Palestrica of the third millennium – Civilization and Sport
Vol. 17, no. 3, July-September 2016, 229–232

The efficiency and safety of L-carnitine and caffeine after short- and long-term administration

Eficacitatea și siguranța L-carnitinei și cafeinei după administrarea pe termen scurt și lung

Amalia Miklos [1], Laura Ciulea [2], Camil Eugen Vari [1], Silvia Imre [1], Bianca Eugenia Ősz [1], Amelia Tero-Vescan [1]

[1] *Faculty of Pharmacy, University of Medicine and Pharmacy Târgu Mureş, Romania*
[2] *Faculty of Medicine, University of Medicine and Pharmacy Târgu Mureş, Romania*

Abstract

L-carnitine and caffeine are excessively used by athletes for increasing or prolonging sport performance due to their ergogenic effects. These supplements are considered harmless among athletes, but the specialized data regarding their safety in long-term administration, in high doses, are not sufficient. On the other hand, the studies that support the effectiveness of these products are numerous, encouraging their use. This review was designed to emphasize the idea that the administration of these supplements is not as safe as it seems to be. Homeostasis of the body can be affected, especially in their long-term administration. Considering these issues, athletes are advised to be cautious and knowledgable before starting to use these supplements.

Key words: efficiency, safety, L-carnitine, caffeine, athletes.

Rezumat

L-carnitina şi cafeina sunt utilizate în mod excesiv de către sportivi pentru creșterea sau susținerea performanței sportive datorită efectelor ergogenice. Aceste suplimente sunt considerate inofensive în rândul sportivilor, însă datele de specialitate privind siguranța lor în administrare pe termen lung și în doze mari, nu sunt suficiente. În schimb, sudiile care susțin eficiența acestor produse sunt numeroase, încurajând utilizarea lor. Acest studiu a fost conceput pentru a sublinia faptul că administrarea acestor suplimente nu este atât de sigură precum pare a fi. Homeostazia organismului poate fi afectată, mai ales în administrarea acestora pe termen îndelungat. Având în vedere aceste aspecte, sportivii sunt sfătuiți să fie prudenți și bine informați înainte de a recurge la utilizarea acestor suplimente.

Cuvinte cheie: eficinență, siguranță, L-carnitină, cafeină, sportivi.

Introduction

The use of nutritional supplements by athletes to improve their performance has gone through a surprising evolution in the last decade. A complete analysis of 51 studies including a total of 10,274 athletes reveals that a share of 46% have constantly used dietary supplements, including ergogenic substances (Apostu, 2014). In addition, these supplements are administered chaotically in terms of frequency, quantity and duration.

The inconvenience is that many nutritional supplements and pharmacological substances such as L-carnitine or caffeine are used excessively, without knowing the clear effects on human homeostasis after acute or chronic administration. In this context, it is important to evaluate efficiency and safety before taking these supplements, because they can be harmful to the body if not administered correctly.

In our review, we aimed to emphasize the efficiency and safety of L-carnitine and caffeine in short- and long-term administration, considering their extensive use in sports field.

L-carnitine

Carnitine is a hydrophilic quaternary amine with important functions in intermediary metabolism, its biological activity being due to the "levo" isomer form. The primary role played by carnitine is in the process of mitochondrial β oxidation. Carnitine translocates the long-chain fatty acids into the mitochondrial matrix, where oxidation occurs and energy results (Pekala et al., 2011; Traina, 2016).

This action is essential in the metabolism of fatty acids,

Received: 2016, July 30; *Accepted for publication:* 2016, August 8;
Address for correspondence: Faculty of Pharmacy, University of Medicine and Pharmacy Târgu Mureş, 38 Gh Marinescu Street, Târgu Mureş, Romania
E-mail: amalia.miklos@yahoo.com
Corresponding author: Amalia Miklos: amalia.miklos@yahoo.com

because without this transport, β oxidation would not occur, leading to accumulation of these compounds, with negative effects on the body (Wu et al., 2015).

Carnitine is biosynthesized from the essential amino acids lysine and methionine in a concentration of 1.2 μmol/kg/day, but can also be obtained through dietary intake. Exogenous carnitine intake can be achieved from lamb (the highest amount), beef steak, chicken, fish, and red meat. A regular diet provides 2-12 μmol/kg/day (El-Hattab & Scaglia, 2015).

