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Review Article | Journal of Nutritional Health & Food Science | Open Access

Are the Bcaas/Leucine Supplementation Effects on Exercise-Induced Muscle Damage Related Immunity Response or to Hmβ?

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Received: March 05, 2014; Accepted: April 25, 2014; Published: April 28, 2014

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Abstract

Branched-chain amino acids (BCAAs), mainly leucine, have been described as potential modulators of resistance exercise-induced muscle adaptations which includes stimulation of muscle protein synthesis and attenuation of proteolysis. However, until the moment, there are no well controlled chronic studies (randomized, double-blind and placebo-controlled) in humans assessing the effects of BCAAs/leucine supplementation on muscle hypertrophy and strength. The most well documented benefits of BCAAs/leucine concerning exercise is the attenuation of muscle damage and soreness. Previous reports support the theory that BCAAs/leucine could act through innate immunity. However, recent studies have demonstrated similar effects in humans with β-hydroxy-β-methylbutyrate (HMβ) supplementation. Since HMβ is a leucine metabolite, it appears that there is a metabolic relation among BCCAs/leucine, HMβ and the attenuation of exercise-induced muscle damage.

Keywords: Delayed onset muscle soreness; Muscle pain; Strength; Essential amino acids

Abbreviations

BCAAs: Branched-chain Amino Acids; HMβ: β-hydroxy-β-methylbutyrate; HMG-CoA: β-hydroxy-β-methylglutaryl-CoA

Background

Branched-chain amino acids (BCAAs) have been described as potential modulators of the exercise-induced muscle adaptations [1]. Among their nutritional properties, BCAAs (especially leucine) have been mainly cited as stimulators of skeletal muscle protein synthesis [2] and attenuation of proteolysis [3] when combined with resistance exercise. However, there are no chronic studies in humans performed in a randomized, double-blind design and with is nitrogenous placebo assessing its effects on muscle structure (hypertrophy) and functionality (strength).Currently, the most well documented effect in humans concerning the mechanical stimuli is the attenuation of exercise-induced muscle soreness/damage and pain[4-7].

The results of BCAAs/leucine supplementation in association with exercise have been attributed to a plasmatic leucine threshold, which is ~3 $mmol \cdot ml^{-1}$, and can be achieved after 2.5-3.0 grams of leucine intake [8]. Studies investigating the effects of leucine or BCAA supplementation on exercise-induced muscle damage do not have clear mechanisms elucidated. Few studies underwent the procedure of muscle biopsy in order to elucidate mechanisms by which these amino acids can alleviate pain and reduce the amount of plasma markers of muscle damage. The few available studies support the theory that leucine/BCAA could act as a potential anti-inflammatory. Our research group has published this theory previously [9] but no current consistent data in humans have tested such hypothesis. This theory does not consider the metabolite HMB as responsible for performing the positive effects on muscle damage, but considers that leucine/BCAAL could act through glutamine metabolism by interactions via transamination.

In this context, recent reports have described similar effects from the intake of the leucine metabolite β-hydroxy-β-methylbutyrate (HMβ) [10,11]. As recently discussed by Molfino et al. [12], HMβ presents nutritional properties related to repairing the exercise-induced damage of the cell membranes due to its metabolite β-hydroxy-β-methylglutaryl-CoA (HMG-CoA). Thus, it is plausible to assume that there is a relation among leucine, HMβ and HMG-CoA regarding exercise and muscle damage.

Therefore, leucine supplementation is necessary to attenuate exercise-induced muscle damage? Or is it possible to strongly achieve such effect through HMβ supplementation? The most recent evidences in humans concerning leucine and HMβ supplementation on exercise and muscle damage are presented in this communication. Therefore, the aim of this short review is to summarize the clinical effects of leucine/BCAA and HMβ in exercise-muscle damage in humans. Such data can provide evidences to verify the need of investigating the molecular mechanisms involved in each intervention in order to improve its application in the clinical practice.

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Results and Discussion

We [1,9,13-15] and others [16,17] have documented the potential therapeutic and ergogenic effects of leucine on skeletal muscle metabolism and adaptations. However, these reports technically assume that leucinemia main is the limiting factor for skeletal muscle adaptation and the effects are mediated by leucine *per se*. According to van Koevering & Nissen [18], approximately 5% of total leucine intake is converted into HMβ. Since the leucine studies recommend a bolus intake of 2.5-3.0 g to achieve to satisfactory plasmatic threshold, it would be expected a endogenous synthesis of ~150 mg of HMβ, which is not accordingly with the daily doses recommended in the studies (3.0 to 6.0 g/day). Thus, we can assume that there are two possible explanations of leucine and HMβ in the attenuation of exercise-induced muscle damage: a) the adequate amount of a bolus of leucine intake promotes a significant increase in leucinemia that induces muscular effects that can be totally or partially mediated by the leucine through an unknown mechanism; or b) leucine intake increases the endogenous synthesis of HMβ and its metabolite HMG-CoA that promotes regeneration of the cell membranes that were damaged by the exercise. If the second possible theory has fundamental, it is conceivable to consider the need of a dose-response study with HMβ in order to evaluate the skeletal muscle sensitivity of distinct plasmatic thresholds, compositions of the supplements, and even the comparison of HMβ with leucine intake.

