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Research Paper

Response of Liver Tissue Bax and Bcl-2 Gene Expression to Aerobic Training with L-Carnitine Supplementation in Rats Toxicated by Boldenone

Mozhgan Ahmadi[1], *Asieh Abbassi Daloii[2], Samira Salehi Kiasari[2]

1. Department of Physical Education and Sport Science Yadegar-e-Imam Khomeini (RAH) Shahre-rey Branch, Islamic Azad University, Tehran, Iran.
2. Department of Physical Education and Sport Science, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran.

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ABSTRACT

Objective This study aimed to compare the response of liver tissue BAX and BCL-2 gene expression to aerobic training with L-carnitine supplementation in rats intoxicated by Boldenone.

Methods In this experimental study, 30 male Wistar rats, aged 12 weeks (weight 195±7.94 g) were randomly divided into five groups: Control, no-treatment, boldenone (5 mg/kg), L-carnitine (100 mg/kg) and aerobic training- L-carnitine. The moderate endurance intensity training program (50%-55% of maximal oxygen consumption) performed for 6 weeks and 5 times a week. Injection once a week in the quadriceps and hamstring was conducted in-depth. After anesthesia, an autopsy was performed, and the liver Isolated. The hepatic apoptosis gene expression in the samples was measured by Real-Time PCR. Data were analyzed by 1-way ANOVA and post hoc Scheffe at the significant level P<0.05.

Results Significant difference was observed between the mean expression of BAX and BCL-2 in the liver tissue of male Wistar rats in different groups (P=0.001). The BAX gene expression of the liver tissue in L-carnitine -aerobic training and L-carnitine groups was significantly lower than the Boldenon group (P=0.001). Also, The BCL-2 gene expression in L-carnitine- aerobic exercise and L-carnitine groups was significantly higher than the Boldenon group (P=0.001).

Conclusion According to the findings of this study, supplementation of L-carnitine with regular aerobic training can have a protective effect against apoptosis induced by anabolic-androgenic steroids.

Extended Abstract

1. Introduction

Long-term administration of high doses of anabolic androgenic steroids reduces the mechanism of liver protection. Side effects of anabolic steroids have been reported on various organs of the body, including hepatic apoptosis [17]. Evidence suggests that exercise activities is associated with the regulation of programmed cell death (apoptosis) in hepatocytes [7]. On the other hand, studies have shown that L-Carnitine has protective effects against drugs that induce damage to body tissues in addition to its known metabolic effects and has an effect on the regulation of gene expression by apoptotic and anti-apoptotic factors [8]. Although the precise mechanisms of the effect of exercise activity and supplementation on the regulation of apoptotic pathway in liver tissue are unclear, however, exercise and supplementation may possibly improve apop-

* *Corresponding Author:*
Asieh Abbassi Daloii, PhD.
Address: Department of Physical Education and Sport Science, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran.
Tel: +98 (911) 1274366
E-mail: abbasi.daloii@gmail.com

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tosis through decreasing Bax and increasing Bcl-2; Accordingly, the present study attempts to investigate the effect of a course of endurance training and consumption of L-Carnitine on the expression of BLC-2 and Bax gene of liver tissue in boldenone-poisoned mice.

2. Materials and Methods

In this experimental study, 30 male Wistar rats (12 weeks old with a mean weight of 195±7.94g) were randomly divided into 5 groups of 6, including: control, untreated, boldenone, L-Carnitine, and L-Carnitine + aerobic exercise". Boldenone group received 5 mg Boldenone per kg body weight and L-Carnitine group received 100 mg L-Carnitine per kg body weight. A five-times-a-week endurance training program with an average intensity of 50 to 55% of maximal oxygen consumption was performed over six weeks [18]. The drug was injected deeply into the hamstring muscles once a week. In this study, ethical principles regarding how to work with laboratory animals such as water and food availability, proper keeping conditions, and non-coercion to do the exercises were observed. After anesthesia, the rats were dissected and their liver tissue removed. Liver apoptosis expression was measured by Real Time PCR. Data were analyzed by one-way ANOVA and Scheffe post hoc test at the significant level P<5%.

