
BCAAs (leucine, isoleucine, and valine), particularly leucine, have anabolic effects on protein metabolism by increasing the rate of protein synthesis and decreasing the rate of protein degradation in resting human muscle. Also, during recovery from endurance exercise, BCAAs were found to have anabolic effects in human muscle. These effects are likely to be mediated through changes in signaling pathways controlling protein synthesis. This involves phosphorylation of the mammalian target of rapamycin (mTOR) and sequential activation of 70-kD S6 protein kinase (p70 S6 kinase) and the eukaryotic initiation factor 4E-binding protein 1. Activation of p70 S6 kinase, and subsequent phosphorylation of the ribosomal protein S6, is associated with enhanced translation of specific mRNAs. When BCAAs were supplied to subjects during and after one session of quadriceps muscle resistance exercise, an increase in mTOR, p70 S6 kinase, and S6 phosphorylation was found in the recovery period after the exercise with no effect of BCAAs on Akt or glycogen synthase kinase 3 (GSK-3) phosphorylation. Exercise without BCAA intake led to a partial phosphorylation of p70 S6 kinase without activating the enzyme, a decrease in Akt phosphorylation, and no change in GSK-3. It has previously been shown that leucine infusion increases p70 S6 kinase phosphorylation in an Akt-independent manner in resting subjects; however, a relation between mTOR and p70 S6 kinase has not been reported previously. The results suggest that BCAAs activate mTOR and p70 S6 kinase in human muscle in the recovery period after exercise and that GSK-3 is not involved in the anabolic action of BCAAs on human muscle.


A mixture of the three branched-chain amino acids (BCAAs) was supplied to subjects during two types of sustained intense exercise, a 30 km cross-country race and a full marathon, and the effect on plasma and muscle concentrations of aromatic and BCAAs was studied. When BCAAs (7.5-12 g) were taken during exercise, the plasma and muscle (vastus lateralis) concentration of these amino acids increased, while in the placebo groups the concentration of BCAAs decreased in the plasma and remained unchanged in the muscle. In the placebo group, both types of exercise caused a 20-40% increase in the muscle concentration of the aromatic amino acids, tyrosine and phenylalanine, and the plasma concentration of these amino acids was increased after the marathon. Since tyrosine and phenylalanine are neither taken up nor metabolized by skeletal muscle, the increases in their concentrations in muscle might indicate net protein degradation during exercise. However, when the subjects were supplied with BCAAs during exercise, the increases in tyrosine and phenylalanine concentrations in both muscle and plasma were prevented. These results suggest that an intake of BCAAs during exercise can prevent or decrease the net rate of protein degradation caused by heavy exercise.


BACKGROUND: The aim of this study was to examine the effects of branched-chain amino acid (BCAA) supplementation on serum indicators of muscle damage after prolonged exercise. We hypothesized that BCAA supplementation would reduce the serum activities of intramuscular enzymes associated with muscle damage.

METHODS: To test this hypothesis, sixteen male subjects were assigned to one of two groups: the supplemental group (consuming 12 g x d(-1) BCAA for 14 d in addition to their normal diet) or the control group (normal diet only). Baseline serum creatine kinase (CK) and lactate dehydrogenase (LDH), shown to be accurate indicators of muscle damage, were determined during the week before the exercise test. The exercise test was administered on day seven and required the subjects to cycle for 120 min on an ergometer at approximately 70% VO2max. Blood samples were taken prior to and immediately following exercise and at 1 hr, 2 hrs, 3 hrs, 4 hrs, 1 d, 3 d, 5 d and 7 d postexercise. All subjects were required have their diets analyzed daily during the 14 d.

RESULTS: Dietary analyses indicated that all subjects consumed the recommended daily intake of BCAA (0.64 g x kg(-1)) in their normal diets. Baseline serum values for CK and LDH were not different between groups in the 7 d prior to the test (p>0.05). However there were significant increases (p<0.05) between the pre-exercise and postexercise values for LDH and
CK until 5 d postexercise test. Importantly, the BCAA supplementation significantly reduced this change in LDH from 2hrs to 5 d posttest, and CK from 4 hrs to 5 d post-test (p<0.05).

