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Mini Review

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Competitive edge: review of the role of glutamine, arginine and β-hydroxy-β-methylbutyrate supplements for enhancing athletic performance in addition to benefiting the body during times of stress, illness and wound healing

Abstract

Glutamine and arginine are conditionally essential amino acids and beta-hydroxy beta-methylbutyrate (HMB which is an amino acid metabolite of leucine). During periods of extreme trauma or stress from thermal injury (burns, electrical shock), sepsis, surgery or wounds, non-essential amino acids become conditionally essential. The demands for these nutrients can become greater than the body's ability to produce them. The diet must then provide the increased needs for these conditionally essential nutrients. Glutamine, arginine, and HMB have been marketed together as an oral nutrition supplement for facilitating wound healing, protein synthesis and promoting lean body mass (LBM) in critically ill patients. These nutrients also show promise for enhancing athletic performance. The purpose of this review is to explore the potential role and effectiveness of supplementation of glutamine, arginine and HMB on promoting athletic performance and LBM. Larger well-designed studies are needed to define the use of these supplements in enhancing athletic performance and LBM.

Keywords: amino acids, conditionally essential, nutrients, supplements, arginine, glutamine, hmb, athletic performance, protein synthesis, LBM

Volume 2 Issue 2 - 2015

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Received: July 11, 2014 | **Published:** March 25, 2015

Abbreviations: HMB, β-hydroxy-β-mehtylbutyrate; hGH, human growth hormone; IGF-1, insulin growth factor 1; LBM, lean body mass; GHB, gamma hydroxybutyrate; PIF, proteolysis-inducing factor

Introduction

Glutamine, arginine and beta-hydroxy beta-methylbutyrate (HMB) are dietary supplements that may enhance athletic performance. Many sports competitions are won by a fraction of a second, so it is not surprising that athletes want to try the latest nutritional supplements to give them that competitive edge. Glutamine, arginine and HMB are just a few of many supplements that can aid performance. Glutamine is the most abundant amino acid in the body that our muscles make, store and release at a high rate. This building block for proteins has many functions in the body. Glutamine serves as a major fuel source for the cells that protect us from disease and aid our immune system. It supports protein synthesis, regulates nitrogen metabolism in catabolic states, preserves muscle glutamine and supports gut integrity.[1–4] During stress (clinical trauma, starvation, or prolonged, strenuous exercise) the concentration of glutamine in blood is decreased.

Because of drops in glutamine levels during times of stress, surgery, injury, and serious illness, it is "conditionally essential" or needed in greater amounts during these conditions. Prolonged endurance exercise like a marathon or triathlon, may also decrease our body's glutamine levels in our muscles and blood. Over trained athletes have been found to have significantly decreased blood concentrations of glutamine when compared with non-over trained athletes.

In theory, glutamine supplementation will enhance immune function, decrease the risk of infection, and help to prevent overtraining syndrome. The benefits of glutamine supplementation in sick patients who have had major trauma or surgery have been well established**.** However, the benefits of glutamine supplementation for athletes during heavy training have not been definitive. A study by Castell and Newsholme[5] looked at the effects of feeding glutamine both at rest in sedentary controls and after exhaustive exercise in middle-distance, marathon and ultra-marathon runners as well as elite rowers during both training and competition. Questionnaires established the incidence of infection for 7d after exercise: infection levels were highest in marathon and ultra-marathon runners, and in elite male rowers after intensive training. They found that the glutamine group showed fewer infections compared to the placebo group.

In another study by Castell[6] published in 2002, he concluded that: "Provision of glutamine or a glutamine precursor has been found to decrease the incidence of illness in endurance athletes. At present, it has not been established precisely which aspect of the immune system is affected by glutamine feeding during the transient immunodepression (suppression that occurs after prolonged, strenuous exercise)".[7] However, evidence indicates that neutrophils might be implicated instead of lymphocytes as previously thought.[5–7]

Glutamine in muscles appears to decrease after periods of intense training which results in lower sugar concentrations.[7] An adequate intake of carbohydrate and calories may prevent muscles from losing sugar and maintain normal glutamine levels. Further research is needed to provide evidence that supplementing endurance athletes with glutamine in addition to dietary carbohydrate intake will further enhance athletic performance.