In the field of sports nutrition, L-carnitine is widely used by athletes as an ergogenic aid to enhance exercise performance and to reduce oxidative stress (Sung et al., 2016; Su et al., 2015).

Several studies have shown that L-carnitine is effective in controlling oxidative stress, holding an antioxidant effect, even after a single oral dose administration (2 g), by increasing the plasma concentrations of superoxide dismutase, glutathione peroxidase, catalase and total antioxidative capacity (Cao et al., 2011).

Regarding the production of nitric oxide after acute administration of L-carnitine at a concentration of 3 g/day and 4 g/day, respectively, it can be observed that the concentration of nitric oxide is increased, which reveals one more time the antioxidant role of L-carnitine (Atalay et al., 2015).

Besides its antioxidant effect, recent studies have shown that L-carnitine fulfills a beneficial function in the recovery process after physical exercises, reducing tissue damage related to hypoxic stress (Huang & Owen, 2012).

Another study aimed to evaluate the benefits of acute administration of L-carnitine on endurance performance in athletes, and the results showed that increasing the concentration of L-carnitine delays physical exhaustion (Orer & Guzel, 2014; Stephens et al., 2013).

On the other hand, regarding the short-term pre-ischemic administration of L-carnitine on isolated rat heart, L-carnitine seems to produce arrhythmogenic activity, which allows concluding that acute administration of L-carnitine supplements in patients with coronary artery disease should be thoroughly studied in the near future (Najafi & Garjani, 2014).

In contradiction to the previously cited study, Lee BJ et al. showed that L-carnitine supplementation at a dose of 1000 mg/day for 12 weeks has a beneficial effect in inflammation of coronary artery disease, probably due to its antioxidant properties (Lee et al., 2015).

It is known in the literature that chronic L-carnitine supplementation in a dose of 2 g/day has the property to reduce metabolic stress after exercise (Broad et al., 2008).

In this context, Parandak et al. (2014) assessed the effect of 2 g/day of L-carnitine supplementation for 2 weeks on lipid peroxidation and muscle damage markers. The conclusion was that long-term L-carnitine supplementation has beneficial effects following an acute bout of exercise in active healthy men.

An interesting issue was assessed by Novakova et al. (2016) in a recent study evaluating the difference between the effect of L-carnitine supplementation on vegetarian and omnivorous males. After oral supplementation of 2 g/day for 12 weeks, it was shown that plasma carnitine concentrations were lower in vegetarian males compared to plasma concentration in omnivorous males, but muscle carnitine stores were maintained, without affecting muscle homeostasis.

According to literature data, it can be concluded that doses ranging from 1-5 g/day are effective to enhance performance exercise and control oxidative stress both in acute and chronic administration. Since only a limited number of studies have focused on the safety of high dose administration of L-carnitine, it is difficult to establish an optimal mode of administration.

However, even if a dietary reference intake has not been officially established by The Food and Nutrition Board, the Ministry of Health and Welfare in Taiwan recommends a dose under 2000 mg/day (Sung et al., 2016).

Caffeine

Caffeine (1,3,7- trimethylxanthine) is a plant-derived alkaloid widely used as a central nervous system stimulant, nowadays being the most consumed psychoactive substance in the world (Holstege & Holstege, 2014; Mitchell et al., 2013).

The mechanism of action on the central nervous system consists of a blockade of adenosine receptors, explaining the stimulation of neuronal activity and other physiological effects, such as an increase in muscle recruitment. Caffeine also inhibits phosphodiesterase activity, increasing the plasma levels of catecholamines, stimulating the glycolysis process with a higher production of energy in muscle during exercise (Meeusen et al., 2013).

The mechanism of the ergogenic effect in high intensity exercise remains unclear, even if the literature reports the efficiency due to a combined action between central and peripheral systems (Astorino & Roberson, 2010; Black et al., 2015).

Caffeine supplementation improves sport performance, especially when consumed in an anhydrous state such as powder or capsules (Duncan et al., 2014), but this improvement is dependent on various other factors including the athlete's condition, the intensity of exercise and the dose of caffeine.

Schubert et al. showed that the consumption of caffeine (3 mg/kg/body weight) before and after a bout of moderate exercise improves fat oxidation and increases energy expenditure, and Olcina et al. showed that 5 mg/kg body weight of caffeine ingested 60 minutes before exercise induce beneficial effects on the plasma total fatty acid profile, providing ergogenic action (Schubert et al., 2014; Olcina et al., 2012).

