Supplementation with β-Hydroxy-β-Methylbutyrate (HMB) and α-Ketoisocaproic Acid (KIC) Reduces Signs and Symptoms of Exercise-Induced Muscle Damage in Man

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This study examined the effects of β-hydroxy-β-methylbutyrate (HMB) and α-ketoisocaproic acid (KIC) supplementation on signs and symptoms of exercise-induced muscle damage following a single bout of eccentrically biased resistance exercise. Six non-resistance trained male subjects performed an exercise protocol designed to induce muscle damage on two separate occasions, performed on the dominant or non-dominant arm in a counter-balanced crossover design. Subjects were assigned to an HMB/KIC (3 g HMB and 0.3 g α-ketoisocaproic acid, daily) or placebo treatment for 14 d prior to exercise in the counter-balanced crossover design. One repetition maximum (1RM), plasma creatine kinase activity (CK), delayed onset muscle soreness (DOMS), limb girth, and range of motion (ROM) were determined pre-exercise, at 1h, 24 h, 48 h, and 72 h post-exercise. DOMS and the percentage changes in 1RM, limb girth, and ROM all changed over the 72 h period ($P < 0.05$). HMB/KIC supplementation attenuated the CK response, the percentage decrement in 1RM, and the percentage increase in limb girth ($P < 0.05$). In addition, DOMS was reduced at 24 h post-exercise ($P < 0.05$) in the HMB/KIC treatment. In conclusion, 14 d of HMB and KIC supplementation reduced signs and symptoms of exercise-induced muscle damage in non-resistance trained males following a single bout of eccentrically biased resistance exercise.

Key Words: eccentric exercise, creatine kinase, DOMS

β-hydroxy-β-methylbutyrate (HMB) is a metabolite of the branch chain amino acid leucine and its ketoacid α-ketoisocaproate (32). HMB has been used as a dietary supplement to increase carcass quality in livestock (31) and has recently gained popularity as a dietary supplement in humans, particularly among strength athletes (27, 28). Today, many commercial HMB supplements also contain a small amount of α-ketoisocaproic acid (KIC).

    In man, the reported benefits of supplementation with dosages of between 1.5 and 3.0 g/d HMB include reduced muscle protein degradation and consequent

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increases in muscle mass and strength following resistance exercise training performed for between 3 and 8 wk (9, 13, 20, 25); there is, however, some evidence that these benefits are not observed in well-trained subjects (16, 26). Creatine kinase activity in blood, which is a commonly used marker of sarcolemmal damage (4, 19, 23), has also been shown to be reduced by HMB supplementation following resistance training (9, 13, 20, 25) and prolonged running (14). Such protection against muscle damage has been attributed to the role of HMB in increasing cell membrane integrity via cholesterol synthesis and therefore reducing damage-induced proteolysis (21); in addition, it has been hypothesized, though not yet tested, that HMB might act as a structural component within the cell (20).

Unaccustomed eccentric exercise has been widely reported to result in muscle damage with symptoms including reduced muscle function, elevated plasma creatine kinase activity, increased pain and swelling, and reduced range of motion (2, 4, 5, 7, 8, 18). To date, only 1 study has identified the effects of HMB supplementation on muscle damage resulting from a single bout of eccentric resistance exercise (24). Paddon-Jones et al. (24) found that 6 d HMB supplementation with 40 mg/kg body mass/d provided no attenuation of symptoms associated with exercise-induced muscle damage following 24 maximal eccentric contractions of the elbow flexors; this finding refutes the proposed mechanisms of HMB enhancing cell membrane integrity. The authors concluded that a longer duration of supplementation could be necessary to determine whether HMB provides a protective effect against exercise-induced muscle damage following a single bout of eccentric exercise.

Issues of product purity are paramount when investigating nutritional supplements. It is well publicized that many sports supplements contain appreciable amounts of contaminants, which can make their use problematic for athletes who compete under World Anti-Doping Authority (WADA) rules. For example, it has been reported that consuming only 1 μg of nandrolone can result in a positive test for norandrosterone under International Olympic Committee (IOC) regulations (10). In addition, contamination with stimulants or anabolic steroids would confound any study investigating the efficacy and ergogenic potential of nutritional supplements. For these reasons, detailed analyses of the active ingredients and possible illegal contaminants (as identified by WADA) were performed on the HMB/KIC supplement used in this study.

