6.5 Enteral Nutrition: Other Formulas: ß Hydroxyl Methyl Butyrate (HMB) May 2015

There were no new randomized controlled trials since the 2013 update and hence there are no changes to the following summary of evidence.

Recommendation: *There are insufficient data to make a recommendation of ß Hydroxyl Methyl Butyrate (HMB) supplementation in critically ill patients.*

Discussion: The committee noted, based on a single level 2 study (Kuhls 2007), that enteral nutrition supplemented with ß Hydroxyl Methyl Butyrate (HMB) had no effect on clinical outcomes but was associated with positive effect on nitrogen balance in critically ill patients when compared to enteral nutrition alone. Given the lack of a treatment effect, the committee decided that further trials in critically ill patients were needed to make a clinical recommendation.

Semi Quantitative Scoring

Values	Definition	2013 Score (0,1,2,3)
Effect size	Magnitude of the absolute risk reduction attributable to the intervention listed--a higher score indicates a larger effect size	0
Confidence interval	95% confidence interval around the point estimate of the absolute risk reduction, or the pooled estimate (if more than one trial)--a higher score indicates a smaller confidence interval	1
Validity	Refers to internal validity of the study (or studies) as measured by the presence of concealed randomization, blinded outcome adjudication, an intention to treat analysis, and an explicit definition of outcomes--a higher score indicates presence of more of these features in the trials appraised	3
Homogeneity or Reproducibility	Similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials	n/a
Adequacy of control group	Extent to which the control group presented standard of care (large dissimilarities=1, minor dissimilarities=2, usual care=3)	3
Biological Plausibility	Consistent with understanding of mechanistic and previous clinical work (large inconsistencies=1, minimal consistencies=2, very consistent=3)	2
Generalizability	Likelihood of trial findings being replicated in other settings (low likelihood i.e. single centre=1, moderate likelihood i.e. multicentre with limited patient population or practice setting=2, high likelihood i.e. multicentre, heterogenous patients, diverse practice settings=3)	1
Low cost	Estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	2
Feasible	Ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	2
Safety	Estimated probability of avoiding any significant harm that may be associated with the intervention listed--a higher score indicates a lower probability of harm	2

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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) might be associated with a trend towards an increase in ICU length of stay but has no effect on ICU length of stay.

3) Supplementation with ß hydroxyl methyl butyrate (HMB might be associated with a significant increase in hospital length of stay and might be associated with a trend towards an increase in hospital length of stay.
4) Supplementation with ß hydroxyl methyl butyrate (HMB) may result in 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) 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	HMB 24.2 ± 12.70 (28)	Placebo 20.9 ± 12.66 (22) WMD 3.30, 95% CI -3.78, 10.38, p=0.36	# 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)

* 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

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