It has been shown by various studies that caffeine supplementation in doses between 3-9 mg/kg body weight increases sport performance proportionally to the dose, improving the aerobic exercise capacity of endurance athletes by 7-35%. When consumed in higher doses (≥ 9 mg/kg), an improvement in performance is no longer noticed (Apostu, 2014) and the incidence of side effects can increase (Pallarés et al., 2013).

Regarding the time of administration in relation to the time of physical activity, caffeine should be ingested 60 minutes prior to exercise, to ensure an optimal absorption (Goldstein et al., 2010).

Pitchford et al. (2014) showed in a recent study that a moderate dose of caffeine supplementation (3 mg/kg body weight) improved the cycling performance and in doses of 5 mg/kg body mass, in acute administration, caffeine proved to delay fatigue during successive taekwondo combats (Santos et al., 2014).

In order to avoid adverse effects resulting from the administration of high doses of caffeine, Spriet aimed to evaluate the efficiency of low doses of caffeine supplementation, concluding that caffeine improves sport performance, vigilance and alertness, even if not consumed in high doses (Spriet, 2014).

In the same context, Diaz-Lara et al. (2015) determined the efficacy of ingestion of caffeine in a moderate concentration (3 mg/kg body mass), showing that this substance enhances high-intensity actions and physical performance.

However, in the literature there are studies that deny the ergogenic effect of caffeine intake.

Some researchers concluded that after supplementation with 6 mg/kg body weight caffeine, performance in judo fitness was not improved and after 5 mg/kg body weight caffeine intake, during simulated taekwondo combat, there were no increases in performance (Lopes-Silva et al., 2014; Lopes-Silva et al., 2015).

In terms of toxicology, chronic consumption of caffeine can lead to tolerance, withdrawal and substance dependence syndrome, consisting of fatigue, headache, irritability, anxiety (Morelli & Simola, 2011; Turnbull et al., 2016).

In addition, studies have confirmed that caffeine could suppress the ossification process in chronic high dose administration, leading to bone loss and predisposition to fractures (O'Keefe et al., 2013; Shin et al., 2015).

Regarding recent studies focused on caffeine administration and blood flow, it has been shown that caffeine consumption combined with physical exercise decreases myocardial blood flow (Higgins & Babu, 2013). Bunsawat et al. (2015) reports that ingestion of 400 mg caffeine followed by a maximal treadmill test to exhaustion stimulates catecholamine release and could lead to a pro-arrhythmogenic state.

Studies evaluating the risks after administration of high (> 600 mg/day) and very high (> 1200 mg/day) doses of caffeine are limited. Therefore, it is difficult to clearly define the level of side effects. Searching for a safe alternative to anhydrous caffeine consumption, Higgins et al. found that coffee containing 3-8.1 mg/kg body weight caffeine should be efficient in improving endurance performance (Higgins et al., 2016).

Conclusions

After reviewing the literature, the following conclusions can be drawn:

1. Although supplementation with L-carnitine is proven to be very effective and safe, data regarding intakes above 2000 mg/day in chronic treatment, especially in people prone to heart disease, are not enough and this issue needs a thorough investigation.

2. Caffeine supplementation improves sports performance taking into account several important factors: the athlete's condition, the intensity of exercise, the pharmaceutical form, and last but not least, the dose of caffeine.

3. Even if L-carnitine and caffeine have been proven to enhance the performance of athletes in acute or chronic administration, there are studies supporting that their efficiency as ergogenic aids is not clear.

4. Considering that only a limited number of studies are focused on safety after chronic and high dose administration, athletes should be careful and knowledgeable before taking these supplements.

Conflict of interests

There were no conflicts of interests.

References

Apostu M. The effect of ergogenic substances over sports performance. Procedia-Soc Behav Scie, 2014; 117:329-334.

Astorino TA, Roberson DW. Efficacy of acute caffeine ingestion for short-term high-intensity exercise performance: a systematic review. J Strength Cond Res. 2010; 24(1):257-265.

Atalay Guzel N1, Erikoglu Orer G, Sezen Bircan F, Coskun Cevher S. Effects of acute L-carnitine supplementation on nitric oxide production and oxidative stress after exhaustive exercise in young soccer players. J Sports Med Phys Fitness 2015;55(1-2):9-15.