The aim of this study was to examine the effects of 14 d HMB and KIC supplementation on the signs and symptoms of exercise-induced muscle damage following a single bout of eccentrically biased resistance exercise.

Methods

Subjects

Eight male volunteers who had not performed any resistance training in the previous 12 months participated in this study. Two subjects were excluded from the data analysis due to one having elevated baseline plasma creatine kinase activity on the second trial and another being unable to complete the exercise protocol on the second occasion. Age, height, and body mass of the subjects ($N = 6$) were (mean ± standard deviation) 23 ± 4 y, 178.3 ± 5.8 cm, and 81.9 ± 18.4 kg, respectively. Prior

to participation, all subjects were informed of the procedures of the investigation and completed a pre-test health-screening questionnaire and provided written informed consent, according to ACSM guidelines (1). All experimental procedures were approved by the Kingston University Research Ethics Committee. Subjects were instructed to refrain from any form of resistance training, plyometrics, or other exercise that could potentially cause muscle damage for the 3 wk prior to and during testing. Adherence to these instructions was confirmed to the test investigator on each visit to the laboratory.

HMB/KIC and Placebo Treatments

Subjects were assigned to the HMB/KIC and placebo treatments in a blind, counter-balanced crossover design. The HMB/KIC treatment comprised a daily dose of 3 g β-hydroxy-β-methylbutyrate with 0.3 g α-ketoisocaproic acid (Maximuscle HMB 1000, Maximuscle Ltd., Watford, U.K.); the placebo treatment comprised 3 g corn flour daily. Each treatment was administered in the form of gelatine capsules taken daily in three equal doses after meals, for 14 d.

The purity of the HMB/KIC supplement was assessed by Fourier Transform Near Infrared (FTNIR) Spectroscopy using wavelengths scanning from 1000 to 2300 nm. The possible presence of the major classes of stimulants and anabolic steroids that have been implicated as contaminants in nutritional supplements were assessed (Table 1). Contamination analyses were performed by an independent laboratory using mass spectrometry-based analytical methods developed specifically to detect contamination in nutritional supplements. These methods were accredited prior to sample analysis to ISO 17025, the required quality standard that underpins WADA testing procedures. The HMB/KIC capsules were homogenized and prepared for analyses using liquid-liquid and solid phase extraction techniques. Stimulants were assessed by liquid chromatography, with mass spectrometric detection to a level of 500 ng per gram of supplement. Steroids were assessed by gas chromatography with mass spectrometric detection to a level of 50 ng per gram of supplement.

Muscle Damage Protocol

Following the 14 d supplementation, subjects performed an exercise protocol designed to induce muscle damage. This was performed on either the dominant or the non-dominant arm, to which subjects were assigned in a counter-balanced crossover design. The exercise protocol consisted of 3 sets of 10 repetitions of single arm biceps curls at 70% of a previously determined 1 repetition maximum (1RM) for the involved arm. The protocol was performed using an adjustable preacher curl bench, set at 140° (York 5, York Barbell UK Ltd, Daventry, U.K.). Repetitions were performed over the full range of motion with a normal concentric contraction followed by a prolonged eccentric contraction lasting a period of 10 s; this time was verbally communicated to the subject so a smooth and even contraction could be maintained. Assistance was provided if subjects were unable to complete the concentric phase of the repetition, however, there was no assistance during the eccentric phase, though verbal encouragement was given by the same test investigator. A rest period of 4 min was taken between sets.