CONCLUSIONS: These results indicate that supplementary BCAA decreased serum concentrations of the intramuscular enzymes CK and LDH following prolonged exercise, even when the recommended intake of BCAA was being consumed. This observation suggests that BCAA supplementation may reduce the muscle damage associated with endurance exercise.


Branched chain amino acids (BCAA) stimulate protein synthesis, and growth hormone (GH) is a mediator in this process. A pre-exercise BCAA ingestion increases muscle BCAA uptake and use. Therefore after one month of chronic BCAA treatment (0.2 gkg(-1) of body weight), the effects of a pre-exercise oral supplementation of BCAA (9.64 g) on the plasma lactate (La) were examined in triathletes, before and after 60 min of physical exercise (75% of VO2 max). The plasma levels of GH (pGH) and of growth hormone binding protein (pGHBP) were also studied. The end-exercise La of each athlete was higher than basal. Furthermore, after the chronic BCAA treatment, these end-exercise levels were lower than before this treatment (8.6+/-0.8 mmol L(-1) after vs 12.8+/-1.0 mmol L(-1) before treatment; p < 0.05 [mean +/- std. err.]). The end-exercise pGH of each athlete was higher than basal (p < 0.05). Furthermore, after the chronic treatment, this end-exercise pGH was higher (but not significantly, p = 0.08) than before this treatment (12.2+/-2.0 ng mL(-1) before vs 33.8+/-13.6 ngmL(-1) after treatment). The end-exercise pGHBP was higher than basal (p < 0.05); and after the BCAA chronic treatment, this end-exercise pGHBP was 738+/-85 pmol L(-1) before vs 1691+/-555 pmol L(-1) after. pGH/pGHBP ratio was unchanged in each athlete and between the groups, but a tendency to increase was observed at end-exercise. The lower La at the end of an intense muscular exercise may reflect an improvement of BCAA use, due to the BCAA chronic treatment. The chronic BCAA effects on pGH and pGHBP might suggest an improvement of muscle activity through protein synthesis.


“Branched-chain amino acid supplementation increases the lactate threshold during an incremental exercise test in trained individuals.” Matsumoto K, Koba T,
The effects of branched-chain amino acid (BCAA) supplementation on the lactate threshold (LT) were investigated as an index of endurance exercise capacity. Eight trained male subjects (21 +/- 2 y) participated in a double-blind crossover placebo-controlled study. The subjects were randomly assigned to two groups and were provided either a BCAA drink (0.4% BCAA, 4% carbohydrate; 1,500 mL/d) or an iso-caloric placebo drink for 6 d. On the 7th day, the subjects performed an incremental loading exercise test with a cycle ergometer until exhaustion in order to measure the LT. The test drink (500 mL) was ingested 15-min before the test. Oxygen consumption VO2 and the respiratory exchange ratio (RER) during the exercise test were measured with the breath-by-breath method. Blood samples were taken before and during the exercise test to measure the blood lactate and plasma BCAA concentrations. The same exercise test was performed again 1 wk later. BCAA supplementation increased the plasma BCAA concentration during the exercise test, while plasma BCAA concentration decreased in the placebo trial. The RER during the exercise test in the BCAA trial was lower than that in the placebo trial (p<0.05). The VO2 and workload levels at LT point in the BCAA trial were higher than those in the placebo trial (VO2: 29.8 +/- 6.8 vs. 26.4 +/- 5.4 mL/kg/min; workload: 175 +/- 42 vs. 165 +/- 38 W, p<0.05, respectively). The VO2max in the BCAA trial was higher than that in the placebo trial (47.1 +/- 5.7 vs. 45.2 +/- 5.0 mL/kg/min, p<0.05). These results suggest that BCAA supplementation may be effective to increase the endurance exercise capacity.


