Indian Journal of Science and Technology, *Vol 8(S8), 440–449, April 2015*

ISSN (Print) : 0974-6846
ISSN (Online) : 0974-5645
DOI: 10.17485/ijst/2015/v8iS8/71212

Comparison of Creatine and Glutamine Supplementation Consumption along withResistance Exercise on the Level of Female Mice' ALP

Eskandari Abbas*, Sharifi Gholam Reza and Modaresi Mehrdad

Islamic Azad University, Isfahan Unit (Khorasgan), Isfahan, Iran

Abstract

Background and Purpose: In recent years, in order to improve power, speed, the increase in the volume of the musculature, preventing sports injuries and maintain the muscle performance athletes use from different resistance exercises and food supplements. In this regard, present study has been conducted with the aim of comparison the influence of an 8 week period consumption of creatine (2 g/kg/day in 1st week and 0.48 g/kg/day during 2nd to 8th weeks) and glutamine (1g/kg/day from first to eight weeks) along with resistance exercise and weight on the level of ALP of small laboratory female rats. **Materials and Methods:** This experimental study was done on 80 Small adult female mice of Surrey species (28 ± 5 gram). The animals were randomly divided into 8 main groups of: resistance exercise, resistance exercise + creatine, resistance exercise + glutamine, resistance exercise + glutamine + creatine, creatine, glutamine, creatine + glutamine and control groups (N = 10). Resistance exercise (5 days a week) was including: climbing (4 sets, 5 times repetition with two minutes rest between the sets) from a ladder (with the height of one meter and including 26 steps) and bearing 30 percent of the weight of the Mouse body (hanging from tail) in the first week and the increasing it up to 200 percent of body weight till the last week of the experiment. During 24 hours after the last practice session of resistance exercise, the blood sample was taken and the the level of ALP has been measured. **Findings:** The results showed that the level of ALP enzyme in groups supplemented with creatine + glutamine (combined with each other) and underwent the resistance exercise had been increased in comparison with the control group (144.3 ± 15.86 in comparison with 234.7 ± 25.69/UL; $P < 0.05$). Also the results of Duncan test showed that the highest gaining of the weight was related to the group of combination of resistance exercise and glutamine and the lowest was related to the control and creatine, creatine + glutamine and resistance exercise + creatine groups. **Conclusion:** The results of this research indicate an increase in the level of ALP enzyme in the liver of mice under effect of the resistance exercise and consumption of creatine-glutamine supplementation and it showed that consumption of glutamine supplementation along with resistance exercise has the most influence upon the animals' weight. Therefore these results suggest more importance of them and more studies are necessary to be done.

Keywords: ALP Enzyme, Creatine, Glutamine, Laboratory Mouse, Liver, Resistance Exercise

1. Introduction

One of the issues, that athletes since long time ago have looked for, is improving the sport performances. In recent years many food supplements have drawn the attention of researchers and their inquiring mind have been directed toward the studying different influences of supplements on muscular power, body shape and other physiological mechanisms. A wide range of researches have investigated the effect of food supplements on the performance of sports.

**Author for correspondence*

Some of the other methods, by which athletes use for increasing and promoting physical fitness level, are resistance exercises. In general, Athletes use different resistance exercises in order to increase the power, the speed, enhancing the muscle volume, preventing sports injuries and maintaining muscle performance[3–5].

On the other hand in recent years along with athletic exercises, consumption of food supplements also has become popular and almost all athletes in their life sports, despite a lack of knowledge about the influence of these supplementations, have used one or few of them[6]. Although researches have shown that many of these supplements have no effect on performance of people, however, it has been proven that one of the most effective diet supplements existing for the athletes is creatine supplement. Therefore, it can be said that creatine is probably the most useful sports supplement for improving athletes' performance. However, still there are some worries about the harmful effect of short term and long term consumption of the creatine on the health[7]. Also, a lack of significant influence of glutamine supplements on some enzymes such as creatine kinase has been reported[8].

In addition, the investigations have shown that low level of glutamine in plasma is as an indicator either of too much exercise and or of fatigue in athletes and following heavy exercises the amount of this amino acid diminishes in blood. In spite of this clear information, still there is no general agreement about consumption of glutamine for prevention of these conditions (such as fatigue and injuries associated with too much exercise)[9].

Therefore, study in this field will lead to achieve better goals in a sport performance. At the end, liver enzymes (including ALP) due to being influenced with resistance exercises and consumption of the diet supplements are utilized as the index for detection effect of food supplements and resistance exercises[10–12]. As, with the increase in body temperature, contraction of active muscles and hitting of sole of foot to the floor during the sport activities, the lifespan of red blood cells becomes shorten and as a result, there will be an increase in bilirubin as a final product in haemoglobin breakdown. A non-conventional increase in bilirubin is a sign of liver damage and disorder, while the best evaluation of the liver is through investigation of alterations in activity of liver enzymes especially ALP, because, in the case of Hepatic Cell Damage the amount of these transaminase elevates in the blood.