Table 1   Stimulants and Steroids Analyzed in HMB and KIC

Stimulants	Ephedrine
	Pseudoephedrine
	Norpseudoephedrine (cathine)
	Phenylpropanolamine
	Methylephedrine
	Caffeine
Steroids	5(6)-androstene-3, 17-dione and/or 4-adrostene-3, 17-dione
	4-androstene-3beta, 17beta-diol
	5a-androst-1-ene-3beta, 17beta-diol
	5a-androstane-3beta, 17beta-diol
	5(6)-androstene-3beta, 17beta-diol
	5(10)-estrene-3, 17-dione (19-nor-5(10)-androstene-3, 17-dione) and/or
	4-estrene-3, 17-dione (19-nor-4 androstene-3, 17-dione) and/or
	5(6)-estrene-3, 17-dione (19-nor-5(6)-androstene-3,17-dione)
	4-estrene-3beta, 17beta-diol (19-nor-4 androstene-3beta, 17beta-diol)
	Nandrolone (19-nor-4-androstene-17beta-hydroxy-3-one)
	Testosterone
	Dehydroepiandrosterone (DHEA)
	1,4-androstene-3, 17-dione
	5a-androst-1-ene-3, 17-dione
	5a-androstane-3,17-dione

Dependent Variables

Measures of concentric 1RM, plasma creatine kinase activity (CK), muscle soreness (DOMS), limb girth, and range of motion (ROM) were taken pre-exercise, and at 1 h, 24 h, 48 h, and 72 h post-exercise.

Concentric One Repetition Maximum (1RM). A preacher curl bench (as previously described) was used for the determination of 1RM. The definition and method of 1RM determination described by Kraemer and Fry (15) was adopted for this study. Reliability data from our laboratory for the determination of 1RM on two consecutive days using this method demonstrate a technical error of measurement (TEM) of 1.1% (i.e., 0.13 kg).

Plasma Creatine Kinase Activity (CK).   A fingertip capillary blood sample collected in a 75 μl heparinized capillary tube (Hawksley & Sons, Ltd., Lancing, U.K.) was centrifuged for 3 min and the blood plasma drawn and frozen at –18 °C for subsequent analysis. CK was determined using enzymatic dry slide chemistry (VITROS DT60II, Ortho-Clinical Diagnostics, Amersham, U.K.). Data from our laboratory for the intra-assay reliability ($N = 10$) of this method to analyze low (87.5 IU/L), medium (636.1 IU/L), and high (1518.4 IU/L) concentrations provide coefficients of variation of 1.1%, 2.6%, and 1.3%, respectively.

Perceived Muscle Soreness Rating (DOMS).   Perceived soreness was determined using the Talag scale (30), a subjective scale from 1 (no pain) to 7 (unbearably painful). Subjects stood with the shoulder of the exercised arm flexed at 90° and the elbow fully extended; subjects were then asked to select a number from the scale that corresponded to the soreness felt.

Limb Girth.   Limb girth of the upper arm was taken midway between acromion and olecranon processes using a flexible anthropometric tape with the arm hung naturally at the side of the body. Reference points on the arm were marked with permanent ink to ensure consistency on subsequent days. Reliability data from our laboratory for the measurement of limb girth on two consecutive days using this method demonstrate a TEM of < 0.3% (i.e., < 0.1 cm).

Range of Motion (ROM).   ROM of the elbow joint in flexion and extension was assessed using a transparent, plastic goniometer (Baseline, Physiomed, Cheshire, U.K.); total ROM was determined using a method previously described (16). Reference points on the arm were again marked with permanent ink to ensure consistency on subsequent days. We have calculated a TEM of < 0.1% (i.e., < 1.1°) when using this procedure for the measurement of ROM on two consecutive days.

Statistical Analyses

Data are presented as means ± standard deviation; data for 1RM, limb girth, and ROM are expressed as percentage change from pre-exercise levels. All dependent variables were analyzed using a 2 factor (treatment, 2 × time, 5) repeated measures analysis of variance (ANOVA). Mauchly's sphericity test was used to check homogeneity of covariance. Violations of the assumption of sphericity were corrected using the Greenhouse-Geisser adjustment. Where a significant interaction effect was found, Tukey's post hoc tests were used to identify significant differences. A significance level of $P < 0.05$ was established prior to analyses.

Results

Eight subjects participated in this study, however, 1 subject was excluded due to elevated baseline CK (508 IU/L) in the second trial and another failed to complete the exercise protocol on the second occasion. Results are therefore presented for $N = 6$.