The authors examined the effect of branched-chain amino acid (BCAA) supplementation on squat-exercise-induced delayed-onset muscle soreness (DOMS) using 12 young, healthy, untrained female participants. The experiment was conducted with a crossover double-blind design. In the morning on the exercise-session day, the participants ingested either BCAA (isoleucine:leucine:valine = 1:2.3:1.2) or dextrin at 100 mg/kg body weight before the squat exercise, which consisted of 7 sets of 20 squats/set with 3-min intervals between sets. DOMS showed a peak on Days 2 and 3 in both trials, but the level of soreness was significantly lower in the BCAA trial than in the placebo. Leg-muscle force during maximal voluntary isometric contractions was measured 2 d after exercise (Day 3), and the BCAA supplementation suppressed the muscle-force decrease (to ~80% of the value recorded under the control conditions) observed in the placebo trial. Plasma BCAA concentrations, which decreased after exercise in the placebo trial, were markedly elevated during the 2 hr postexercise in the BCAA trial. Serum myoglobin concentration was increased by exercise in the placebo but not in the BCAA trial. The concentration of plasma elastase as an index of neutrophil activation appeared
to increase after the squat exercise in both trials, but the change in the elastase level was significant only in the placebo trial. These results suggest that muscle damage may be suppressed by BCAA supplementation.


In this study, five men exercised the knee extensor muscles of one leg for 60 min (71 +/- 2% maximal work capacity) with and without (control) an oral supplement (77 mg/kg) of branched-chain amino acids (BCAA). BCAA supplementation resulted in a doubling (P < 0.05) of the arterial BCAA levels before exercise (339 +/- 15 vs. 822 +/- 86 microM). During the 60 min of exercise, the total release of BCAA was 68 +/- 93 vs. 816 +/- 198 mumol/kg (P < 0.05) for the BCAA and control trials, respectively. The intramuscular BCAA concentrations were higher (P < 0.05) for the BCAA trial and remained higher (P < 0.05) throughout exercise. In both trials, substantial quantities of NH3 were released, and when NH3 production equivalent to IMP accumulation was subtracted the net NH3 production was 1,112 +/- 279 and 1,670 +/- 245 mumol/kg (P < 0.05) for the control and BCAA trials, respectively. In contrast, the release of the essential amino acids (EAA) was much lower for the BCAA than the control trial (P < 0.05). When the BCAA were subtracted from the EAA (EAA-BCAA), the total release of EAA minus BCAA was lower (P < 0.05) for the BCAA (531 +/- 70 mumol/kg) than the control (924 +/- 148 mumol/kg) trial. These data suggest that BCAA supplementation results in significantly greater muscle NH3 production during exercise. Furthermore, the increased intramuscular and arterial BCAA levels before and during exercise result in a suppression of endogenous muscle protein breakdown during exercise.


PURPOSE: The purpose of this study was to examine the role of branched-chain amino acid (BCAA) supplementation during recovery from intense eccentric exercise.

METHODS: Twenty-four non-weight-trained males were assigned to one of two groups: one group (supplementary, SUP) ingested BCAA beverages (n = 12); the second group (placebo, PLA) ingested artificially flavored water (n = 12). Diet was controlled throughout the testing
period to match habitual intake. The eccentric exercise protocol consisted of 12 x 10 repetitions of unilateral eccentric knee extension exercise at 120% concentric one repetition maximum. On the day of the exercise, supplements were consumed 30 min before exercise, 1.5 h after exercise, between lunch and dinner, and before bed. On the following 2 d, four supplements were consumed between meals. Muscle soreness, muscle function, and putative blood markers of muscle damage were assessed before and after (1, 8, 24, 48, and 72 h) exercise.

RESULTS: Muscle function decreased after the eccentric exercise (P < 0.0001), but the degree of force loss was unaffected by BCAA ingestion (51% +/- 3% with SUP vs -48% +/- 7% with PLA). A decrease in flexed muscle soreness was observed in SUP compared with PLA at 48 h (21 +/- 3 mm vs 32 +/- 3 mm, P = 0.02) and 72 h (17 +/- 3 mm vs 27 +/- 4 mm, P = 0.038). Flexed muscle soreness, expressed as area under the curve, was lower in SUP than in PLA (P = 0.024).

CONCLUSIONS: BCAA supplementation may attenuate muscle soreness, but it does not ameliorate eccentric exercise-induced decrements in muscle function or increases in reputed blood markers of muscle damage, when consumed before exercise and for 3 d after an eccentric exercise bout.


