Readmission and Mortality in Malnourished, Older, Hospitalized Adults Treated with a Specialized Oral Nutritional Supplement: A Randomized Clinical Trial.

Deutz NE, et al. *Clin Nutr*. 2015. (http://dx.doi.org/10.1016/j.clnu.2015.12.010)

Objectives:

Evaluation of a high-protein (HP) oral nutritional supplement with beta-hydroxy-beta-methylbutyrate (HMB) on post-discharge outcomes of non-elective hospital readmission and mortality in malnourished, hospitalized older adults.

Methods:

- This study is referred to as NOURISH: **N**utrition effect **O**n **U**nplanned **R**eadmissions and **S**urvival in **H**ospitalized Patients.
- Multicenter, randomized, placebo-controlled, double-blind trial with inpatients and post-hospital discharge patients over 65 years with congestive heart failure (CHF), acute myocardial infarction (AMI), pneumonia (PNA), or chronic obstructive pulmonary disease (COPD), who were determined by the Subjective Global Assessment (SGA) to be malnourished (Class B: Moderate or Suspected Malnutrition and Class C: Severe Malnutrition).
- Inclusion criteria were patients over 65 with a recent hospital admission (within 72 hours) with a primary diagnosis of CHF, AMI, PNA, or COPD.
- Additional inclusion criteria included: anticipated length of hospital stay > 3 days and < 12 days, expected to consume ≥ 2-8 fl oz (237 mL) of study product while in hospital, able to consume foods and beverages orally, and functionally ambulatory during the 30 days prior to admission.
- Exclusion criteria were diabetes mellitus (Type 1 or 2), current active or treated cancer, and impaired renal or liver function.
- 313 patients were randomized to receive standard care and 2 servings/day (and 90-days post discharge) of the intervention formula (HP-HMB) which provided 350 calories, 20 g protein, 1.5 g HMB, 11 g fat, 44 g carbohydrate, 160 IU vitamin D, and other essential nutrients/serving (Ensure® Enlive®).
- 309 patients were randomized to receive standard care and 2 servings/day (and 90-days post discharge) of the placebo formula which provided 48 calories, 12 g carbohydrate, 10 mg vitamin C/serving.
- Prior to unbinding the data and finalizing the statistical analysis, the primary endpoint was modified to the composite incidence of non-elective readmission or death within 90-days post-discharge.

Results:

- There was no significant difference between groups for the primary composite endpoint of non-elective hospital readmission and death (HP-HMB 26.8% and placebo 31.1%) or for the 90-day hospital readmission rate alone (HP-HMB 25.2% and placebo 25.6%).
- 90-day mortality was significantly lower in the HP-HMB group as compared to placebo group (4.8% vs. 9.7%; $p = 0.018$) at each of the evaluated time points (30, 60, 90 days post-discharge).
- The SGA score improved to SGA-A (well nourished) in both groups with a higher likelihood that at 90 days, the HP-HMB group would achieve better nutritional status as compared to the placebo group ($p = 0.009$).
- 121 patients in the HP-HMB group (38.7%) and 126 in the placebo group (40.8%) exited the study prior to the 90-day visit resulting in 192 patients in the HP-HMB group and 183 in the placebo group.

Conclusions:

No effects were observed for the primary endpoint, compared with placebo. The intervention group, supplemented with a total of 700 calories and 40 g of protein/day had less mortality and improved indices of nutritional status during the 90-day observation period as compared to the placebo group supplemented with 96 calories and 0 g protein/day.

Summary prepared by Nestlé HealthCare Nutrition.

The complete study citation is: *Clin Nutr.* 2016 Feb;35(1):18-26. doi: 10.1016/j.clnu.2015.12.010. Epub 2016 Jan 18.

Key Facts to Consider

Intervention vs. Placebo Group:

- The intervention group received 700 calories and 40 g protein/day from the HP-HMB formula.
- The placebo group received 96 calories and 0 g protein/day from their formula.
- The formulas were not matched for calories and/or protein.
- The study did not track or measure total calories and protein consumed by each group.
- It is not surprising that those who received 700 extra calories and 40 extra g protein/day had better outcomes.

High Dropout Rate:

- The intervention group started with 313 patients and ended with 192 (38.7% drop-out rate).
- The placebo group started with 309 patients and ended with 183 (40.8% drop-out rate).

Primary Endpoint Changed:

- As per the study protocol, the primary endpoint was the composite incidence of non-elective hospital readmissions **and** death within 90-days post-discharge.
- When the data was analyzed for death alone within 90-days post hospital discharge, statistical differences were demonstrated between the groups. It is not customary to change study objectives once a study has been initiated.
- The study provides the intent to treat (ITT) data (all patients who began the study, including those who dropped out) as opposed to the per protocol (PP) data (patients who actually completed the study). It is customary to analyze and present both data sets.

Variables Not Measured:

- The study did not track or measure the amount of protein and/or calories provided each day from food, which would also influence outcomes.
- Self-reported adherence to the protocol of 2 servings per day was tracked for only 30-days post discharge, not for the full 90-day post discharge period.

Effect of Specific Nutrients:

- The study was not designed to determine the effect of specific nutrients.
- The effect of HMB on mortality or hospital readmission cannot be determined from this study.
- This study further supports the well-documented evidence that an oral nutritional supplement consumed for 30 or more days after hospital discharge will help improve outcomes in vulnerable patient populations, such as the elderly, who are malnourished or at risk for malnutrition when admitted to the hospital or during their hospitalization.

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Summary prepared by Nestlé Healthcare Nutrition