Figure 1 illustrates the percentage change in 1RM (lower panel) and CK (upper panel) for the two treatment conditions. There was a significant change in 1RM over the 72 h period ($F = 31.122$, $P < 0.001$), decreasing from $131.3 ± 10.8$ N in the placebo treatment and from $123.5 ± 25.5$ N in the HMB/KIC treatment at pre-exercise, by approximately 20 N at 1 h post-exercise. There was a significant difference between HMB/KIC and placebo treatments for the percentage change in 1RM ($F = 13.267$, $P < 0.05$). Despite similar decreases at 1 h post-exercise in the 2 treatments, the HMB/KIC treatment attenuated the decrement in 1RM over the 72 h period. In addition, although not significant, there was a slight increase in 1RM (~ 2.5 N) over pre-exercise levels after 48 h in the HMB/KIC treatment (Figure 1, lower panel). There was a significant difference in the CK response between treatments ($F = 7.814$, $P < 0.05$), which increased over the 48 h following exercise in the placebo treatment reaching a peak of $315.2 ± 194.6$ IU/L; the HMB/KIC
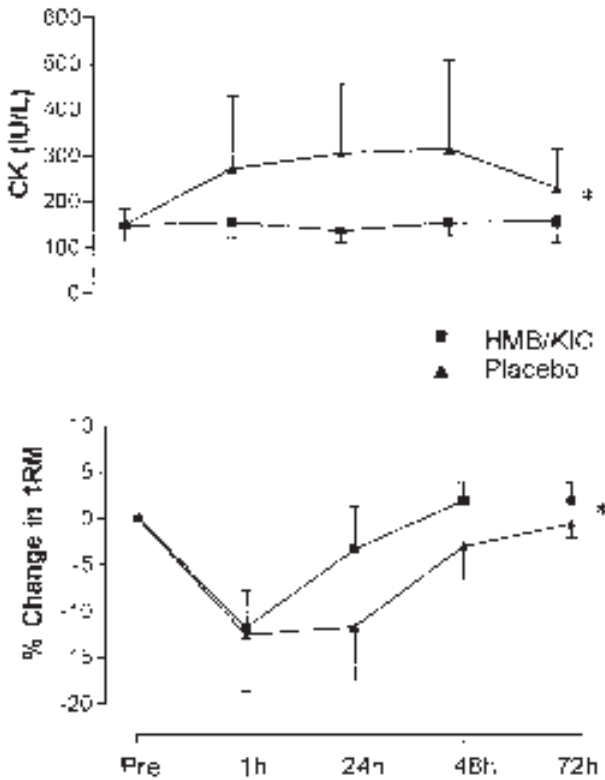
Figure 1 — 1RM (percentage change) and CK in HMB/KIC and placebo treatments; lower and upper panels, respectively.
*significant difference between treatments ($P < 0.05$).

treatment, however, showed very little increase in CK, rising from baseline levels of 147.0 ± 33.8 IU/L to a peak of 154.5 ± 35.6 IU/L at 1 h post-exercise. No significant change over time or treatment by time interaction were found for CK.