Table 1 presents the result of the studies in humans evaluating the effects of BCAAs/leucine and HMβ supplementation in the attenuation of the exercise-induced muscle damage.

Conclusions and Perspectives

According to the studies presented and discussed, both

Table 1: Effects of BCAAs/leucine HMβ supplementation on exercise-induced muscle damage in healthy humans.

Reference	Sample	Experimental Design	Supplementation Protocol	Exercise Protocol	Placebo	Dietary Control	Results
Nosaka et al. [4]	38 men, untrained	Randomized, double-blind, crossover	Essential amino acids enriched with BCAAs (60%) 30 min before, immediately post, and 8 more occasions over 4-day post exercise	1 bout of 900 muscle actions of arm curl with 1.80 to 3.44 kg range of workload	Maltitol	Y	↓ CK, myoglobin, and muscle soreness
Shimomura et al. [5]	12 women, untrained	Randomized, double-blind, crossover	100 mg·kg^{-1} of BCAAs 15 min before exercise	1 bout of 7 sets x 20 reps of squat exercise	Dextrin	N	↓ Peak time muscle soreness
Sharp & Pearson [6]	10 men, trained	Randomized, double-blind, crossover, placebo-controlled	BCAAs (1.8 g of leucine) 3 weeks before and 1 week during the exercise protocol	Whole-body resistance exercise (8 exercises; 3 sets x 8 RM at 80% 1RM)	Capsules of lactose	N	↓ CK
Jackman et al. [7]	24 men, untrained	Randomized, single-blind	4 doses of 1.75 g of BCAAs on the following 2 days after exercise	1 bout of 12 sets x 10 reps of eccentric exercise at 120% of concentric 1RM	Sweetened and flavored water	Y	↔ CK and myoglobin ↓ Muscle soreness
Wilson et al. [19]	16 men, untrained	Randomized, crossover	3 g of HMβ before exercise	55 maximal eccentric knee extension	Rice maltodextrin	Y	↓ CK, LDH, Muscle soreness
Kraemer et al. [20]	17 men, untrained	Randomized, double-blind, placebo-controlled	2 daily doses of1.5 g of calcium HMβ + 7 g of arginine + 7 g of glutamine + 3 g of taurine + 5.824 g of dextrose	12 weeks of periodized whole-body resistance exercise	Isocaloric, isonitrogenous	N	↓ CK
Wilson et al. [9]	20 men, trained	Randomized	3 g of HMβ free acid 30 min before exercise, with lunch and with the evening meals	1 bout of 3 sets x 12 maximal reps of whole-body resistance exercise	Food-grade orange flavours and sweeteners	Y	↓ CK and DOMS

BCAAs – branched-chain amino acids; CK – creatine kinase; DOMS – delayed onset muscle soreness; HMβ – β-hydroxy-β-methylbutyrate; LDH – lactate dehydrogenase; RM – repetition maximum.

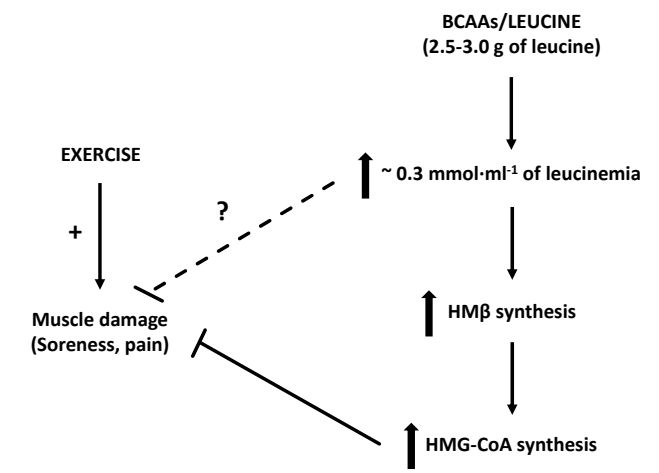

Figure 1: BCAAs/leucine and HMβ relation in the attenuation of exercise-induced muscle damage. BCAA, branched-chain amino acids; HMβ: β-hydroxy-β-methylbutyrate; HMG-CoA: β-hydroxy-β-methylglutaryl-CoA.

BCAAs/leucine and HMβ are effective supplements in the attenuation of exercise-induced muscle damage. There are two potential explanations for the effect of BCAA/leucine in the attenuation of exercise-induced muscle damage (Figure 1): an effect dependent or independent of HMβ endogenous synthesis. If the effect is dependent of HMβ synthesis, there is a need of studies evaluating the possible dose-response effect as well as forms of administration and association with other nutrients. However, if there is a leucine effect *per se*, the interaction between leucinemia and skeletal muscle response is determinant and the cellular mechanisms should be investigated. Importantly, it has been demonstrated that the effects of HMβ can be observed in both trained and untrained subjects, which supports the fact that the training variables are the most limiting factors of HMβ effectiveness.

Author's Contributions

HN was a significant writer and responsible for the concept and design of the manuscript; NM was a significant writer and responsible for the review of the manuscript. All authors read and approved the final manuscript.

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