

## Journal Watch

### **Reversal of cancer-related wasting using oral supplementation with combination of $\beta$ -hydroxy- $\beta$ -methylbutyrate, arginine, and glutamine**

Eubanks May P, Barber A, D'Olimpio JT, Hourihane A, Abumrad NN.. *The American Journal of Surgery* 2002; 183: 471-479

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#### **Abstract:**

Background: Cancer-related cachexia is caused by a diverse combination of accelerated protein breakdown and slowed protein synthesis. The hypothesis proposed in this study is that supplementation of specific nutrients known to positively support protein synthesis and reduce protein breakdown will reverse the cachexia process in advanced cancer patients.

Methods: Patients with solid tumors who had demonstrated a weight loss of at least 5% were considered for the study. Patients were randomly assigned in a double-blind fashion to either an isotrogenous control mixture of nonessential amino acids or an experimental treatment containing  $\beta$ -hydroxy- $\beta$ -methylbutyrate 93g/d, L-arginine (14 g/d), and L-glutamine (14 g/d [HMB/Arg/Gln]). The primary outcomes measured were the change in body mass and fat-free mass (FFM), which were assessed at 0, 4, 8, 12, 16, 20, and 24 weeks.

Results: Thirty-two patients (14 control, 18 HMB/Arg/Gln) were evaluated at the 4-week visit. The patients supplemented with HMB/Arg/Gln gained  $0.95 \pm 0.66$  kg of body mass in 4 weeks, whereas control subjects lost  $0.26 \pm 0.78$  kg during the same time period. This gain was the result of a significant increase in FFM in the HMB/Arg/Gln-supplemented group ( $1.12 \pm 0.68$  kg), whereas the subjects supplemented with the control lost  $1.34 \pm 0.78$  kg of FFM ( $P = 0.02$ ). The response to 24-weeks of supplementation was evaluated by an intent-to-treat statistical analysis. The effect of HMB/Arg/Gln on FFM increase was maintained over the 24 weeks ( $1.60 \pm 0.98$  kg; quadratic contrast over time,  $P < 0.05$ ). There was no negative effect of treatment on the incidence of adverse effects or quality of life measures.

Conclusions: The mixture of HMB/Arg/Gln was effective in increasing FFM of advanced (stage IV) cancer. The exact reasons for this improvement will require further investigation, but could be attributed to the observed effects of HMB on slowing rates of protein breakdown, with improvements in protein synthesis observed with arginine and glutamine.

#### **Comments:**

##### Strengths/uniqueness:

The study incorporates a randomized, double-blind control design. The process of randomization and reasons for patient withdrawal are discussed. An intent-to-treat analysis is completed for the 24-week response to supplementation. Solid assessments/equipment is used to evaluate body composition.

##### Weaknesses:

There is a high dropout rate of study participants as the weeks progressed. Patients who did not complete the 4-week follow-up were excluded from analysis.

Although multiple safety assessments are used, there is limited documentation of specific safety data. The subjective outcomes of quality of life assessments are broad and not specific enough.

for evaluation of anorexia-cachexia i.e. absence of inquiry of effect on appetite. Although statistically significant increases in body weight gain and fat-free mass are reported for the treatment group, the clinical significance of the modest weight change is uncertain.

Relevance to Palliative Care:

The reported beneficial effects of the three amino acids on cancer-related cachexia are intriguing but preliminary. The study is deserving of further evaluation that includes a larger sample size.