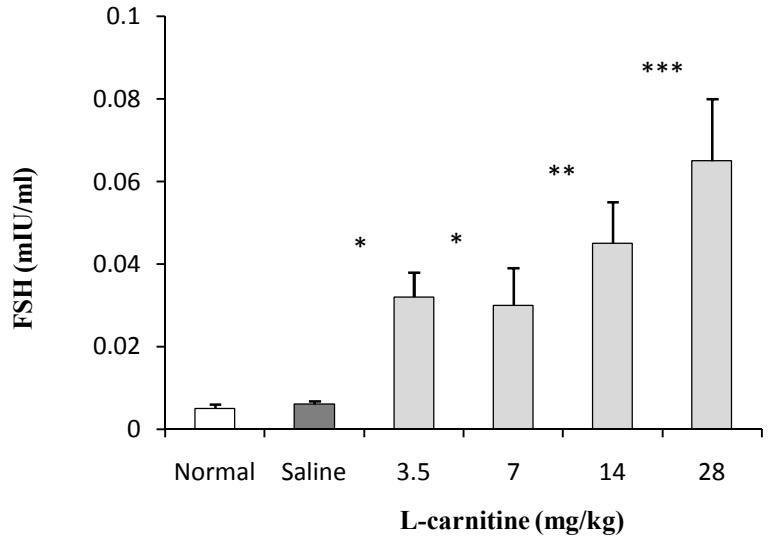


Fig 3- Effect of i. p. L-carnitine treatment at doses 3.5, 7, 14 and 28 mg/kg body weight on serum FSH level in adult male rats. Each column represents mean ± SEM for 8 rats. Control saline group was administrated with saline as vehicle. *p<0.05, **p<0.01, ***p<0.001 different from control saline group.

The evidence reported here, that carnitine increases serum sexual hormone and gonadotropins levels in treated rats. In agreement, Krsmanovic et al reported pulsatile gonadotropin-releasing hormone (GnRH) secretion from perifused hypothalamic cells and GT1-1 neuronal cells was significantly increased after culture in medium containing 100 μM acetyl-L-carnitine (ALC). This action of ALC was largely due to an increase in the spike amplitude of GnRH release. In addition, the receptor-mediated release of GnRH by *N*-methyl-d-aspartic acid and endothelin was significantly increased in perifused cells cultured in ALC-enriched medium. Stimulatory effects of ALC on basal, high $K^+$- and agonist-induced GnRH release were also observed during long-term culture of primary hypothalamic neurons. Similar effects of ALC were evident in cultured GT1-1 cells and were accompanied by a significant increase in cell number. These observations in normal and transformed GnRH neurons demonstrate that ALC promotes the growth and secretory activity of neuropeptide-producing cells of the hypothalamus [13].

Furthermore, Garoll et al showed phospholipid hydroperoxide glutathione peroxidase has an important role in male infertility, and carnitine treatment might improve sperm motility in the presence of normal mitochondrial function [14].

It is reported L-carnitine therapy was effective in increasing semen quality, especially in groups with lower baseline levels in 100 infertile patients [15].

Also, administration of L-carnitine and L-acetyl carnitine is effective in increasing sperm kinetic features in patients affected by idiopathic asthenozoospemia and improves the total oxyradical scavenging capacity of the seminal fluid in the same population [16].

Al-Rubiey reported L-carnitine plus meloxicam treatment have a beneficial effect in decreasing, restoring and maintaining the number of testicular leydig cells in experimental varicocelized rats close to that control of non-varicocelized rats [17].

It is shown that propionyl-L-carnitine and acetyl-L-carnitine proved are safe and reliable in improving the efficacy of sildenafil in restoring sexual potency after bilateral nerve-sparing radical retropubic prostatectomy in 96 patients who had undergone bilateral nerve-sparing radical retropubic prostatectomy [18].

Also, it is reported L-carnitine with other ingredients (*Panax ginseng* C.A. Meyer extract, *Lepidium meyenii* root extract, yeast extract, egg white peptide, *Mucuna pruriens* extract, black ginger extract, polyphenol, L-arginine, L-carnitine, coenzyme $Q_{10}$, vitamin E, black pepper extract, and zinc) is useful for treatment of mild-to-moderate erectile dysfunction [19].

Ismail et al reported adding L-carnitine when treating clomiphene-resistant PCOS patients not only improved the quality of ovulation and the pregnancy rate with an acceptable patient tolerability, but also enhanced the patient lipid profile and body mass index [20].

In contrast, Kozink et al showed indicators of semen quality were not enhanced by dietary supplementation of L-carnitine in boars [21].
Also, Sigman et al reported carnitine supplementation demonstrated no clinically or statistically significant effect on sperm motility or total motile sperm counts in men with idiopathic asthenospermia [22].
In conclusion, our results showed treatment of L-carnitine elevated releasing testosterone, LH and FSH and could improve sexual potency. So, improvement of male reproduction and semen parameters may be related to sexual hormone elevations.

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