The Antiseptic

Estd.1904

Indexed in IndMED

A MONTHLY JOURNAL OF MEDICINE AND SURGERY

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Vol. 114 • No. 11 NOVEMBER 2017 ISSN 003-5998 • ₹ 100

AN UNUSUAL CAUSE OF ABDOMINAL PAIN - LEAD TOXICITY!

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THE ANTISEPTIC - A MONTHLY JOURNAL OF MEDICINE & SURGERY

Vol 114 No 11 **NOVEMBER 2017**

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Nutrition and Nutraceuticals for Muscle Maintenance and Recovery

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Background

In the past 40 years there has been substantial progress in the ability to provide nutrition support to hospitalized patients, especially those that are critically ill. Small bore and percutaneous feeding tubes allow safe enteral nutrition (EN) in circumstances and disease states previously considered impossible or inadvisable. Patients with a dysfunctional gastrointestinal tract can receive their full nutrition needs via parenteral nutrition (PN). However, while providing adequate nutrition reduces muscle breakdown, nutrition alone cannot completely preserve lean muscle mass in hospitalized adult patients.

In the early phase of critical illness, catabolism is unavoidable. Research has demonstrated that the negative nitrogen balance associated with the early stage of critical illness is not completely reversed even when calories and protein are provided far in excess of requirements. Furthermore, the lack of exercise and general immobilization that occurs in hospitalized patients results in breakdown of skeletal muscle regardless of nutrition intake. The loss of skeletal muscle during hospitalizations exacerbates muscle weakness, which can hamper weaning from mechanical ventilation, delay recovery, and increase the need for and duration of rehabilitation services. A study of ARDS survivors revealed that discharge body weights were 18% less than preadmission weight, and there was a prolonged functional disability in many patients that persisted, even when pulmonary function returned to normal. Intensive Care Unit acquired weakness has been reported in 50% of patients ventilated > 1 week and was still present in 25% of ICU patients 7 days later.

However, studies of arginine supplemented enteral feedings have also revealed increased mortality in septic patients and a study of supplemental arginine in patients with cardiovascular disease was halted due to significantly increased mortality in the arginine supplemented group. Although there is data to suggest that supplemental arginine could have potential benefits for strength, muscle, rehabilitation and wound healing, there are no randomized studies of the effect of arginine on any functional endpoints that matter such as the need for rehabilitation after hospitalization, time for recovery, or actual healing of wounds. Considering that randomized studies have demonstrated unexpected negative effects of supplemental arginine in some circumstances, arginine supplementation appears to be an area worthy of further investigation rather than routine clinical use at this time.

Branched Chain Amino Acids and Leucine

Studies of isolated muscle tissue and animal models have provided evidence that the branched chain amino acids, particularly leucine, stimulate muscle protein synthesis. In healthy young adults, adding additional leucine to an oral amino acid supplement (3.5g leucine) increased muscle anabolic signaling, but did not stimulate muscle protein synthesis more than an amino acid supplement with a normal leucine content (1.7g leucine). However, in an elderly population (66 +/- 2 years) increasing the concentration of leucine in an amino acid supplement to 2.8g increased protein synthesis by 20% compared to the standard amino acid supplement containing 1.7 gm leucine.25 Healthy elderly subjects who ingested a leucine-rich amino acid supplement had rates of protein synthesis similar to younger patients (30 +/- 2 years).

There were no significant differences in muscle mass or strength between the placebo and leucine groups at the end of 3 months. There is evidence that resistance exercise may have a synergistic effect on protein synthesis with branched-chain enriched proteins, therefore it would be worthwhile to study the potential for leucine as an adjunct to resistance exercise in patients undergoing rehabilitation or in elderly patients with sarcopenia. Due to the fact that leucine stimulates protein synthesis by increased signaling through a pathway that is increased in some forms of cancer, some experts have questioned if leucine could accelerate growth of existing tumors. Colon cancers with an unfavorable prognosis were reported to have increased leucine

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Specially Contributed to "The Antiseptic"
Vol. 114 No. 11 & P : 9 - 11

uptake, and branched-chain enriched amino acid mixtures appear to stimulate tumor growth. While supplemental branched-chain amino acids or leucine may not be advisable during treatment of existing malignancy, there is sufficient evidence for an effect of leucine on protein synthesis to justify further investigations.

Beta - hydroxy - beta - methylbutyrate (HMB)

Beta-hydroxy-beta-methylbutyrate (HMB) is a metabolite derived from the amino acid leucine. HMB has been studied in athletes, the elderly and in various pathological states after studies demonstrated an increase in lean muscle mass and protein synthesis in animals with HMB supplementation. Randomized studies in athletes have demonstrated that the beneficial effects of HMB on muscle appear to be limited to novice athletes, because elite or highly trained athletes do not appear to benefit from HMB supplementation.31, 32 A small randomized study of HMB supplementation (3 gm/day) in 48 critically ill trauma patients, demonstrated that HMB significantly improved nitrogen balance from the first 7 days compared to the last 7 days, more than placebo or a combination of 3g HMB, 14 gm arginine and 14g glutamine (Juven). Interestingly, the addition of arginine and glutamine to HMB in trauma patients appears to negate any benefits of HMB on protein metabolism. The group that received the combination of HMB with arginine and glutamine had numerically lower nitrogen balance compared to control patients.