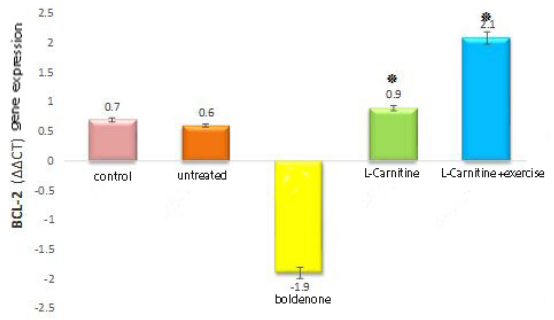
3. Results

The data showed that the mean expression of BCL-2 gene in liver tissue of male Wistar rats was different in each group (P=0.001). Results of Scheffe's post hoc test showed that BCL-2 and Bax gene expression in liver tissue was significantly lower in Boldenone group than in control group (P=0.001). Changes of liver tissue BCL-2 gene expression were significantly higher in L-Carnitine and L + -carnitine groups than in Boldenone group (P=0.001) (Figure 1). Also, the results of Scheffe's post hoc test showed that the Bax gene expression in liver tissue was significantly increased in Boldenone group compared to the control group (P=0.001). Liver tissue changes of Bax gene expression in the L-Carnitine and L-Carnitine + groups were significantly lower than the Boldenone group (P=0.001) (Figure 2).

4. Discussion

In the present study, L-Carnitine supplementation with regular aerobic exercise increased the anti-apoptotic factor of BCL-2 in liver tissue after using Boldenone [19]. One of the beneficial mechanisms of L-Carnitine on hepatotoxicity is the ability to stabilize the cell membrane fluidity by regulating sphingomyelin levels. In addition, L-Carnitine has been shown to have antioxidant properties with protective effects against free radical damage [20]. The results of the present study also showed that L-Carnitine, by enhancing tissue anti-apoptotic factor BCL-2, has protective effects against apoptosis induced by boldenone administration. According to some recent studies, exercise results in increased levels of BCL-2 [21, 22], which is consistent with the findings of the present study [23, 24].

The precise mechanisms of exercise activity in regulating the apoptotic pathway of liver tissue are not well understood, but according to previous research, exercise activity can inhibit caspase-9 activation and also eventually can positively regulate apoptosis process by reducing pro-apoptotic Bax protein and increasing anti-apoptotic Bcl-2 protein, thereby inhibiting cytochrome c release. [13, 25]. However, the results of the present study are not consistent with some previous studies [7, 26, 27]. The inconsistency in these results may be due to factors such as short duration of exercise in each session or training period or abnormal levels of apoptotic regulators in the subjects. According to the results of the present study, supplementation of L-



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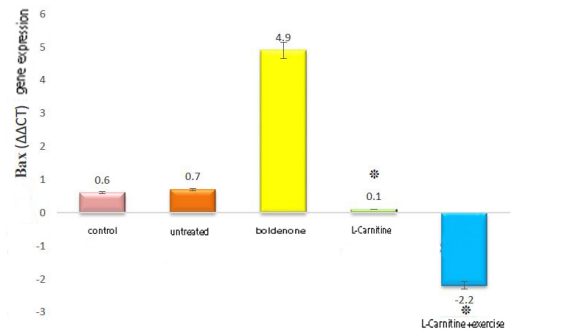
Arak University of Medical Sciences

Figure 1. mean changes of BCL-2 gene expression in liver tissue of male Wistar rats in different groups
* significant increase compared to Boldenone group



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Arak University of Medical Sciences

Figure 2. changes of mean BAX gene expression in liver tissue of male Wistar rats in different groups after intervention
* significant decrease compared to Boldenone group

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Carnitine with regular aerobic exercise reduced the expression of apoptosis factor Bax gene in liver tissue following Boldenone administration [26, 28]. This increase appears to be one of the mechanisms of Bax suppression [28-31].

5. Conclusion

Briefly, L-Carnitine supplementation with regular aerobic exercise reduced apoptotic factor and increased anti-apoptotic factor of liver tissue following Boldenone administration; therefore, it appears that L-Carnitine supplementation combined with regular aerobic exercise may have a protective effect against apoptosis induced by androgenic anabolic steroids.

Ethical Considerations

Compliance with ethical guidelines

All experiments were conducted in accordance with the Declaration of Helsinki: Statement of Ethical Principles for Medical Research. This plan was reviewed by the Ethics Committee of Ferdowsi University and approved under No. 3/19753.

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Authors' contributions

Conceptualization: Asieh Abbassi Daloii; Investigation: Samira Salehi Kiasari; Writing – review & editing: Mozhgan Ahmadi

Conflicts of interest

There was no conflict of interest in conducting this study.

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