Black CD, Waddell DE, Gonglach AR. Caffeine's ergogenic effects on cycling: neuromuscular and perceptual factors. Med Sci Sports Exerc. 2015;47(6):1145-1158.

Broad EM, Maughan RJ, Galloway SD. Carbohydrate, protein, and fat metabolism during exercise after oral carnitine supplementation in humans. Int J Sport Nutr Exerc Metab. 2008;18(6):567-584.

Bunsawat K, White DW, Kappus RM, Baynard T. Caffeine delays autonomic recovery following acute exercise. Eur J Prev Cardiol. 2015; 22(11):1473-1479.

Cao Y, Qu HJ, Li P, Wang CB, Wang LX, Han ZW. Single dose administration of L-carnitine improves antioxidant activities in healthy subjects, Tohoku J Exp Med. 2011; 224(3):209-213.

Diaz-Lara FJ, Del Coso J, Portillo J, Areces F, García JM, Abián-Vicén J. A moderate dose of caffeine enhances high-intensity actions and physical performance during a simulated brazilian Jiu-Jitsu competition. Int J Sports Physiol Perform. 2015, [Epub ahead of print] DOI:10.1123/ijspp.2015-0686.

Duncan MJ, Thake CD, Downs PJ. Effect of caffeine ingestion on torque and muscle activity during resistance exercise in men. Muscle Nerve 2014;50(4):523-527.

El-Hattab AW, Scaglia F. Disorders of carnitine biosynthesis and transport. Mol Genet and Metab 2015; 116(3):107-112.

Goldstein ER, Ziegenfuss T, Kalman DKreider R, Campbell B, Wilborn C, Taylor L, Willoughby D, Stout J, Graves BS, Wildman R, Ivy JL, Spano M, Smith AE, Antonio J. International society of sports nutrition position stand: caffeine and performance. J Int Soc Sports Nutr. 2010;7(1):5.

Higgins JP, Babu KM. Caffeine reduces myocardial blood flow during exercise. Am J Med 2013;126(8):730-738.

Higgins S, Straight CR, Lewis RD. The effects of preexercise caffeinated coffee ingestion on endurance performance: An evidence-based review. Int J Sport Nutr Exerc Metab. 2016;26(3):221-239.

Holstege CP & Holstege E. Caffeine. Reference Module in Biomedical Sciences. Encyclopedia of Toxicology (Third Edition) 2014, 617-620.

Huang A, Owen K. Role of supplementary L-carnitine in exercise and exercise recovery. Med Sport Sci. 2012;59:135-142. doi: 10.1159/000341934.

Lee BJ, Lin JS, Lin YC, Lin PT. Antiinflammatory effects of L-carnitine supplementation (1000 mg/d) in coronary artery disease patients. Nutrition, 2015;31(3):475-479.

Lopes-Silva JP, Felippe LJ, Silva-Cavalcante MD, Bertuzzi R, Lima-Silva AE. Caffeine ingestion after rapid weight loss in judo athletes reduces perceived effort and increases plasma lactate concentration without improving performance. Nutrients. 2014;6(7):2931-2945.

Lopes-Silva JP, Silva Santos JF, Branco BH, Abad CC, Oliveira LF, Loturco I, Franchini E. Caffeine Ingestion Increases Estimated Glycolytic Metabolism during Taekwondo Combat Simulation but Does Not Improve Performance or Parasympathetic Reactivation. PLoS One. 2015;10(11):e0142078.

Meeusen R, Roelands B, Spriet LL. Caffeine, exercise and the brain. Nestle Nutr Inst Workshop Ser. 2013;76:1-12.

Mitchell DC, Knight CA, Hockenberry J et al. Beverage caffeine intakes in the US. Food Chem Toxicol 2013;63:136–142. doi: 10.1016/j.fct.2013.10.042.

Morelli M, Simola N. Methylxanthines and drug dependence: a focus on interactions with substances of abuse. Handb. Exp. Pharmacol. 2011;(200):483-507. doi: 10.1007/978-3-642-13443-2_20.

Najafi M, Garjani A. Short term administration of L-carnitine can be detrimental to the ischemic heart. Adv Pharm Bull. 2014;4(1):1-3.