In a study done by Waldron et al, it was detected that consuming creatine supplement during exercise has no meaningful effect on hepatic disorder (amount of ALP enzyme activity)[23]. In the other hand, Saki et al also investigated the impact of supplement consumption on the level of various enzymes in athletes whom were doing resistance exercises. Their results showed that level of ALP has elevated[28].

With regard to the above cases and existing contradictions about the impact of supplements and athletic exercises on the health and weight of athletes and especially combination effect of these supplements on the liver, that has an important and fundamental role in many body functions, Therefore the present research with the aim of determining influence of resistance exercises and creatine and glutamine supplements consumption on the levels of ALP and weight of laboratory small female mice was conducted.

2. Materials and Methods

In this research, all the cares of the animals were performed based on ethical guideline in animal experiment research of Brazil (COBEA) and animal scientific research committee of university of Vale do Paraiba (ethical code of present research: 493059).

3. Experimental Design

The present investigation is an experimental study and was done on 80 laboratory adult female mouse three month old (28.00 ± 5.0 gram) which were kept separately (22 ± 2 degrees centigrade, with air moisture of the 50 ± 5 % and the cycle of light to darkness 12:12 hours). Water and food was freely available. The study was done for eight weeks and animals were randomly separated to 8 Groups (N = 10): resistance exercise, resistance exercise + creatine, resistance exercise + glutamine, resistance exercise + glutamine + creatine, creatine, glutamine, creatine + glutamine and control groups.

4. Resistance Exercise

Climbing from a ladder with the height of one meter (with 26 steps, with 2cm distance and slope of 85 degrees) and connection of sinker to the tail of mouse as a resistance

exercise were used. Mice got familiar with the exercise for one week. After acquaintance, resistance exercises got started using cylinder contained sinker which was closed with an adhesive to the tail of mice (2-3 cm from the proximal end). After closing the weight to the tail of small laboratory female mice, they encouraged to climb. In the third week in which mice were adapted to exercise protocol, in the beginning for adaptation we used encouragement with food and touch, but after a few weeks the mice used to do them and immediately when they placed in the foot of ladder began to climb. In the first week the amount of closed traction was up to 30 precents of weight of their body that was gradually increased and it reached about 200 precents of their weight in the last week (Table 1). Resistance exercises were including five days in a week containing 4 sets, 5 time repetitions with one minute rest between repetitions and two minutes between the sets for eight weeks.

Table 1. The resistance exercise program in 4 sets of 5 repetitions on the one meter ladder with 26 steps and 2cm distance

Week	I	II	III	IV	V	VI	VII	VIII
Load (Percentage of the Body Weight)								

5. Supplements

Supplements either alone, along with resistance exercise and or in combination with each other were given to mice as the following. Animals received the supplements via gavage.

5.1 Creatine Supplement

The creatine supplement was started along with resistance exercise. Dosage used for creatine was 2 g/kg/day (loading stage) in the first week and 0.48 g/kg/day during 2nd to 8th weeks (maintenance stage). The dose was administered 30 minutes before exercise resistance to the animals.

5.2 Glutamine Supplement

The glutamine supplement was begun along with resistance exercise. Dosage used for glutamine was 1g /kg/day from in all eight weeks. The considered dose was given to the animals 60 minutes after resistance exercise (or after feeding with creatine supplement to groups without resistance exercise).

6. Enzyme Level Measurement

Twenty four hours after the last resistance exercise, the animals were killed and blood sample was taken. In order to separate the serum from blood cells, obtained blood samples were centrifuged at temperature of 4 degrees celcius with the speed of 5000 round per minute (rpm) for 10 minutes. The measurement of activity levels of Alkaline phosphatase (ALP) were performed with ELISA method (Enzyme-linked immunosorbent) and with the utilizing the kits of HANGZHOU EASTBIOPHARM company with the help of the auto- analyser RA- 1000 made of Technicom company of the US.

7. Statistical Method

We applied kolmogorov-smirnov test for determining the normality of data. Of one-way analysis of variance and LSD post hoc test and Duncan's multiple range tests for comparison of difference among groups were used. For analysis of data SPSS software version 19 (version 19, SPSS Inc, Chicago, IL) was used and significant level was considered $P< 0.05$. Also the results were presented based on the mean and Standard Deviation.

8. Result

According to the given results in the Table 2, Kolmogorov-Smirnov test showed that data correlated to ALP liver enzyme and weight of the mice followed a normal distribution ($P > 0.05$). Moreover, data have had a homogeneous variance ($P > 0.05$).