Results for DOMS and percentage change in limb girth are shown in Figure 2 (upper and lower panels, respectively). DOMS significantly increased following the exercise bout ($F = 51.457$, $P < 0.001$), reaching a peak at 24 h post-exercise in both treatments. There was a significant treatment by time interaction ($F = 2.895$, $P < 0.05$), revealing that DOMS was lower at 24 h post-exercise in the HMB/KIC treatment, reaching 2.66 ± 0.51 in contrast to 3.33 ± 0.81 in the placebo treatment ($P < 0.05$). There was an increase in limb girth following the exercise bout ($F = 8.350$, $P < 0.01$), which peaked at 24 h post-exercise in both treatments (increasing by 1.3% and 1.2% in placebo and HMB/KIC treatments, respectively). There was a significant difference in limb girth between treatments ($F = 9.511$, $P < 0.05$); Figure 2 (lower panel) illustrates that the percentage increase in limb girth was
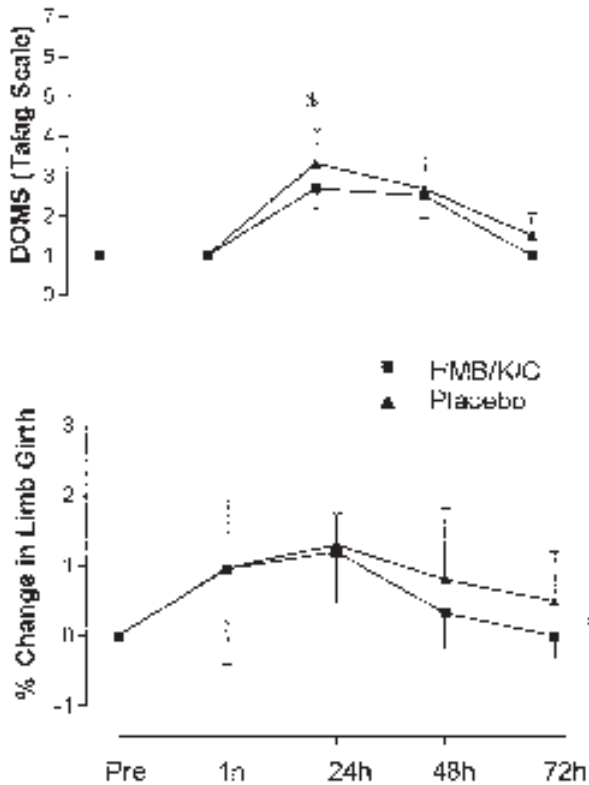
Figure 2 — Limb girth (percentage change) and DOMS in HMB/KIC and placebo treatments; lower and upper panels, respectively.
$ significant difference in DOMS between treatments at 24 h post-exercise, ($P < 0.05$).
*significant difference between treatments ($P < 0.05$).

attenuated in the HMB/KIC treatment over the 72 h post-exercise period. In addition, limb girth returned to pre-exercise levels at 72 h post-exercise in the HMB/KIC treatment though it remained slightly elevated in the placebo treatment.

There was a change in ROM over the 72 h period ($F = 11.784$, $P < 0.001$); similar trends were found in both treatment conditions, with decreases measured for up to 24 h post-exercise (Figure 3). Although not significantly different, the percentage decrease in ROM was slightly lower in the HMB/KIC treatment (4.2° and 8.3° at 24 h post-exercise in the HMB/KIC and placebo treatments, respectively). ROM increased from 24 h to 72 h post-exercise in both treatments though it did not reach baseline levels.

The results of the HMB and KIC analyses demonstrated both to be 98% pure, the remaining 2% being primarily moisture. No stimulants or anabolic steroids were found in the HMB/KIC supplement.
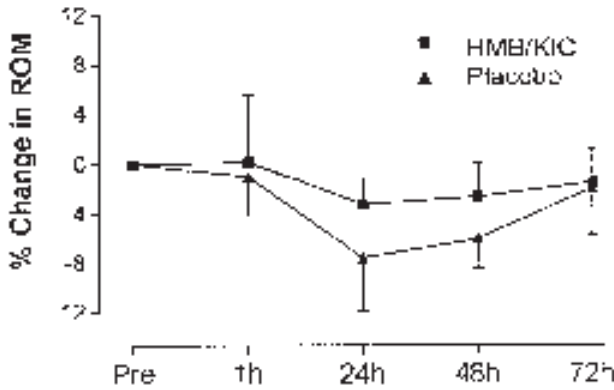
Figure 3 — ROM (percentage change) in HMB/KIC and placebo treatments.

Discussion

This is the first study to show that HMB and KIC supplementation attenuates muscle damage in non-resistance trained males following a single bout of eccentrically biased resistance exercise. Supplementation for 14 d significantly attenuated the increase in CK, DOMS, and limb girth, and the decrement in 1RM. The only variable not affected by HMB and KIC supplementation was the percentage change in ROM. Our findings are in contrast to those of the only other study reporting the effects of HMB supplementation on muscle damage consequent to a single bout of eccentric resistance exercise (24); however, we used a supplementation period of 14 d rather than 6 d as previously examined (24) and a supplement that also contained KIC.

The exercise protocol used in this study was effective in causing muscle damage as shown by the significant changes in 1RM, DOMS, limb girth, and ROM over time. Although CK did not demonstrate a change over time, there was a difference between treatments, with increases in CK in the placebo treatment. These results support previous research identifying that a single bout of eccentric exercise causes significant increases in signs and symptoms of muscle damage (5, 7, 8, 12, 22, 23).