The present study was conducted to examine alterations in plasma free amino acid concentrations induced by squat exercise and branched-chain amino acid (BCAA) supplementation in young, untrained female subjects. In the morning on the exercise session day, participants ingested drinks containing either BCAA (isoleucine:leucine:valine=1:2.3:1.2) or dextrin (placebo) at 0.1 g/kg body weight 15 min before a squat exercise session, which consisted of 7 sets of 20 squats, with 3 min intervals between sets. In the placebo trial, plasma BCAA concentrations were decreased subsequent to exercise, whereas they were significantly increased in the BCAA trial until 2 h after exercise. Marked changes in other free amino acids in response to squat exercise and BCAA supplementation were observed. In particular, plasma concentrations of methionine and aromatic amino acids were temporarily decreased in the BCAA trial, being significantly lower than those in the placebo trial. These results suggest that BCAA intake before exercise affects methionine and aromatic amino acid metabolism.


BCAA catabolism in skeletal muscle is regulated by the branched-chain alpha-keto acid dehydrogenase (BCKDH) complex, located at the second step in the BCAA catabolic pathway. The activity of the BCKDH complex is regulated by a phosphorylation/dephosphorylation cycle. Almost all of BCKDH complex in skeletal muscle under normal and resting conditions is in an inactive/phosphorylated state, which may contribute to muscle protein synthesis and muscle growth. Exercise activates the muscle BCKDH complex, resulting in enhanced BCAA catabolism. Therefore, exercise may increase the BCAA requirement. It has been reported that BCAA supplementation before exercise attenuates the breakdown of muscle proteins during exercise in humans and that leucine strongly promotes protein synthesis in skeletal muscle in humans and rats, suggesting that a BCAA supplement may attenuate muscle damage induced by exercise and promote recovery from the damage. We have examined the effects of BCAA supplementation on delayed-onset muscle soreness (DOMS) and muscle fatigue induced by squat exercise in humans. The results obtained showed that BCAA supplementation prior to squat exercise decreased DOMS and muscle fatigue occurring for a few days after exercise. These findings suggest that BCAAs may be useful for muscle recovery following exercise.


OBJECTIVE: Intense long-duration exercise has been associated with immunosuppression, which affects natural killer cells, lymphokine-activated killer cells, and lymphocytes. The mechanisms involved, however, are not fully determined and seem to be multifactorial, including endocrine changes and alteration of plasma glutamine concentration. Therefore, we evaluated the effect of branched-chain amino acid supplementation on the immune response of triathletes and long-distance runners.

METHODS: Peripheral blood was collected prior to and immediately after an Olympic Triathlon or a 30k run. Lymphocyte proliferation, cytokine production by cultured cells, and plasma glutamine were measured.

RESULTS: After the exercise bout, athletes from the placebo group presented a decreased plasma glutamine concentration that was abolished by branched-chain amino acid supplementation and an increased proliferative response in their peripheral blood mononuclear
cells. Those cells also produced, after exercise, less tumor necrosis factor, interleukins-1 and -4, and interferon and 48% more interleukin-2. Supplementation stimulated the production of interleukin-2 and interferon after exercise and a more pronounced decrease in the production of interleukin-4, indicating a diversion toward a Th1 type immune response.

CONCLUSIONS: Our results indicate that branched-chain amino acid (BCAA) supplementation recovers the ability of peripheral blood mononuclear cells to proliferate in response to mitogens after a long distance intense exercise, as well as plasma glutamine concentration. The amino acids also modify the pattern of cytokine production leading to a diversion of the immune response toward a Th1 type of immune response.


OBJECTIVE: The influence of branched-chain amino acid (BCAA) supplementation on urinary urea nitrogen, hydroxyproline (HP), and 3-methylhistidine (3MH) concentrations after 25 min of breast stroke exercise (65-70% maximum heart rate reserved, 65-70% HRRmax) followed by a 600 m crawl stroke competition was investigated in a double-blind, counter-balanced study.

METHODS: Male university students (19-22 years old) majoring in physical education participated in the study. Based on the previous swimming time of a 600 m crawl stroke, the participants were divided into two groups: placebo (n = 9, BMI = 24.2 +/- 2.1 kg/m2; 12 g of glucose/day; in capsules) and BCAA (n = 10, BMI = 22.7 +/- 1.5 kg/m2; 12 g of BCAAs/day; in capsules: leucine 54%, isoleucine 19%, valine 27%) groups. The participants maintained a regular dietary intake (except the prescribed breakfast on day 15) and exercise activity at a moderate/low intensity (60-70% HRRmax, swimming and rowing, approximately 1.5 hour/day) during the 15-day study. A prescribed exercise program was performed on day 15. Urinary and blood samples were collected before, during, and after the prescribed exercise for the measurements of the urinary urea nitrogen, HP, and 3MH concentrations in urine, as well as the glucose, lactate, glutamine, alanine, and BCAA concentrations in plasma.