Table 2. The test results of Kolmogorov-Smirnov test and homogeneity of variances for ALP liver enzyme and weight of mice

Variable	Kolmogorov-Smirnov	Significance Level	Homogeneity of Variances
ALP Enzyme (IU/L)			
Weight of Mice (gram)			

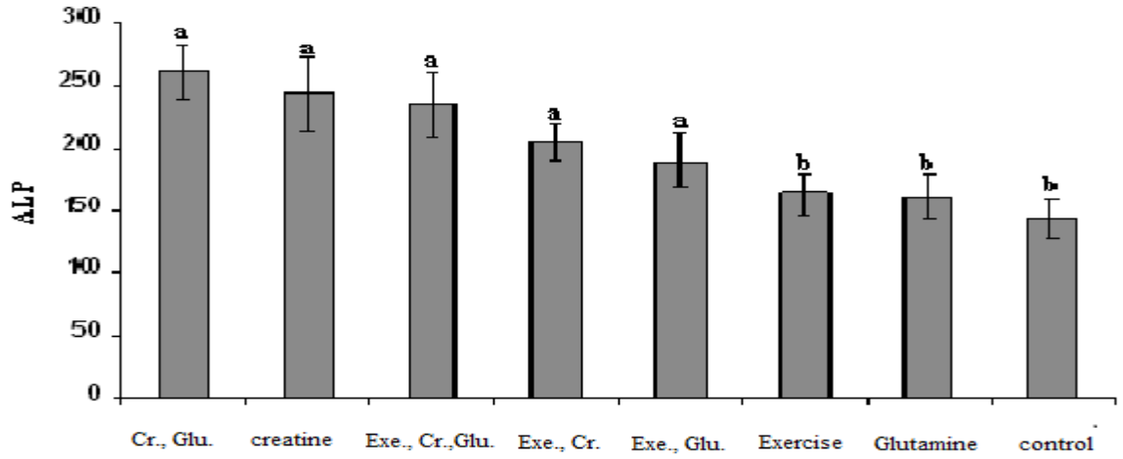

Figure 1. Comparison of the level of ALP enzyme of control group with 7 applied groups using the LSD test (Cr.: Creatine, Glu.: Glutamine, Exe.: Exercise).

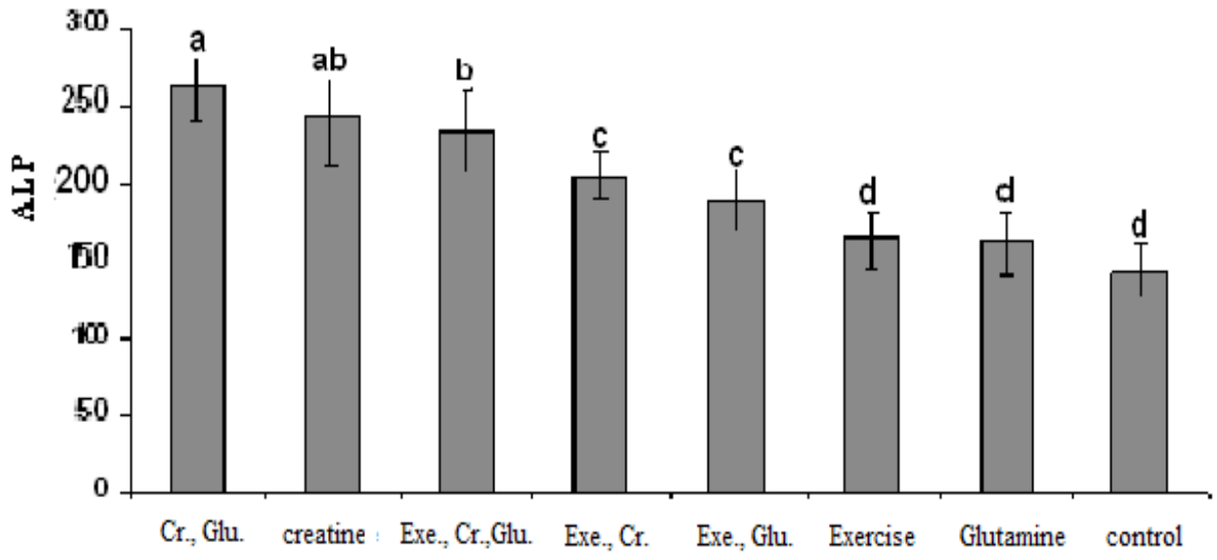

Figure 2. Comparison of the level of ALP in eight groups of mice under applied treatments by using Duncan test (Cr.: Creatine, Glu.: Glutamine, Exe.: Exercise).