In 2008, a study by Lighthart-Melis et al.,[8] showed that glutamine is an important precursor for the synthesis of arginine in humans. Arginine is another amino acid that is "conditionally essential" during periods of illness and stress. Arginine has been shown to support protein synthesis, improve nitrogen balance and support wound healing.[9–11] There is a theory that consuming arginine will raise the blood level of human growth hormone (hGH) and insulin.[9] The performance advantage would be that increases in these two hormones (hGH and insulin) would help build more body mass by natural growth (accretion) and the decrease of body fat.

Earlier studies were done with competitive weightlifters who have been given arginine with another amino acid or a placebo.[10,11] Insulin levels and hGH were measured daily. The researchers did not see a difference between the arginine or the placebo group. In 2007, a Portuguese study was done with 17 male volunteers who were given 7grams of arginine per day versus a placebo for 7days to validate the effect of L-arginine supplementation on growth hormone and IGF-1 (insulin growth factor 1) in adults. The L-arginine supplement dose was found to be ineffective to augment levels of either of those parameters in 7days.[12] This author speculates that a higher dose might be effective.

More recently, in 2008, a review by Kanaley[10] concluded that studies have shown that resting growth hormone responses increase with oral ingestion of L-arginine and the dose range is 5-9g of arginine.[13] This review also indicated that exercise alone is the more potent stimulator of growth hormone response regardless of age. "The supplementation of L-arginine did not appear to stimulate the production of insulin, GH, and IGF-1 and, thus, provided no benefit in hormonal response or exercise performance in trained runners".[14] HMB (β-hydroxy-β-mehtylbutyrate) is a normal constituent of muscle that has been hypothesized to protect muscle from stress-related damage, to build lean body mass (LBM) and to decrease muscle breakdown.[15] Studies from 2004 and 2005 demonstrate the role of HMB in preventing muscle loss in cancer patients.[16,17]

HMB is not an essential nutrient, so there is no established requirement. HMB is found in small amounts in citrus fruit and catfish. However, to get a therapeutic dosage, you need to take a supplement in powder or pill form. HMB is not to be confused with gamma hydroxybutyrate (GHB), a similar supplement. GHB can cause severe sedation, especially when combined with other sedating substances, such as alcohol or anti-anxiety drugs. HMB helps reverse muscle breakdown and increase protein synthesis. In 2004, Smith et al.,[16,17] studied how HMB may reduce the inflammatory response by down-regulating the action of proteolysis-inducing factor (PIF), normalize metabolism and help prevent muscle breakdown in cancer-related weight loss. The action of HMB on protein breakdown and intracellular signaling leading to increased proteasome expression by the tumor factor proteolysis-inducing factor (PIF) was studied in vitro using murine myotubes as a surrogate model of skeletal muscle. Results suggest that HMB attenuates PIF-induced activation and increased gene expression of the ubiquitin-proteasome proteolytic pathway, reducing protein degradation.[16] In 2005, Smith et al.,[17] further studied the attenuation of proteasome expression reflected as a reduction in protein degradation in gastrocnemius muscle of cachectic mice treated with HMB. In addition, HMB produced a significant stimulation of protein synthesis in skeletal muscle. These results suggest that HMB preserves lean body mass and attenuates protein degradation through down-regulation of the increased expression of key regulatory components of the ubiquitin-proteasome proteolytic pathway, together with stimulation of protein synthesis.

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May et al.,[18] studied the effect of using oral supplementation of glutamine, arginine and HMB on cancer-related wasting syndrome. They conducted a randomized, double-blind, placebo-controlled study of 49 patients with advanced cancer (stage IV solid tumors). The participants began the study with a greater than 5% weight loss. The study group was supplemented with 14g glutamine, 14g arginine and 3g HMB per day over 24weeks. The control group ate an isocaloric, isonitrogenous diet. Calorie and protein intake was measured but not standardized between the study and control group.