HMB and KIC supplementation had a significant effect on the percentage decrement in muscle function following the eccentrically biased bout of resistance exercise. The results demonstrate that although there was a similar decrease in 1RM at 1 h post-exercise in both treatments, there was a greater decrement in strength in the placebo treatment over the study period. It is interesting to note that 1RM actually exceeded pre-exercise levels by 48 h post-exercise in the HMB/KIC trial, though this increase was not significant. Although improved strength gains have been previously reported following HMB supplementation during a resistance training program (9, 13, 20, 25), Paddon-Jones et al. (24) found supplementation to have no effect on isometric or isokinetic muscle function over 10 d following a single bout of eccentric resistance exercise. In contrast, however, smaller decrements in muscle

force have been reported with HMB supplementation, following downhill running (3). Any protective effect HMB and KIC might provide against exercise-induced muscle damage would be expected to result in diminished damage-induced proteolysis (21), thereby maintaining muscle tissue and attenuating losses in strength, as evidenced in this study.

HMB and KIC supplementation significantly attenuated the CK response, indicating that muscle damage was reduced following the exercise protocol, perhaps via enhanced cell membrane integrity with a consequent reduction in CK efflux from the cell. Although no direct evidence exists as to exact mechanisms, HMB has been hypothesized to act as a precursor for cholesterol synthesis via its metabolism to β-hydroxy-β-methylglutaryl CoA (HMG-CoA), thus providing a carbon source for cholesterol synthesis (21). An increase in intracellular cholesterol could enhance cell membrane integrity and therefore reduce muscle damage following unaccustomed or intense exercise (21). Another hypothesis is that HMB serves as a structural component within the cell membrane (20). The mechanisms by which KIC might reduce muscle damage are again unclear; however, given that KIC is a precursor to HMB, it is likely that it acts on the muscle cell in the same way. Although the results of the present study do not directly confirm these hypotheses, it is clear that HMB and KIC supplementation did provide protection and attenuated muscle damage following a single bout of eccentrically biased resistance exercise. Our finding of reduced CK concurs with a number of previous studies reporting HMB supplementation to reduce CK following resistance training (9, 13, 20, 25) and prolonged running (14). The only other study found in the literature to have reported the effects of HMB supplementation on muscle damage caused by a single bout of eccentric resistance exercise (24) did not, however, measure CK.

Large inter-subject variation in CK in response to exercise has previously been reported as a limitation in its use in establishing the extent of muscle damage (6, 11, 29). It is therefore interesting to note that in the current study, although there is considerable variation between subjects in the placebo trial (Figure 1), the HMB/KIC trial showed very little inter-subject variation, indicating that HMB and KIC provided a protective effect in all subjects.

Muscle soreness was significantly lower in the HMB/KIC treatment at 24 h post-exercise. This is in contrast to the findings of Paddon-Jones et al. (24) who found that muscle soreness assessed using a 10 point visual analog scale was not reduced with 6 d HMB supplementation following a single bout of eccentric exercise. HMB supplementation for 28 d has, however, been previously shown to reduce muscle soreness following 30 min downhill running (3). Any mechanism by which HMB and KIC could affect soreness has not yet been identified (27), though it is likely to be a consequence of the reduced myofibrillar damage due to enhanced cell membrane integrity manifested by HMB and KIC supplementation.

Limb girth was measured in this study as an indirect marker of swelling and edema. HMB and KIC supplementation significantly attenuated the increase in limb girth following exercise. Since CK, 1RM, and DOMS all indicated reduced muscle damage with HMB/KIC supplementation, it is concordant that swelling and edema were reduced. Again, our finding is in contrast to that of Paddon-Jones et al. (24) who found HMB supplementation to have no effect on post-exercise limb girth. This difference might be attributable to the longer supplementation period used in our study.

Independent testing of the active ingredients in the HMB/KIC supplement demonstrated 98% purity. The analyses of stimulants and steroids showed that consumption of the HMB and KIC as performed in this study would not infringe IOC rules. These analyses also demonstrate that the effects of the HMB/KIC supplement were not due to stimulant or steroid contaminants.