9. ALP Enzyme of Mice Liver

Corresponding to the results presented in the table No. 3, one-way analysis of variance showed that the amount of ALP enzyme of mice liver of control group in comparison with mice groups underwent different treatments (glutamine, creatine, creatine + glutamine, exercise + creatine, exercise + glutamine, exercise + creatine + glutamine and exercise) had a meaningful difference ($P < 0.05$). So that, according to LSD test results, in mice which had consumed the creatine and glutamine supplementations along with resistance exercise and group under resistance exercise, in comparison with the control group the levels of liver enzyme ALP had increased (Figure 1).

The letter (b) expresses lack of significant effect and letter (a) indicates a meaningful influence of groups on the amount of the hepatic ALP in comparison with control group.

Also Duncan test results showed that there was a significant difference in the amount of liver enzyme ALP of mice among groups under influence of consumption of the dietary supplements with each other and with the control group. In a way that the highest value of ALP level was related to those mice that had consumed creatine + glutamine and the least value associated to groups of exercise, the group consumer of glutamine and control group (Figure 2). Latin letters from (a) to (d) respectively show the highest and lowest influence on the amount of ALP.

10.1 Weight of Mice under the Influence of Different Groups of Treatments during the 8 Weeks

According to the results presented in the Table 4, the test results of one-way analysis of variance showed that there is a meaningful difference between weights of mice in different weeks ($P<0.05$).

Table 3. Comparison of ALP enzyme of mice liver under the influence of consumption of supplements and resistance exercise tests using LSD and Duncan tests

Group	The Mean and Standard Deviation of ALP	Comparison with LSD Test	Comparison with Duncan Test
Resistance Exercise		B	D
Exercise + Creatine + Glutamine		A	B
Exercise + Glutamine		**A**	**C**
Exercise + Creatine		**A**	**C**
Creatine + Glutamine		**A**	**A**
Creatine		**A**	**AB**
Glutamine		**B**	**D**
Control		**B**	**D**

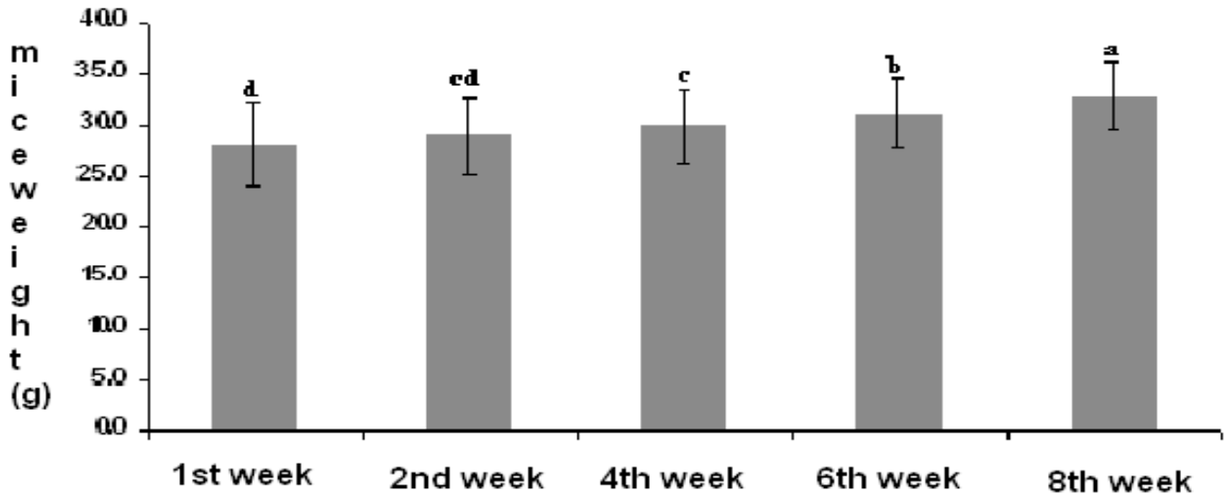

Figure 3. Comparison of mice weight during the period of experiment using Duncan test.

(Latin letters from (a) to (d) respectively indicate the highest and lowest amount of influence on the weight of the body).

Table 4. Comparison of mice weight during the period of experiment using Duncan test

Time	The Average and Standard Deviation of Mice Weight	Comparison with Duncan Test
First Week		D
Second Week		CD
Fourth Week		C
Sixth week		B
Eighth week		A

Additionally, the result of Duncan test showed that the highest mice weight is related to eighth week and the least was associated to first week (Figure 3).

