

Issue 171 In a nutshell

Cachexia (weight loss, particularly muscle tissue) is a serious complication of cancer that is difficult to treat.

Omega-3 fatty acids and essential amino acids may have specific roles to play in treatment, along with general measures to increase appetite, exercise to promote muscle synthesis etc.

Cancer cachexia

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NUTRITION RESEARCH REVIEW

Study 1: Essential amino acids help

A recent American trial found that essential amino acid (EAA) supplements increased weight and muscle mass in cancer cachexia patients.

Subjects: 32 patients with advanced (stage IV) solid cancers who had lost at least 5% of body weight.

Method: Randomised, controlled, double-blinded trial (RCT). Active treatment was a mixture of essential amino acids (L-arginine 14 g, L-glutamine 14 g and the leucine metabolite beta-hydroxy-beta-methylbutyrate 3 g daily). Control treatment was an isonitrogenous non-essential amino acid supplement.

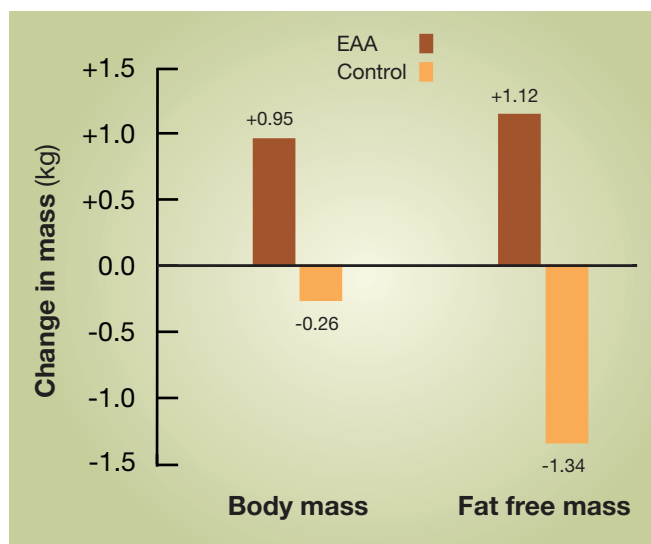
Results: Only the EAA supplemented patients gained weight. This was due to a significant increase in fat free (i.e. muscle) mass at 4 weeks ($p=0.02$, see Graph), even more so at 24 weeks (mean increase in fat free mass in active treated group = 1.6 kg, $p<0.05$). There were no adverse effects.

Reference: May PE, et al. Reversal of cancer-related wasting using oral supplementation with a combination of beta-hydroxy-beta-methylbutyrate, arginine, and glutamine. Am J Surg. 2002 Apr;183(4):471-9.

Study 2: EFA helpful in cachexia

Adding omega-3 essential fatty acids (EFAs) and antioxidants to energy/protein supplements may have advantages in treating cancer cachexia, according to results from a new multi-centre international trial.

Subjects: 200 patients with pancreatic cancer and



Graph: Change in weight with supplementation

weight loss of at least 5% over the preceding 6 months. Of the initial subjects, only 110 were available for analysis at the 8 week end-point of the trial.

Method: RCT. Patients were given a supplement containing 620 Kcal of energy (including 32 g protein) either with or without 2.2 g EFA along with extra antioxidants (vitamin A, C, E and selenium, to help protect the extra fatty acids from lipid peroxidation).

Results: In both groups there was a substantial reduction in the rate of loss of weight and lean body mass (LBM). However, there were no significant differences between the two groups in relation to this change. Also, in neither group did patients manage to consume the full allocated supplement dose.

An analysis was therefore done of dose taken vs effect. There were significant correlations between supplement dose and increase in both weight and LBM, seen only in the EFA-supplemented and not in

Table (Study 2): Correlations with supplement intake

	EFA	Control
Weight	$r=0.50$ ($p<0.001$)	$r=0.16$ ($p>0.2$)
LBM	$r=0.33$ ($p<0.04$)	$r=0.09$ ($p>0.4$)

the control supplemented group. See Table (page 1).