RESULTS: Two weeks of dietary supplementation did not induce any changes in the plasma glucose and total BCAA concentrations of either group, nor in the urinary urea nitrogen, HP, and 3MH concentrations in urine. On day 15, after 25 min of breast stroke exercise and a 600 m crawl stroke competition, plasma glucose concentration decreased significantly (p < 0.05) whereas plasma lactate concentration increased significantly (p < 0.05) in both groups. The exercise program prescribed in the study did not affect urinary urea nitrogen, HP, and 3MH concentrations. Twenty hours after the competition, however, a significant increase in the
CONCLUSIONS: The results obtained in this study suggest that swimming induced muscle proteolysis was prevented by BCAA supplementation. The mechanism could be attributed to the availability of ammonia provided by the oxidation of supplemented BCAAs during exercise.


INTRODUCTION: Intense long-duration exercise could lead to immune suppression through a decrease in the circulating level of plasma glutamine. The decrease in plasma glutamine concentration as a consequence of intense long-duration exercise was reversed, in some cases, by supplementing the diet of the athletes with branched-chain amino acids (BCAA). To better address this question, we have evaluated some blood parameters (lymphocyte proliferation, the level of plasma cytokines, plasma glutamine concentration, and in vitro production of cytokines by peripheral blood lymphocytes) before and after the São Paulo International Triathlon, as well as the incidence of symptoms of infections between the groups.

METHODS: Twelve elite male triathletes of mean age 25.5 +/- 3.2 yr (ranging from 21.4 to 30.1 yr), weighing 74.16 +/- 3.9 kg, swam 1.5 km, cycled 40 km, and ran 10 km (Olympic triathlon) in the São Paulo International Triathlon held in April 1997 and April 1998. In both events, six athletes received BCAA and the others, placebo. RESULTs: Athletes from the BCAA group (BG) presented the same levels of plasma glutamine, before and after the trial, whereas those from the placebo group showed a reduction of 22.8% in plasma glutamine concentration after the competition. Changes in the proliferative response of peripheral blood lymphocytes were accompanied by a reduction in IL-1 production after exercise (22.2%), which was reversed by BCAA supplementation (20.3%), without changes in IL-2 production.

DISCUSSION: The data obtained shows that BCAA supplementation can reverse the reduction in serum glutamine concentration observed after prolonged intense exercise such as an Olympic triathlon. The decrease in plasma glutamine concentration is paralleled by an increased incidence of symptoms of infections that results in augmented proliferative response of lymphocytes cultivated in the absence of mitogens. The prevention of the lowering of plasma glutamine concentration allows an increased response of lymphocytes to ConA and LPS, as well as an increased production of IL-1 and 2, TNF-alpha, and IFN-gamma, possibly linked to the lower incidence of symptoms of infection (33.84%) reported by the supplemented athletes.

GLUTAMINE STUDIES


The purpose of this study was to determine the efficacy of glutamine in promoting whole body carbohydrate storage and muscle glycogen resynthesis during recovery from exhaustive exercise. Postabsorptive subjects completed a glycogen-depleting exercise protocol, then consumed 330 ml of one of three drinks, 18.5% (wt/vol) glucose polymer solution, 8 g glutamine in 330 ml glucose polymer solution, or 8 g glutamine in 330 ml placebo, and also received a primed constant infusion of [1-13C]glucose for 2 h. Plasma glutamine concentration was increased after consumption of the glutamine drinks (0.7-1.1 mM, P < 0.05). In the second hour of recovery, whole body nonoxidative glucose disposal was increased by 25% after consumption of glutamine in addition to the glucose polymer (4.48 +/- 0.61 vs. 3.59 +/- 0.18 mmol/kg, P < 0.05). Oral glutamine alone promoted storage of muscle glycogen to an extent similar to oral glucose polymer. Ingestion of glutamine and glucose polymer together promoted the storage of carbohydrate outside of skeletal muscle, the most feasible site being the liver.