10.2 Weight of Mice under the Influence of Different Treatment Groups

According to the results listed in Table 5, the results of one-way analysis of variance test showed that there was a meaningful difference between weights of mice under the influence of consumption of supplements and or different treatment groups ($P<0.05$). Additionally, based on LSD test results, a significant difference between weight of mice in control group and other groups was observed (Figure 4). The results of Duncan test showed that weight of mice among different groups (glutamine, creatine,creatine + glutamine, exercise + creatine, exercise + gluta mine, exercise + creatine + glutamine and exercise)had a meaningful difference, in a way that the highest weight related to the mice in combination group of resistance exercise + glutamine and the lowest is for control group (Figure 5). The letter (b) indicates lack of significant influence and letter (a) shows a significant effect of groups on the amount of the weight of the body in comparison with control group.

11. Discussion

Based on the results of this research, 8 week resistance exercise and consumption of supplementations has a significant influence on the level of the ALP liver enzyme and body weight of the mice. The other researchers have achieved to the similar results as our study[11,13].

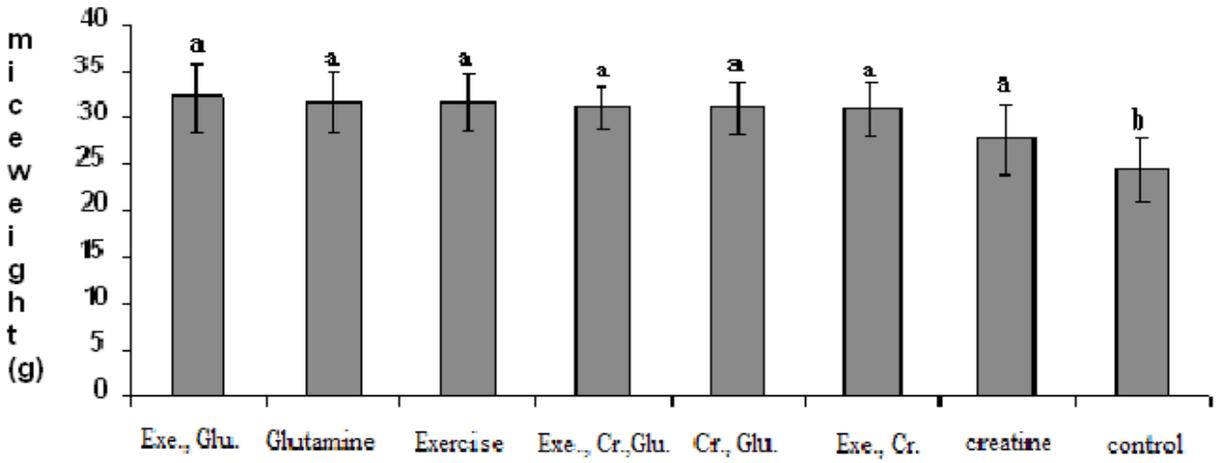

Figure 4. Comparison of mice weight among control group and other groups using LSD (Cr.: Creatine, Glu.: Glutamine, Exe.: Exercise).

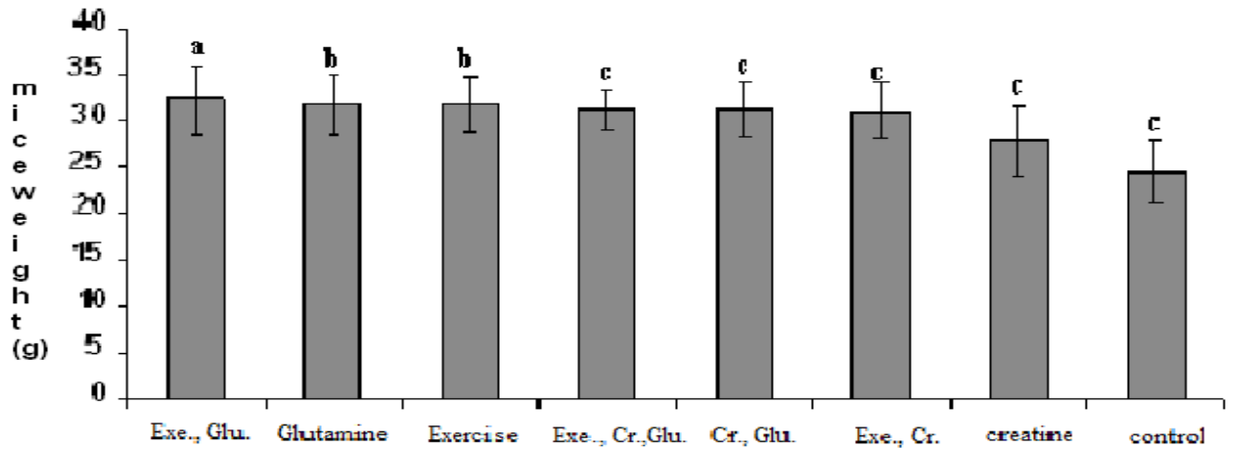

Figure 5. Comparison of mice weight under influence of different groups using Duncan Test (Cr.: Creatine, Glu.: Glutamine, Exe.: Exercise).