In conclusion, and in contrast to previous literature examining shorter duration supplementation (24), we found that 14 d supplementation with HMB and KIC reduced signs and symptoms associated with exercise-induced muscle damage in non-resistance trained male subjects. This is the first study to demonstrate that HMB/KIC supplementation is effective in the management and reduction of muscle damage following a single bout of eccentrically biased resistance exercise. Further research is required to confirm these findings and to elucidate the mechanisms by which HMB/KIC supplementation could provide protection against exercise-induced muscle damage. In addition, investigation of the protective effects of HMB and KIC supplementation for acute exercise in resistance-trained populations is warranted.

Acknowledgments

References

1. American College of Sports Medicine. Policy statement regarding the use of human subjects and informed consent. *Med. Sci. Sports Exerc.* 32:vi, 2000.
2. Armstrong, R.B., G.L. Warren, and J.A. Warren. Mechanisms of exercise-induced muscle fibre injury. *Sports Med.* 12:184-207, 1991.
3. Byrd, P.L., P.M. Mehta, P. DeVita, D. Dyck, and R.C. Hickner. Changes in muscle soreness and strength following downhill running: effects of creatine, HMB, and betagen supplementation. (abstract). *Med. Sci. Sports Exerc.* 31:S263, 1999.
4. Clarkson, P.M., K. Nosaka, and B. Braun. Muscle function after exercise-induced muscle damage and rapid adaptation. *Med. Sci. Sports Exerc.* 24:512-520, 1992.
5. Cleak, M.J., and R.G. Eston. Muscle soreness, swelling, stiffness, and strength losses after intense eccentric exercise. *Br. J. Sports Med.* 26:267-272, 1992.
6. Ebbeling, C.B., and P.M. Clarkson. Exercise-induced muscle damage, repair and adaptation in humans. *Sports Med.* 7:207-234, 1989.
7. Eston, R.G., S. Finney, S. Baker, and V. Baltzopoulos. Muscle tenderness and peak torque changes after downhill running following a prior bout of isokinetic eccentric exercise. *J. Sports Sci.* 14:291-299, 1996.
8. Fridén, J., M. Sjostrom, and B. Ekblom. Myofibrillar damage following intense eccentric exercise in man. *Int. J. Sp. Med.* 4:170-176, 1983.
9. Gallagher, P.M., J.A. Carrithers, M.P. Godard, K.E. Schulze, and S.W. Trappe. β-hydroxy-β-methylbutyrate ingestion, part 1: effects on strength and fat free mass. *Med. Sci. Sports Exerc.* 32:2109-2115, 2000.
10. Geyer, H., M.K. Parr, U. Mareck, U. Reinhart, Y. Schrader, and W. Schänzer. Analysis of non-hormonal nutritional supplements for anabolic-androgenic steroids—results of an international study. *Int. J. Sports Med.* 25:124-129, 2004.

11. Hortobágyi, T., and T. Denahan. Variability in creatine kinase: methodological, exercise, and clinically related factors. *Int. J. Sports Med.* 10:69-80, 1989.

12. Howatson, G., and K.A. van Someren. Ice massage: effects on exercise-induced muscle damage. *J. Sports Med. Phys. Fitness.* 43(4):500-505, 2003.

13. Jowko, E., P. Ostaszewski, M. Jank, J. Sacharuk, A. Zieniewicz, J. Wilczak, and S. Nissen. Creatine and β-hydroxy-β-methylbutyrate (HMB) additively increase lean body mass and muscle strength during a weight-training programme. *Nutr.* 17:558-566, 2001.

14. Knitter, A.E., L. Panton, J.A. Rathmacher, A. Peterson, and R. Sharp. Effects of β-hydroxy-β-methylbutyrate on muscle damage after a prolonged run. *J Appl. Physiol.* 89:1340-1344, 2000.

15. Kraemer, W.J., and A.C. Fry. Strength testing: development and evaluation of methodology. In: Maud, P.J., and C. Foster. (eds). *Physiological assessment of human fitness.* Champaign, IL: Human Kinetics, 115-138, 1995.