The study group demonstrated a lean body mass gain of 1.14kg and the control group had a weight loss of 1.32kg. Statistically significant at P=0.02 at 4weeks. Mean calorie intake at baseline and during 4weeks was 1441kcal/day and 1478kcal/day for the study group and 1864kcal/day and 2169kcal/day for the control group. The study group also consumed less protein than the control group both at baseline and fourweeks.[19]

HMB naturally occurs in the body when the amino acid leucine breaks down. Leucine is a branched-chain amino acid found in high concentrations in muscles. During athletic training, damage to the muscles results in the breakdown of leucine as well as increased HMB levels. Evidence suggests that taking HMB supplements might facilitate the body to slow down the destruction of muscle tissue.[15–29] Therefore, HMB has been studied as a sports performance supplement for enhancing strength and muscle mass. The research is promising but contradictory and limited to small studies.[18,20–25,30–35] Some studies of small double-blind trials have been negative.[30,35] Kreider et al.,[35] conducted a double-blind and randomized manner, 40 experienced resistance-trained athletes were matched and assigned to supplement their diet for 28d with a fortified carbohydrate/protein powder containing either 0, 3 or 6gxd(-1) of calcium HMB. Their results indicate that 28days of HMB supplementation of 3 to 6g/ during resistance-training in experienced resistance-trained males, does not reduce muscle catabolism.[26]

Many of the older small double-blind studies have indicated that HMB seems to improve muscle-growth response to weight training.[18,20–25] The main problem with these studies is that they have too small a sample size. Nissen et al.,[21] studied the effect of HMB on muscle metabolism during resistance-exercise training. In this study, 41 healthy males were randomly assigned to receive either 0, 1.5 or 3grams of HMB per day in orange juice. Diets were meat-free for 3days each week during which blood and urine were collected. Subjects were weight-trained 3times per week for three weeks. The group who consumed 3 grams per day of HMB showed a 55% increase (over the control) in lean tissue over the 3-week study. Most studies done on human research subjects use dosages up to 3grams of HMB per day whether for improved exercise performance or for improvement of LBM in cancer cachexia or in HIV patients with wasting syndrome. Safety has been shown up to a dosage of 6 grams per day.

A more recent study by Vukovich et al.,[25] studied the body composition in 70year-old adults (both men and women) in response to beta-hydroxy-beta methylbutyrate and found results similar to that of young adults. The study subjects underwent resistance exercises 2times per week while consuming 3g HMB per day, orally. Study subjects showed an average of 42.4% increase in one repetition maximum leg curl strength after 8weeks compared with 18% for the placebo subjects. Muscle measurement indicated that lean body mass increased by an average of 1.5kg for HMB group with only average of 0.5kg increase for the placebo group.

The body can produce small amounts of HMB (0.3 to 1gram per day) in muscle tissue. It can be found in relatively high concentrations in plant and animal foods such as alfalfa, grape fruit and cat fish. However, one would need to take supplements to obtain the therapeutic levels needed to achieve results indicated in the smaller studies. HMB has been shown to improve wound healing as well as promoting and preserving lean body mass in hospitalized patients. This review of the role of HMB related to improved exercise performance and strength indicates that larger population studies are needed before definitive conclusions can be made.

Conclusion

Though more studies are needed, from existing studies we can conclude that there is a potential role for combined supplementation of glutamine, arginine, and HMB in adequate doses to promote lean body mass and exercise performance.[18,20–29]

Acknowledgements

None.

Conflict of interest

Author declares that there is no conflict of interest.