(Latin letters (a) to (c) respectively show the highest and lowest amount of influence on the weight of the body).

Table 5. Comparison of weight of mice in control group and other groups with LSD and Duncan Tests

Group	The Average and Standard Deviation	Comparison with LSD Test	Comparison with Duncan Test
Exercise		B	B
Exercise + Creatine + Glutamine		A	C
Exercise + Glutamine		A	A
Exercise + Creatine		A	C
Creatine + Glutamine		A	C
Creatine		A	C
Glutamine		A	B
Control		B	C

Also the results of this study showed that resistance exercise doesn't cause a meaningful change in the amount of ALP liver enzymes in patients with liver disorder and it could be one of the distinctions of exercise resistance in comparison with supplements such as creatine. Barani and his colleagues also stated that resistance exercise with a reduction in the level of ALP enzyme and an improvement in physical fitness parameters can be effective in recovery of patients with fatty liver[13].Also Bemben et al have found the similar results and reported that resistance exercise doesn't change the level of ALP meaningfully[14].

Additionally based on the results of this research, the amount of ALP enzyme in the liver of rats under the influence of glutamine supplementation consumption in comparison with the control was without a significant difference. Faokhshahi Nia et al also in a study in order to determine the effect of glutamine supplementation on these varity of perceived pain stated that this supplement has no effecton the Index of muscle damage and causes a reduction in muscle pain created with exercises[8].

In the field of how glutamine affects, Pithon and colleagues stated that glutamine in improving and control of inflammatory processes including activity of neutrophils has an effective role in the increase of host defense mechanism and lead to the decrease of the inflammatory periods and the fibrous death[15]. Cruzat et al about the influence of glutamine supplement consumption on indices of muscle damage mentioned that consumption of glutamine supplementation decrease the release of enzyme immediately after exercise protocol[16]. So this is one of the reasons that this glutamine supplement is important for athletes. The results of Dabidi et al' study indicates a lack of meaningful influence of glutamine supplement on some of immune indices due to sport activities[17].

On the other hand creatine supplement consumption has caused the significant increase in the amount of liver enzymes of ALP in liver of mice in comparison with both control group and other studied groups. Researchers in this field have studied the liver enzyme changes and have achieved to various results. In the sense that creatine probably can prevent the increase in the activity of these enzymes[18,19]. While, some of the researches have reported the role of creatine in the increase of these enzyme, in other it is indicated that consumption of creatine on the level of Serum enzymes is in effective[20,21].

This fact regarding the influence of creatine consumption on the serum indices of liver injury is more acute. For example, Kreider announced that creatine supplementa tion will increase the amount of some ofthe hepatic enzymes[22]. On the other hand the results of Mayhew and colleagues in contrary with present research results showed that consumption of creatine supplementation doesn't cause a significant increase in liver enzymes[23]. So for definitive comment in this regard, more researches are necessary.

Of the other findings of this study was that effect of a combination of resistance exercise along with creatine and with glutamine + creatine though caused a significant increase in amount of liver enzyme of ALP compared to the control group but it had less effect compared to mice that had consumed creatine and creatine + glutamine.

Therefore generally, based on finding of this part of the research it can be concluded that if resistance exercise is done along with consuming different supplementations, to a great extent causes an adjustment in the amount of release of ALP enzyme.

Robinson et al also stated that simultaneous use of combination of creatine supplement with athletic exercises will not increase the liver enzymes significantly[20]. Bashiri and his colleagues stated that its reason is the type, duration and intensity of sport activities that can be effective on activation of liver enzymes as well. Also they acknowledged long term and Endurance activities with which energy production is more aerobic are more effective on the amount of activity of liver enzymes, because for continuing of these types of activities need more energy production via the aerobic system[24]. In this regard, Mougios mentioned that liver enzymes are involved in the liver metabolism, since liver is involved in this kind of activities more than other activities[25]. Therefore, the possibility of hepatic cell membrane damage is higher in long term and endurance activities. In the other way, if the exercise is kind of resistance exercise, most part of energy required for such activities are provided through the anaerobic way thereby, damage to the cells and especially enzymes of liver, which are not involved in providing required energy, will be much less. Contrary to results of present research, findings of some of the researchers showed the increase in Liver enzymes with athletic exercises[26].

