6.5 Enteral Nutrition: Other Formulas: ß Hydroxyl Methyl Butyrate (HMB)

There were no new randomized controlled trials since the 2015 update and hence there are no changes to the following summary of evidence.

Question: Does the use of a formula supplemented with ß hydroxyl methyl butyrate (HMB) result in better outcomes in the critically ill adult patient?

Summary of evidence: There was 1 level 2 study that studied the effect of supplementation of enteral formulas with ß hydroxyl methyl butyrate (HMB), alone to a isonitrogenous isocaloric placebo in trauma patients. The data pertaining to the second intervention from this study comparing enteral nutrition supplemented with ß hydroxyl methyl butyrate, arginine and glutamine (Juven®) to standard enteral nutrition alone is described in section 4.1: Diets supplemented with Arginine and select other nutrients.

Mortality: When the HMB group was compared to the control group, formula supplemented with HMB had no effect on mortality (RR 0.16, 95% CI 0.01, 3.14, p=0.23).

Infections: When the HMB group was compared to the control group, formula supplemented with HMB had no effect on the number of infectious complications per patient (WMD 0.20, 95% CI -1.33, 1.73, p=0.80).

ICU LOS: When the HMB group was compared to the control group, there was a trend towards an *increase* in ICU LOS for the group that received formula supplemented with HMB (WMD 6.50, 95% CI -3.22, 16.22, p=0.19).

Hospital LOS: When the HMB group was compared to the control group, formula supplemented with HMB was associated with a *significant increase* in hospital LOS (WMD 14.10, 95% CI 1.19, 27.01, p=0.03).

Ventilator days: When the HMB group was compared to the control group, formula supplemented with HMB had no effect on the number of ventilator days (WMD 3.30, 95% CI -3.78, 10.38, p=0.36).

Other: There was no effect of the supplementation on nitrogen intake. Nitrogen balance was significantly better in the HMB group (p=0.05).

Conclusions:

1) Supplementation with ß hydroxyl methyl butyrate (HMB) has no effect on mortality or duration of mechanical ventilation.

2) Supplementation with ß hydroxyl methyl butyrate (HMB) may be associated with an increase in ICU length of stay.
3) Supplementation with ß hydroxyl methyl butyrate (HMB) is associated with a significant increase in hospital length of stay.
4) Supplementation with ß hydroxyl methyl butyrate (HMB) is associated with better nitrogen balance in trauma patients.

Level 1 study: If all of the following are fulfilled: concealed randomization, blinded outcome adjudication and an intention to treat analysis.
Level 2 study: If any one of the above characteristics are unfulfilled.

Table 1. Randomized studies evaluating other enteral formulas in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
1) Kuhls 2007*	Trauma patients in ICU Injusry Severity Score >18 N=100	C.Random: No/not sure ITT: No** Blinding: Double (10)	Standard EN + supplement of 3 gms ß hydroxyl methyl butyrate (HMB) vs. Standard EN + isonitrogenous placebo supplement Isonitrogenous/isocaloric 25kcal/kg/day, 1.5g pro/kg/day	HMB 0/28 (0)	Placebo 2/22 (9) RR 0.16, 95% CI 0.01, 3.14, p=0.23	HMB (# per patient) 4.8 ± 2.65 (28)	Placebo (# per patient) 4.6 ± 2.81 (22) WMD 0.20, 95% CI -1.33, 1.73, p=0.80

Table 1. Randomized studies evaluating other enteral formulas in critically ill patients (continued)

Study	LOS days		Ventilator days		Other
1)) Kuhls 2007*	HMB ICU 28.9 ± 17.46 (28) Hospital 44.4 ± 23.28 (28)	Placebo ICU 22.4 ± 17.35 (22) Hospital 30.3 ± 22.98 (22)	HMB 24.2 ± 12.70 (28)	Placebo 20.9 ± 12.66 (22)	# Patients with SIRS Score >3 or >4 Significantly less in HMB group on day 3 (p<0.01) and day 7 (p<0.02) Average Nitrogen Balance HMB -6.50 ± 6.35 Placebo -9.0 ± 6.10 Change in Nitrogen Balance Comparing Week 1 to Week 2 Greater in HMB vs placebo (p<0.05)
	ICU WMD 6.50, 95% CI -3.22, 16.22, p=0.19 Hospital WMD 14.10, 95% CI 1.19, 27.01, p=0.03		WMD 3.30, 95% CI -3.78, 10.38, p=0.36		

* all "standard error" reported in the Kuhls 2007 study have been converted to "standard deviation"
** 100 pts randomized but only 72 reported on as 72 received at least 7 days of supplementation. Additional statistical exclusion criteria were established based on 50% treatment compliance.therefore 72 pts were used.
† presumed hospital mortality unless otherwise specified
‡ refers to the # of patients with infections unless specified

ICU: Intensive care unit
C. Random: concealed randomization
ITT: intent to treat
EN: enteral nutrition
SIRS: systemic inflammatory response syndrome
WMD: weighted mean difference; CI: Confidence interval

Data pertaining to enteral nutrition supplemented with ß hydroxyl methyl butyrate, arginine and glutamine (Juven®) to standard enteral nutrition alone not shown here. Refer to section 4.1: Diets supplemented with Arginine and select other nutrients