References

1. Kadawaki M, Kanazawa T. Amino acids as regulators of proteolysis. *J Nutr.* 2003;133(6 Suppl 1):2052S–2056S.
2. Vinnars E, Hammarqvist F, von der Decken A, et al. Role of glutamine and its analogs in posttraumatic muscle protein and amino acid metabolism. *JPEN J Parenter Enteral Nutr*. 1990;14(4 Suppl):125S–129S.
3. Halecek M. Relation between glutamine, branched-chain amino acids, and protein metabolism. *Nutrition*. 2002;18(2):130–133.
4. Sauba WW, Smith RJ, Wilmore DW. Blutamine metabolism by the intestinal tract. *JPEN J Parenter Enteral Nutr.* 1985;9(5):608–617.
5. Castell LM, Newsholme EA. The effects of oral glutamine supplementation on athletes after prolonged, exhaustive exercise. *Nutrition.* 1997;13(7–8):738–742.
6. Castell LM. Can Glutamine Modify the Apparent Immunodepression Observed After Prolonged, Exhaustive Exercise? *Nutrition*. 2002;18(5):371–375.
7. Castell LM, Poortmans JR, Leclercq R, et al. Some aspects of the acute phase response after a marathon race, and the effects of glutamine supplementation. *Eur J Appl Physiol Occup Physiol*. 1997;75(1):47–53.
8. Ligthart-Melis GC, van de Poll MC, Boelens PG, et al. Glutamine is an important precursor for de novo synthesis of arginine in humans. *Am J Clin Nutr*. 2008;87(5):1282–1289.
9. Fayh AP, Friedman R, Sapata KB, et al. Effect of L-arginine supplementation on secretion of human growth hormone and insulin-like growth factor in adults. *Arq Bras Endocrinol Metabol.* 2007;51(4):587–592.
10. Kanaley JA. Growth hormone, arginine and exercise. *Curr Opin Clin Nutr Metab Care*. 2008;11(1):50–54.
11. da Silva DV, Conte-Junior CA, Paschoalin VM, et al. Hormonal response to L-arginine supplementation in physically active individuals. *Food Nutr Res*. 2014;58.
12. Kirk SJ, Hurson M, Regan MC, et al. Arginine stimulates wound healing and immune function in elderly human beings. *Surgery.* 1993;114(2):155–160.
13. Pan M, Chaudry H, Epler MJ, Meng Q, Karinch A (2004) Arginine transport in catabolic disease states. *J Nutr*. 2004;134(10 Suppl):2826S–2829S.
14. Barbul A, Lazarou SA, Efron DT, et al. Arginine enhances wound healing and lymphocyte immune responses in humans. *Surgery.* 1990;108(2):331–337.
15. Nissen, SL, Abumrad NN. Nutritional role of leucine metabolite β-hydroxy-β-methylbutyrate. *The Journal of Nutritional Biochemistry.* 1997;8(6):300–311.
16. Smith HJ, Wyke SM, Tisdale MJ. Mechanisim of the attenuation of proteolysis-inducing factor stimulated protein degradation in muscle by β-hydroxy-β-methylbutyrate. *Cancer Res*. 2004;64(23):8731–8735.
17. Smith HJ, Mukerji P, Tisdale MJ. Attenuation of proteasome-induced proteolysis in skeletal muscle by β-hydroxy-β-methylbutyrate. *Cancer Res.* 2005;65(1):277–283.
18. Slater GJ, Jenkins D. Beta-hydroxy beta-methylbutyric acid (HMB) supplementation and the promotion of muscle growth and strength. *Sports Med*. 2000;30(2):105–116.
19. May PE, Barber A, D'Olimpio JT, et al. Reversal of cancer-related wasting using oral supplementation with a with a combination of β-hydroxy-β-methylbutyrate, arginine, and glutamine. *Am J Surg.* 2002;183(4):471–479.
20. Ostaszewski P, Kostiuk S, Balasinska B. The effect of leucine metabolite 3-hydroxy-3-methylbutyrate (HMB) on muscle protein synthesis and protein breakdown in chick and rat muscle. *J Anim Sci*. 1996;74(Suppl 1):138.
21. Nissen S, Sharp R, Ray M, et al. Effect of leucine metabolite beta-hydroxy-beta-methylbutyrate on muscle metabolism during resistance-exercise training. *J Appl Physiol (1985).* 1996;81(5):2095–2104.
22. Nissen S, Panton L, Fuller J. Effect of feeding beta-hydroxy-beta-methylbutyrate (HMB) on body composition and strength of women. *FASEB J*. 1997;11:A150.
23. Panton LB, Rathmacher JA, Baier S, et al. Nutritional supplementation of the leucine metabolite beta-hydroxy beta-methylbutyrate (HMB) during resistance training. *Nutrition.* 2000;16(9):734–739.
24. Gallagher PM, Carrithers JA, Godard MP, et al. Beta-hydroxy-beta-methylbutyrate ingestion, Part I: effects on strength and fat free mass. *Med Sci Sports Exerc.* 2000;32(12):2109–2115.
25. Vukovich MD, Stubbs NB, Bohlken RM. Body composition in 70year-old adults responds to dietary beta-hydroxy-beta-methylbutyrate similarly to that of young adults. *J Nutr*. 2001;131(7):2049–2052.
26. Eley HL, Russell ST, Baxter JH, et al. Signaling pathways initiated by beta-hydroxy-beta-methylbutyrate to attenuate the depression of protein synthesis in skeletal muscle in response to cachectic stimuli. *Am J Physiol Endocrinol Metab*. 2007;293(4):E923–E931.
27. Eley HL, Russell ST, Tisdale MJ. Mechanism of attenuation of muscle protein degradation induced by tumor necrosis factor-alpha and angiotensin II by beta-hydroxy-beta-methylbutyrate. *Am J Physiol Endocrinol Metab*. 2008;295(6):E1417–E1426.
28. Escobar J, Frank JW, Suryawan A, et al. Leucine and alpha-ketoisocaproic acid, but not norleucine, stimulate skeletal muscle protein synthesis in neonatal pigs. *J Nutr.* 2010;140(8):1418–1424.