PURPOSE OF REVIEW: Glutamine is largely synthesized in skeletal muscles and provides fuel to rapidly dividing cells of the immune system and precursors to gluconeogenesis in the liver. Physical exercise is known to affect glutamine synthesis and to modulate glutamine uptake. Overtraining is frequently associated with reduced availability of glutamine and decreased immunocompetence. Inactivity affects glutamine metabolism, but this subject was poorly investigated.

RECENT FINDINGS: Strenuous physical exercise as well as exhaustive training programs lead to glutamine depletion due to lowered synthesis and enhanced uptake by liver and immune cells. Evidence suggests that postexercise glutamine depletion is associated with immunodepression. Counterwise, moderate training leads to improved glutamine availability due to a positive balance between muscle synthesis and peripheral clearance. Physical inactivity, as investigated by experimental bed rest in healthy volunteers, reduced glutamine synthesis and availability.
**SUMMARY:** After exercise, a reduced glutamine availability may be considered as a marker of overtraining. An increased glutamine availability may contribute to decreased inflammation and health benefits associated with optimal training. Thus, glutamine supplementation may enhance immunocompetence after strenuous exercise. The potential of glutamine supplementation during physical inactivity needs to be explored.


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**OBJECTIVE:** High-intensity and prolonged exercise significantly enhances the levels of plasma ammonia, a metabolite with toxic effects on the central nervous system. The main purpose of the present study was to evaluate the metabolic response of athletes to glutamine (Gln) and alanine (Ala) supplementation, since these amino acids have a significant influence on both anaplerosis and gluconeogenesis.

**METHODS:** Professional football players were assigned to groups receiving either Gln or Ala supplementation (100 mg kg(-1) body weight); this supplementation was either short-term or long-term and was given immediately before exercise. The players were evaluated using two exercise protocols, one with intervals (n = 18) and the other with continuous intensity (n = 12).

**RESULTS:** Both types of exercises increased ammonia, urate, urea and creatinine in blood. Chronic Gln supplementation partially protected against hyperammonemia after a football match (intermittent exercise: Gln -140 (SEM 13)% vs Ala -240 (SEM 37)% and after continuous exercise at 80% of the maximum heart rate (Gln -481 (SEM 44)% vs placebo -778 (SEM 99)%). Urate increased by 10-20% in all groups, independently of supplementation. Glutamine once a day supplementation induced a greater elevation in urate as compared to alanine at the end of the game; however, long-term supplementation provoked a lesser increment in urate. Exercise induced similar increases in creatinine as compared to their respective controls in either acute or chronic glutamine administration.

**CONCLUSIONS:** Taken together, the results suggest that chronically supplemented Gln protects against exercise-induced hyperammonemia depending on exercise intensity and supplementation duration.


There is an increased risk of infections in athletes undertaking prolonged, strenuous exercise. There is also some evidence that cells of the immune system are less able to mount a defence against infections after such exercise. The level of plasma glutamine, an important fuel for cells of the immune system, is decreased in athletes after endurance exercise; this may be partly responsible for the apparent immunosuppression which occurs in these individuals. We monitored levels of infection in more than 200 runners and towers. The levels of infection were lowest in middle-distance runners, and highest in runners after a full or ultramarathon and in elite rowers after intensive training. In the present study, athletes participating in different types of exercise consumed two drinks, containing either glutamine (Group G) or placebo (Group P) immediately after and 2 h after exercise. They subsequently completed questionnaires (n = 151) about the incidence of infections during the 7 days following the exercise. The percentage of athletes reporting no infections was considerably higher in Group G (81%, n = 72) than in Group P (49%, n = 79, p < 0.001).