Novakova K, Kummer O, Bouitbir J, Stoffel SD, Hoerler-Koerner U, Bodmer M, Roberts P, Urwyler A, Ehrsam R, Krähenbühl S. Effect of L-carnitine supplementation on the body carnitine pool, skeletal muscle energy metabolism and physical performance in male vegetarians. Eur J Nutr. 2016;55(1):207-217.

O'Keefe JH, Bhatti SK, Patil HR, DiNicolantonio JJ, Lucan SC, Lavie CJ. Effects of habitual coffee consumption on cardiometabolic disease, cardiovascular health, and all-cause mortality. J Am Coll Cardiol. 2013;62(12):1043-1051.

Olcina G, Munoz D, Kemp J, Timona R, Maynarc J, Caballerod MJ, Maynar M. Total plasma fatty acid responses to maximal incremental exercise after caffeine ingestion. J Exerc Sci Fit 2012;10:33-37.

Orer GE, Guzel NA. The effects of acute L-carnitine supplementation on endurance performance of athletes. J Strength Cond Res. 2014;28(2):514-519.

Pallarés JG, Fernández-Elías VE, Ortega JF, Muñoz G, Muñoz-Guerra J, Mora-Rodríguez R. Neuromuscular responses to incremental caffeine doses: performance and side effects. Med Sci Sports Exerc. 2013;45(11):2184-2192.

Parandak K, Arazi H, Khoshkhahesh F, Nakhostin-Roohi B. The effect of two-week L-carnitine supplementation on exercise-induced oxidative stress and muscle damage. Asian J Sports Med. 2014;5(2):123-128.

Pekala J, Patkowska-Sokoła B, Bodkowski R, Jamroz D, Nowakowski P, Lochyński S, Librowski T. L-carnitine-metabolic functions and meaning in humans life. Curr Drug Metab. 2011;12(7):667-678.

Pitchford NW, Fell JW, Leveritt MD, Desbrow B, Shing CM. Effect of caffeine on cycling time-trial performance in the heat. J Sci Med Sport. 2014;17(4):445-449.

Santos VG, Santos VR, Felippe LJ, Almeida JW Jr, Bertuzzi R, Kiss MA, Lima-Silva AE. Caffeine reduces reaction time and improves performance in simulated-contest of taekwondo. Nutrients. 2014;6(2):637-649.

Schubert MM, Hall S, Leveritt M, Grant G, Sabapathy S, Desbrow B. Caffeine consumption around an exercise bout: effects on energy expenditure, energy intake, and exercise enjoyment. J Appl Phys 2014;117(7):745-754.

Shin J, Choi Y, Kim J, Yu AR, Shin JS, Choi YY, Roh J. High doses of caffeine reduce in vivo osteogenic activity in prepubertal rats. J Anat. 2015;227(1):10-20.

Spriet LL. Exercise and sport performance with low doses of caffeine. Sports Med. 2014;44(2):175-184.

Stephens FB, Wall BT, Marimuthu K Shannon CE, Constantin-Teodosiu D, Macdonald IA, Greenhaff PL. Skeletal muscle carnitine loading increases energy expenditure, modulates fuel metabolism gene networks and prevents body fat accumulation in humans. J Physiol. 2013;591(18):4655-4666.

Su CC, Chang CS, Chou CH, Wu YHS, Yang KT, Tseng JK, Chang YY, Chen YC. L-carnitine ameliorates dyslipidemic and hepatic disorders induced by a high-fat diet via regulating lipid metabolism, self-antioxidant capacity, and inflammatory response. J Funct Foods 2015;15:497-508.

Sung DJ, Kim S, Kim J, And HS, So WY. Role of l-carnitine in sports performance: Focus on ergogenic aid and antioxidant. Sci & Sports 2016, [Epub ahead of print]. doi:10.1016/j.scispo.2016.02.005.

Traina G. The neurobiology of acetyl-L-carnitine. Front Biosci (Landmark Ed). 2016;21:1314-1329.

Turnbull D, Rodricks JV, Mariano GF. Neurobehavioral hazard identification and characterization for caffeine. Regul Toxicol and Pharm 2016;74:81-92. doi: 10.1016/j.yrtph.2015.12.002.

Wu T, Guo A, Shu Q, Qi Y, Kong Y, Sun Z, Sun S, Fu Z. L-Carnitine intake prevents irregular feeding-induced obesity and lipid metabolism disorder. Gene 2015;554(2):148-154.