16. Kreider, R.B., M. Ferreira, M. Wilson, and A.L. Almada. Effects of calcium β-hydroxy-β-methylbutyrate (HMB) supplementation during resistance training on markers of catabolism, body composition and strength. *Int. J. Sports Med.* 20:503-509, 1999.

17. Maud, P.J., and M.Y. Cortez-Cooper. Static techniques for the evaluation of joint range of motion. In: Maud, P.J., and C. Foster. (eds). *Physiological assessment of human fitness.* Champaign, Ill: Human Kinetics Publishers, 221-243, 1995.

18. McHugh, M.P. Recent advances in the understanding of the repeated bout effect: the protective effect against muscle damage from a single bout of eccentric exercise. *Scand. J. Med. Sci. Sports.* 13:88-97, 2003.

19. Newham, D.J., D.A. Jones, and R.H.T. Edwards. Plasma creatine kinase changes after eccentric and concentric contractions. *Musc. Nerve.* 9:59-63, 1986.

20. Nissen, S., R. Sharp, M. Ray, J.A. Rathmacher, D. Rice, J.C. Fuller, Jr., A.S. Connelly, and N. Abumrad. The effect of leucine metabolite β-hydroxy-β-methylbutyrate on muscle metabolism during resistance exercise training. *J. Appl. Physiol.* 81:2095-2104, 1996.

21. Nissen, S., and N.N. Abumrad. Nutritional role of the leucine metabolite β-hydroxy-β-methylbutyrate (HMB). *J. Nutr. Biochem.* 8:300-311, 1997.

22. Nosaka, K., and P.M. Clarkson. Variability in serum creatine kinase response after eccentric exercise of the elbow flexors. *Int. J. Sports Med.* 17:120-127, 1995.

23. Nosaka, K., and K. Sakamoto. Effects of joint angle on the magnitude of muscle damage to the elbow flexors. *Med. Sci. Sports Exerc.* 24:512-520, 2001.

24. Paddon-Jones, D., A. Keech, and D. Jenkins. Short-term β-hydroxy-β-methylbutyrate supplementation does not reduce symptoms of eccentric muscle damage. *Int. J. Sport Nutr. Exerc. Metab.* 11:442-450, 2001.

25. Panton, L.B., J.A. Rathmacher, S. Baier, and S. Nissen. Nutritional supplementation of the leucine metabolite β-hydroxy-β-methylbutyrate (HMB) during resistance training. *Nutr.* 16:734-739, 2000.

26. Slater, G., D. Jenkins, P. Logan, H. Lee, M. Vukovich, J.A. Rathmacher, and A.G. Hahn. β-hydroxy-β-methylbutyrate (HMB) supplementation does not affect changes in strength or body composition during resistance training in trained men. *Int. J. Sport Nutr. Exerc. Metab.* 11:384-396, 2001.

27. Slater, G.J., and D. Jenkins. β-hydroxy-β-methylbutyrate (HMB) supplementation and the promotion of muscle growth and strength. *Sports Med.* 30:105-116, 2000.

28. Sallis, R.E., and K. Jones. Dietary supplement use among college football players. (abstract). *Med. Sci. Sports Exerc*. 31:S118, 1999.
29. Sorichter, S., B. Puschendorf, and J. Mair. Skeletal muscle injury induced by eccentric muscle action: protein markers of muscle fiber injury. *Exerc. Immunol. Review*. 5:5-21, 1999.
30. Talag, T. Residual muscle soreness as influenced by concentric, eccentric and static contractions. *Res. Q. Exerc. Sport*. 44:458-469, 1973.
31. Van Koevering, M.Y., H.G. Dolezal, D.R. Gill, F.N. Owens, C.A. Strasia, D.S. Buchanan, R. Lake, and S. Nissen. Effects of β-hydroxy-β-methyl butyrate on performance and carcass quality of feedlot steers. *J. Anim. Sci*. 72:1927-1935, 1994.
32. Van Koevering, M., and S. Nissen. Oxidation of leucine and α-ketoisocaproate to β-hydroxy-β-methylbutyrate in vivo. *Am. J. Physiol*. 262:E27-E31, 1992.