At normal intakes, dietary glutamine and glutamate are metabolized by the small intestine and essentially all glutamine within the body is synthesized de novo through the action of glutamine synthetase. The major sites of net glutamine synthesis are skeletal muscle, lung, and adipose tissue and, under some conditions, the liver. In addition to the small intestine, where glutamine is the major respiratory fuel, other sites of net glutamine utilization include the cells of the immune system, the kidneys, and the liver. The intestine expresses pyrroline 5-carboxylate (P5C) synthase, which means that proline is an end product of intestinal glutamine catabolism. Proline can also be synthesized from ornithine and the exact contribution of the 2 pathways is not certain. Infusion of proline i.v. to increase circulating concentrations is associated with increased proline oxidation and decreased proline synthesis. In contrast, conditions of proline insufficiency, after feeding low-proline diets or in response to high rates of proline catabolism in burn patients, do not result in increased proline synthesis. Glutamine supplementation is widespread and up to 0.57-0.75 g.kg(-1).d(-1) is well tolerated. Similarly, the only study of proline supplementation, in which patients with gyrate atrophy were given 488 mg.kg(-1).d(-1), reported no deleterious side effects. In the absence of controlled trials, it is currently not possible to estimate a safe upper limit for either of these 2 amino acids.

An oral glutamine load was administered to nine healthy subjects to determine the effect on plasma glutamine, bicarbonate, and circulating growth hormone concentrations. Two grams glutamine were dissolved in a cola drink and ingested over a 20-min period 45 min after a light breakfast. Forearm venous blood samples were obtained at zero time and at 30-min intervals for 90 min and compared with time controls obtained 1 wk earlier. Eight of nine subjects responded to the oral glutamine load with an increase in plasma glutamine at 30 and 60 min before returning to the control value at 90 min. Ninety minutes after the glutamine administration load both plasma bicarbonate concentration and circulating plasma growth hormone concentration were elevated. These findings demonstrate that a surprisingly small oral glutamine load is capable of elevating alkaline reserves as well as plasma growth hormone.


Endogenous production of glutamine may become insufficient during critical illness. The shortage of glutamine is reflected as a decrease in plasma concentration, which is a prognostic factor for poor outcome in sepsis. Because glutamine is a precursor for nucleotide synthesis, rapidly dividing cells are most likely to suffer from a shortage. Therefore, exogenous glutamine supplementation is necessary. In particular, when i.v. nutrition is given, extra glutamine supplementation becomes critical, because most present formulations for i.v. use do not contain any glutamine for technical reasons. The major part of endogenously produced glutamine comes from skeletal muscle. For patients staying a long time in the intensive care unit (ICU), the muscle mass decreases rapidly, which leaves a tissue of diminishing size to maintain the export of glutamine. The metabolic and nutritional adaptation in long-staying ICU patients is poorly studied and is one of the fields that needs more scientific evidence for clinical recommendations. To date, there is evidence to support the clinical use of glutamine supplementation in critically ill patients, in hematology patients, and in oncology patients. Strong evidence is presently available for i.v. glutamine supplementation to critically ill patients on parenteral nutrition. This must be regarded as the standard of care. For patients on enteral nutrition, more evidence is needed. To guide administration of glutamine, there are good arguments to use measurement of plasma glutamine concentration for guidance. This will give an indication for treatment as well as proper dosing. Most patients will have a normalized
plasma glutamine concentration by adding 20-25 g/24 h. Furthermore, there are no reported adverse or negative effects attributable to glutamine supplementation.


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**ELECTROLYTE/HYDRATION STUDIES**


**Context:** Exercise-associated muscle cramps (EAMCs) are common among physically active individuals and are temporarily disabling; therefore, prevention is of great interest.

**Objective:** To determine the role of hydration and electrolyte supplementation in the prevention of EAMCs.

**Design:** Each subject completed 2 counterbalanced trials in a repeated-measures design.

**Setting:** University of Alabama. Patients or Other Participants: College-aged men (n = 13) with a history of EAMCs.

**Intervention(s):** In each trial, participants performed a calf-fatiguing protocol to induce EAMCs in the calf muscle group. Each trial was performed in a hot environment (dry bulb temperature of 37 degrees C, relative humidity of 60%). In the carbohydrate-electrolyte trial, subjects consumed, at a rate similar to sweat loss, a carbohydrate-electrolyte beverage with sodium chloride added. In the hypohydration trial, subjects were not allowed to consume any fluids.