According the results of this study, if a resistance exercise is done parallel with consumption of supplement, to a large extent it will decrease the amount of ALP enzyme in the liver. Bashiri and his colleagues also expressed that using a combination of resistance exercise and consumption of creatine monohydrate as the index of liver Cell Damage, there is no likely an

undesirable increase in liver enzymes (AST and ALT)[24].

11.1 Weight of Mice under Consumption of Supplements and Resistance Exercise

As expected the results of this research showed that with the progress of time, mice' weight increased with consumption of different supplementations and resistance exercise. And also based on the results, weight of mice in control group was the lowest and mice with resistance exercise, those under the supplement consumption and group of a combination of exercise + glutamine had the highest weight.

Kilduff et al acknowledged that using of supplements with resistance exercises during 4 to 12 weeks lead to increase performance of individuals[27]. Also some of the other researchers reported the weight of the body by consuming food supplements in comparison with the control group had a meaningful increase[28–30]. The reason of increasing of the body weight following consumption of supplements such as creatine is because of increase in the protein synthesis and consequently increases in the weight[31].

12. Conclusion

Generally based on the findings of this study, weight of mice using supplements and resistance exercise in contrast to impact of the eight groups is to a large extent influenced by the amount of the secretion of ALP. In the other words, the consumption of glutamine supplement with resistance exercise had the least influence in secretion of ALP of liver and the highest influence on the weight of the mice body.

But consumption of creatine supplement had the highest influence on the secretion of the ALP and the least effect on the weight of the body. Therefore it may be possible to determine the influence of supplements on the body weight with detecting the amount of these cretion liver enzymes. Of course to achieve the definite answer it is needed more studies to be done. At the end results of this investigation indicates the distinction between influence of creatine and glutamine supplement. Because glutamine had less influence in secretion of ALP enzyme and more important role in the increase in weight of the body and its effects was almost parallel and close with resistance exercise. Of course it should be mentioned that a combination of supplementation of glutamine + creatine has much effecton liver enzymes ALP secretion, though this can be related to some extent to the effect of the creatine, however more investigations are mandatory.

13. References

1. Okudan N, Gokbel H. The effects of creatine supplementation on performance during the repeated bouts of supramaximal exercise. J sport Med. 2005 Dec; 45(4):507–11.
2. Havenetidis K, Boone T. Assessment of ergogenic properties of creatin using an intermittent exercise protocol. Journal of exercise physiology. 2005 Feb; 8(1):26–33.
3. Shackelford LC, Leblance AD, Driscoll TB, Evans HJ, Rianon NJ, Smith SM. Resistance exercise as a counter measure to disuse-induced bone loss. J Appl Physiol. 2004 July; 97: 119-120
4. Guzel NA, Hazar S, Erbas D. Effect of different resistance exercise protocols on nitric oxide, lipid peroxidation and creatine kinase activity in sedentary males. J Sports Sci Med. 2007 Jun; 6(4):17–22.
5. Matsus H, Shiba N, Umezu Y, Nago T, Maeda T, Tagawa Y, et al. Effects of hybrid exercise on the activities of myogenic enzymes in plasma. Kurume Med J. 2006 Sep; 53(3–4):47–51.
6. Williams HS. A history of science. Modern Development of the Chemical and Biological Sciences. New York: Harper and Brothers; 2007.
7. Pettersson J, Hindorf U, Persson P, Bengtsson T, Malmqvist U, Werkstrom V, et al. Muscular exercise can cause highly pathological liver function tests in healthy men. Br J Clin Pharmacol. 2008 Feb; 65(2):253–9.
8. Farokhshahi R, Rahmaninia F, Farzaneh E. The effect of glutamine supplementation on intensity of perceived pain and creatine kinase after eccentric contraction in untrained men. Sport Physiology. 2013 May; 19:97–110.
9. Nissen S, Sharp R, Ray M, Rathmacher J, Rice D, Fuller J. Effect of leucine metabolite beta-hydroxy-beta-methylbutyrate on muscle metabolism during resistance-exercise training. J Appl Physiol. 1996 Nov; 81(5):2095–104.
10. Hann HW, Wan S, Myers RE, Hann RS, Xing J, Chen B. Comprehensive analysis of common serum liver enzymes as prospective predictors of hepatocellular carcinoma in HBV patients. PLoS One. 2012 Oct; 7(10):1–10.
11. Kawanishi N, Yano H, Mizokami T, Takahashi M, Oyanagi E, Suzuki K. Exercise training attenuates hepatic inflammation, fibrosis and macrophage infiltration during diet induced-obesity in mice. Brain Behav Immun. 2012 Aug; 26(6):931–41.