Fish Oil

Fish oil provides the n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which influence a wide variety of cellular functions. Among other actions, EPA and DHA supplementation decreases production of proinflammatory cytokines in stressed states, alters the sensitivity of skeletal muscle to the effects of insulin, and may decrease protein breakdown. Early unblinded studies of fish oil supplementation in cancer patients reported decreased weight loss, preserved lean muscle mass, and improved appetite. However, larger randomized studies of fish oil supplementation in cancer patients did not report significant advantages compared to placebo.

Glutamine

Serum and intracellular concentrations of glutamine are decreased in critical illness, and provision of parenteral glutamine (PG) was reported to improve nitrogen balance in adult patients after surgery or trauma. Supplemental glutamine induces heat shock proteins, which allows cells and tissues to become more stress tolerant in experimental models. Two studies in critically ill patients who received parenteral nutrition (PN) supplemented with PG reportedly had improved 6-month survival, compared to patients who received glutamine-free PN. Supplemental PG did not result in any significant difference in short-term mortality (ICU or hospital) in these studies.

Strategies to Help Limit Loss of Lean Body Mass

- Decrease the time patients are without nutrition prior to procedures
- Accelerate the transition back to oral/enteral intake post-procedures
- Add D5 to standing IV fluids in patients not receiving nutrition support
- Evaluate the practice of NPO status prior to procedures and consider continuing nutrition (at least nutritional liquids/enteral feeding) until 2 hours before many procedures
- Enlist Early Recovery After Surgery (ERAS) pathway or modifications
- Keep EN going (especially in those jejunely fed) for tests/procedures that require no, or only a local anesthetic.
- Provide an evening snack (or two) for patients that must be NPO after midnight.
- Provide adequate amounts of high-quality protein.
- Evaluate protocols for mobility and physical therapy and collaborate with other disciplines to eliminate barriers for activity.

Nutrition and Feeding Strategies

Although full nutrition does not completely prevent muscle loss in hospitalized patients, it is clear that inadequate nutrition accelerates muscle loss, and prolonged or recurrent periods without nutrition cause large amounts of body protein to be burned for energy. Healthy adults that are deprived of food have an adaptation to starvation within several days, with decreased metabolic rate and protein oxidation and increased utilization of fat for fuel. However, patients with illness or injury experience hypermetabolism and rapid protein breakdown even when starved. Fat cannot be converted directly into glucose, therefore, when glycogen stores are quickly depleted, large amounts of body proteins are catabolized to meet the needs of cells that are dependent on glucose. Many patients arrive at the hospital with a history of weight loss or decreased oral intake, and thus have depleted glycogen stores on admission.

Discussion

The loss of lean muscle mass during hospitalizations very likely contributes to functional impairments, reduced quality of life and increased costs for rehabilitation. The elderly, who are an expanding segment of our population, are especially susceptible to the negative effects of muscle loss. While there are a number of nutritional supplements that show promise and are worthy of additional research, there is a need for adequately powered studies that investigate meaningful outcomes and cost effectiveness before they are routinely used in clinical practice. OKG is the only anabolic nutraceutical with demonstrated outcome improvements in controlled studies, but there is limited data in acutely or critically ill patients receiving OKG. Some nutraceuticals that increase anabolism may have the potential to accelerate tumor growth and available research does not adequately address potential safety risks. Randomized studies over the past 20 years have repeatedly demonstrated unexpected harmful effects of relatively benign nutrients or nutraceuticals that initially appeared promising in animal or small scale human studies. Some critically or acutely ill populations may be at particular risk from enhancing protein synthesis because it is possible that reversing catabolism in the earlier stages of illness may have unexpected negative effects. The use of anabolic steroid oxandrolone in ventilator dependent surgical patients resulted in a significantly longer period of mechanical ventilation and intensive care unit stay, which may be related to increased collagen deposition leading to increased fibrotic pulmonary changes.

Conclusions

There are a number of nutritional supplements that have demonstrated potential as agents to help maintain or recover muscle during and after illness. However, there is a need for larger studies examining patient outcomes and cost effectiveness before routine clinical use can be recommended. Nutritional strategies and protocols that minimize time without nutrition during hospitalizations may reduce muscle loss and can generally be implemented without increasing costs. Optimizing existing efforts to prevent time without nutrition and increase physical activity are concrete steps that can be implemented now to reduce and restore muscle mass until additional research with anabolic nutraceuticals are available. Future nutrition studies should investigate not only short term outcomes such as survival and length of stay at ICU, but also include longer term outcomes such as functional status and requirements for rehabilitation as outcomes. Programs that optimize physical activity and combined exercise and nutrition programs should be studied in the future.

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Streptococcus gallolyticus subspecies (subsp.) gallolyticus (formerly bovis bioptype I) bacteremia has been long associated with underlying colonic adenocarcinoma.

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