**Main Outcome Measure(s):** We measured the incidence and time to onset of EAMCs.

**Results:** Nine participants experienced cramps in the carbohydrate-electrolyte trial, compared with 7 in the hypohydration trial. Of the 7 individuals who had EAMCs in both trials, exercise duration before onset was more than doubled in the carbohydrate-electrolyte trial (36.8 +/- 17.3 minutes) compared with the hypohydration trial (14.6 +/- 5.0 minutes, P < .01).

**Conclusions:** Consumption of a carbohydrate-electrolyte beverage before and during exercise in a hot environment may delay the onset of EAMCs, thereby allowing participants to exercise longer. However, it appears that dehydration and electrolyte loss are not the sole causes of EAMCs, because 69% of the subjects experienced EAMCs when they were hydrated and supplemented with electrolytes.


Prolonged exercise leads to a progressive water and electrolyte loss from the body as sweat is secreted to promote heat loss. The rate of sweating depends on many factors and is increased in proportion to the work rate and the environmental temperature and humidity. Sweat rate is highly variable between individuals, and can exceed 21 h-1 for prolonged periods. Since it is established that dehydration will impair exercise capacity and can pose a risk to health, the intake of fluid during exercise to offset sweat loss is important. Fluid intake is also aimed at providing a source of substrate, usually in the form of carbohydrate. The availability of ingested fluids may be limited by gastric emptying or by intestinal absorption. Gastric emptying of liquids is slowed by the addition of carbohydrate in proportion to the carbohydrate concentration and osmolality of the solution. With increasing glucose concentration, the rate of fluid delivery to the small intestine is decreased, but the rate of glucose delivery is increased. Water absorption in the small intestine is a passive process and is stimulated by the active absorption of glucose and sodium. The optimum fluid for rehydration during exercise depends on many factors, particularly the intensity and duration of the exercise, the environmental conditions, and the individual physiology of the athlete. There is no advantage to fluid intake during exercise of less than 30 min duration. The composition of fluids to be used will depend on the relative needs to replace water and to provide substrate. Where rehydration is a priority the solution should contain some glucose and sodium and should not exceed isotonicity: this will require the glucose concentration to be low (20-309 g l-1) or the substitution of glucose polymers, and the sodium content to be high (perhaps as much as 60 mmol l-1). Where substrate provision is more important, a more concentrated solution, incorporating large amounts of glucose polymers in concentrations of 150-200 g l-1, is to be preferred. To minimize the limitation imposed by the rate of gastric emptying, the volume of fluid in the stomach should be kept as high as is comfortable by frequent ingestion of small amounts of fluid. Addition of sodium, and perhaps also of potassium, may be important for rehydration after exercise.


Rapid and complete restoration of fluid balance after exercise is an important part of the recovery process, especially in hot, humid conditions, when sweat losses may be high. Rehydration after exercise can only be achieved if the electrolytes lost in sweat, as well as the lost water, are replaced. However, the amount of electrolytes lost in sweat is highly variable between individuals and although the optimum drink may be achieved by matching drink electrolyte intake with sweat electrolyte loss, this is virtually impossible in sport settings. The
composition of sweat varies considerably not only between individuals, but also with time during exercise and it is further influenced by the state of acclimatization. A moderate excess of salt intake would appear to be beneficial as far as hydration status is concerned, without any detrimental effects on health, provided that fluid intake is in excess of sweat loss and the renal function is not impaired. To achieve effective rehydration following exercise in the heat, the rehydration beverage should contain moderately high levels of sodium (at least 50 mmol l-1), and possibly also some potassium. The addition of substrate is not necessary for rehydration, although a small amount of carbohydrate (< 2%) may improve the rate of intestinal uptake of sodium and water. The volume of beverage consumed should be greater than the volume of sweat lost to provide for the ongoing obligatory urine losses. Therefore, the palatability of the beverage is important. Many individuals may lose substantial amounts of sweat and will therefore have to consume large amounts of replacement fluids and this is more likely to be achieved if the taste is perceived as being pleasant. Water alone is adequate for rehydration purposes when solid food is consumed, as this replaces the electrolytes lost in sweat. However, there are many situations where intake of solid food is not possible or is deliberately avoided and, in these instances, the inclusion of electrolytes in rehydration beverages is essential. Where a second exercise bout has to be performed, replacement of sweat losses is an essential part of the recovery process. Exercise performance will be impaired if complete rehydration is not achieved.