29. Wilkinson DJ, Hossain T, Hill DS, et al. Effects of leucine and its metabolite β-hydroxy-β-methylbutyrate on human skeletal muscle protein metabolism. *J Physiol*. 2013;591(Pt 11):2911–2923.

30. Slater G, Jenkins D, Logan P, et al. Beta-hydroxy-beta-methylbutyrate (HMB) supplementation does not affect changes in strength or body composition during resistance training in trained men. *Int J Sport Nutr Exerc Metab*. 2001;11(3):384–396.

31. Ransone J, Neighbors K, Lefavi R, et al. The Effect of beta-Hydroxy beta-Methylbutyrate on Muscular Strength and Body Composition in Collegiate Football Players. *J Strength Cond Res*. 2003;17(1):34–39.

32. Thomson JS. β -Hydroxy- β -Methylbutyrate (HMB) supplementation of resistance trained men. *Asia Pac J Clin Nutr*. 2004;13(Suppl):S59.

33. Hoffman JR, Cooper J, Wendell M, et al. Effects of beta-Hydroxy beta-Methylbutyrate on power performance and indices of muscle damage and stress during high-intensity training. *J Strength Cond Res*. 2004;18(4):747–752.

34. Lamboley CR, Royer D, Dionne IJ. Effects of beta-hydroxy-beta-methylbutyrate on aerobic-performance components and body composition in college students. *Int J Sport Nutr Exerc Metab*. 2007;17(1):56–69.

35. Kreider RB, Ferreira M, Wilson M, et al. Effects of calcium beta-hydroxy-beta-methylbutyrate (HMB) supplementation during resistance-training on markers of catabolism, body composition and strength. *Int J Sports Med*. 1999;20(8):503–509.

Citation: Funk P. Competitive edge: review of the role of glutamine, arginine and β-hydroxy-β-methylbutyrate supplements for enhancing athletic performance in addition to benefiting the body during times of stress, illness and wound healing. *J Nutr Health Food Eng.* 2015;2(2):38–41. DOI: 10.15406/jnhfe.2015.02.00046