Reference: Fearon KC. et al. Effect of a protein and energy dense n-3 fatty acid enriched oral supplement on loss of weight and lean tissue in cancer cachexia: a randomised double blind trial. *Gut*. 2003 Oct;52(10):1479-1486.

Study 3: Fish oil ineffective

Fish oil supplements were not effective in countering anorexia or cachexia associated with advanced cancer, according to new research from Texas.

Subjects: 60 patients with advanced cancer who had loss of weight and appetite.

Method: Randomised, placebo-controlled trial. Active treatment consisted of fish oil capsules over 2 weeks (subjects in this group achieved a mean of 1.8 g of eicosapentaenoic acid and 1.2 g of DHA daily).

Results: There were no significant differences between placebo and active treatment in post- vs pre-treatment appetite, tiredness, well being, weight or other nutritional parameters that were measured.

Reference: Bruera E. et al. Effect of fish oil on appetite and other symptoms in patients with advanced cancer and anorexia/cachexia: a double-blind, placebo-controlled study. *J Clin Oncol*. 2003 Jan 1;21(1):129-34.

Comments

Cachexia is a condition of weight loss, particularly involving muscle and fat tissue. It often occurs in patients with active cancer or HIV infection.

The causes are multifactorial and not fully understood. Cachexia usually involves the obvious factors which decrease nutrient intake (e.g. anorexia) or increase catabolism (e.g. surgery, chemotherapy). But it is also involves catabolic substances generated by the tumour or by the body's reaction to it. For example, inflammatory mediators such as cytokines (e.g. interleukins and tumor necrosis factor) and a recently identified substance produced by cancer tissue known as proteolysis-inducing factor ¹.

Whatever its cause, cachexia is a serious condition, leading to increased mortality, morbidity and impaired quality of life ². Various treatments have been suggested, ranging from simple measures that decrease energy expenditure and extra protein-energy intake to medication using substances including melatonin and thalidomide. But results of trials have been modest - mostly reducing the rate of weight loss rather than significantly increasing lean tissue mass ¹⁻³.

Many people believe that the eicosanoids are central to the puzzle of cachexia, both the eicosanoids that cause catabolism and those that can treat it. The omega-3 essential fatty acids (EFAs) have been shown to have a direct effect in countering some of the catabolic mediators involved in cancer and cachexia ⁵.

In a previous issue (#45, April 1998) we reported on evidence that fish oil supplementation can prolong cancer survival and speculated that this may be due in part to its action in reversing the cachexic process.

The two new trials (Studies 2 and 3 above) add to our knowledge and are interesting in several ways.

They remind us that clinicians treating cachexia must measure not just weight, but also muscle mass. They also remind us how difficult it can be to get patients to consume enough supplement. And they confirm how modest the gain in lean tissue mass often is. Study 3 had no gain (perhaps due to the short time frame) whilst Study 2 had only a small increase in 6 months.

Study 1 focuses on which specific amino acids may promote protein anabolism. This certainly makes sense, since cancer cachexia is characterised by higher rate of protein turnover and breakdown, in part due to failure of fat utilisation to adequately 'spare' protein in energy metabolism. This is likely to particularly affect nutrient balance of EAAs. At the same time, clinicians should not forget the value of resistance exercise in promoting muscle mass ⁶.

So far we do not have enough trial data to say which particular combination of EAAs is the 'best bet' for treating cachexia. We referred in a recent issue (#163, July 2003) to evidence that branched chain amino acids are also helpful in this situation ².

It is clear that we will need to take a much more sophisticated approach to supplementation in treating cachexia, perhaps tailored to the individual metabolic environment of each patient. We have a long way to go in this task, but identifying what kind of fat and protein is most often effective is a positive first step.

References: 1. MacDonald N. et al. Understanding and managing cancer cachexia. *J Am Coll Surg*. 2003 Jul;197(1):143-61.
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