12. Slentz CA, Bateman LA, Willis LH, Shields AT, Tanner CJ, Piner LW, et al. Effects of aerobic vs. resistance training on visceral and liver fat stores, liver enzymes, and insulin resistance by HOMA in overweight adults from STRRIDE AT/RT. Am J Physiol Endocrinol Metab. 2011 Nov; 301(5):E1033–9.
13. Barani F, Afzalpour ME, Ilbiegi S, Kazemi T, Mohammadi Fard M. The effect of resistance and combined exercise on serum levels of liver enzymes and fitness indicators in women with nonalcoholic fatty liver disease. Birjand University of Medical Sciences. 2014 Jun; 21(2):188–202.
14. Bemben MG, Lamont HS. Creatine supplementation and exercise performance: recent findings. Sports Med. 2005 Feb; 35(2):107–25.
15. Pithon-Curi TC, Schumacher RI, Freitas JJ, Lagranha C, Newsholme P, Palanch AC, et al. Glutamine delays spontaneous apoptosis in neutrophils. Am J Physiol Cell Physiol. 2003 Jun; 284(6):55–61.
16. Cruzat VF, Rogero MM, Tirapegui J. Effects of supplementation with free glutamine and the dipeptide alanyl-glutamine on parameters of muscle damage and inlfammation in rats submitted to prolonged exercise. J Cell Biochem Funct. 2010 Jan; 28(1):24–30.
17. Dabidi Roshan V, Barzegarzadeh H. The effect of the short-term glutamine supplementation on exhaustive exercise-induced changes in immune system of active boys. World J Sport Sci. 2009 Aug; 2(4):222–30.
18. Cooke M. The effects of nutritional supplementation on regeneration of muscle function after damage. A dissertation submitted in total fulfilment of the requirements of the degree of Doctor of Philosophy. Faculty of Health. Engineering and Science Victoria University Footscray Park Campus:Victoria University; 2005.
19. Santos RV, Bassit RA, Caperuto EC, Costa Rosa LF. The effect of creatine supplementation upon inflammatory and muscle soreness markers after a 30km race. Life Sci. 2004 Sep; 75(16):1917–24.
20. Robinson TM, Sewell DA, Casey A, Steenge G, Greenhaff PL. Dietary creatine supplementation does not affect some hematological indices, or indices of muscle damage and hepatic and renal function. Br J Sports Med. 2000 Aug; 34(4):284–8.
21. Waldron JE, Pendlay GW, Kilgore TG, Haff GG, Peeves JS, Kilgore JL. Concurrent creatine monohydrate supplementation and resistance training does not affect markers of hepatic function in trained weight lifters. JEP 2002 Feb; 5(1):57–64.
22. Kreider RB. Creatine supplementation: analysis of ergogenic value, medical safety, and concerns. J Exerc Physiol. 1998 April; 1(1):7–18.
23. Mayhew DL, Mayhew JL, Ware JS. Effects of long-term creatine supplementation on liver and kidney functions in American college football players. Int J Sport Nutr Exerc Metab. 2002 Dec; 12(4):453–60.
24. Bashiri J, Gaeini A, Nikbakht H, Hadi H, Bashiri M. Effect of concurrent creatine monohydrate ingestion and resistance training on hepatic enzymes activity levels in non-athlete males. Iranian Journal of Endocrinology and Metabolism. 2010 May; 12(1):42–7.
25. Mougios V. Exercise Biochemistry. In: Rahnema N, Nouri R, Rouhani H, Shadmehri S, Aghaee N, Saberi Y, editors. Tehran: Samt Publishing; 2009.
26. Parikh DJ, Ramanathan NL. Exercise induced serum enzyme changes in untrained subjects. Indian J Physiol Pharmacol. 1977 Jul; 21(3):175–80.
27. Kilduff LP, Pitsiladis YP, Tasker L, Attwood J, Hyslop P, Dailly A, et al. Effect of Creatine on body composition and strength gains after 4 week of resistance training in previously nonresistance-trained humans. Int J Sport Nutr Exerc Metab. 2003 Dec; 34(4):504–20.
28. Garazhian Y, Rahmani-Nia F, Rahnama F. The comparative effects of oral creatine supplementation and high protein on muscular strength and body composition. Int J Sports Sci Eng. 2008 Sep; 2(4):223–30.
29. Kutz MR, Gunter MJ. Creatine monohydrate supplementation on body weight and percent body fat. J Strength Condit Res. 2003 Nov; 17(4):817–21.
30. Becque MD, Lochmann JD, Melrose DR. Effects of oral creatine supplementation on muscular strength and body composition. Med Sci Sports Exerc. 2000 Mar; 32(3):654–8.
31. Kocak S, Karli U. Effects of high dose oral creatine supplementation on anaerobic capacity of elite wrestlers. J Sport Med Phys Fitness. 2003 Dec; 43(4):488–92.