4.3 Composition of Enteral Nutrition: Protein/Peptides

January 31st, 2009

Recommendation:
Based on 4 level 2 studies, when initiating enteral feeds, we recommend the use of whole protein formulas (polymeric).

Discussion: The committee noted that despite no safety concerns and the ease of implementation of peptide based enteral formulas, there were no studies demonstrating any favourable treatment effects with their use. The higher cost of peptide based formulas compared to standard was noted. The committee also noted that peptide based formulas may be considered for their other components i.e. fat content, MCT, glutamine composition, etc and that patients with gastrointestinal complications (short bowel syndrome, pancreatitis, etc.) may benefit from peptide based formulas but there are insufficient data to put forward a recommendation.

Values	Definition	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	2
Homogeneity or Reproducibility	Similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials	1
Adequacy of control group	Extent to which the control group represented 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 inconsistencies =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, heterogeneous patients, diverse practice settings =3.	1
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	3
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	3

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Question: Does the use of peptide based enteral formula, compared to an intact protein formula, result in better outcomes in the critically ill adult patient?

Summary of evidence: There were 4 level 2 studies that compared a peptide based enteral formula to one with intact proteins.

Mortality: Only two studies reported mortality and found no difference (Meredith, Brinson) (RR = 0.42, 95 % confidence intervals 0.06, 2.88, p=0.4) (figure 1).

Infections: Based on the two studies that reported on infections, there were no difference between the groups (Heimburger, Mowatt-Larsen) (RR 0.85, 95 % confidence intervals 0.64, 1.13, p = 0.3) (figure 2).

LOS: One study found a trend towards fewer hospital days (p =0.17) in the peptide based group (Meredith) (figure 3).

Ventilator days: Not reported.

Other complications: A trend towards an increase in diarrhea with the use of peptides was seen in one study (Heimburger p =0.07), whereas another study showed a decrease in the incidence of diarrhea in the peptide group (Meredith). A third study found no differences in diarrhea between the two groups in another study (Mowatt-Larsen). In one study of hypoalbuminemic patients (Brinson et al), 3/5 patients in the control group (standard) crossed over to the experimental group (peptide based) because of diarrhea. Meta analysis showed no difference in diarrhea between the peptide based and standard groups (RR 0.76, 95 % confidence interval 0.25, 2.33, p= 0.6). There were no differences in calorie or protein intake between the groups.

Conclusions:

1) No difference in mortality or infections between patients receiving a peptide based vs. a standard formula.
2) No difference in diarrhea between the groups receiving peptides vs. standard formula.
3) Peptide based formulas vs. standard may be associated with a trend towards fewer hospital days.

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 enteral PROTEIN/PEPTIDES in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)	
1. Brinson 1988	Mixed ICU's patients with MOF, hypoalbuminemia, malnutrition from 2 ICUs N= 12	C.Random: no ITT: yes Blinding: nsingle (5)	Peptide based formula (vital HN) vs whole protein formula (Osmolite HN)	0/7	2/5 (40)	NR	NR
2. Meredith 1990	ICU patients, Trauma, N = 18	C.Random: yes ITT: yes Blinding: no (8)	Peptide based formula vs whole protein formula	1/9 (11)	1/9 (11)	NR	NR
3. Mowatt-Larsen 1992	Critically ill, acutely injured patients, albumin < 30 n = 41	C.Random: not sure ITT: no Blinding: no (6)	Peptide based formula vs whole protein formula	NR	NR	12/21 (60)	14/20 (70)
4. Heimburger 1997	ICU patients from 2 ICUs N = 50	C.Random: not sure ITT: no Blinding: no (7)	Small peptide formula vs whole protein formula	Peptide NR	Whole protein NR	Peptide 17/26 (65)	Whole protein 18/24 (75)

Table 2. Randomized studies evaluating enteral PROTEIN/PEPTIDES in critically ill patients

Study	LOS days		Ventilator days		Cost		Other	RR (CI) **
1. Brinson 1988	NR	NR	NR	NR	NR	NR	Diarrhea 1/7 (14) 3/5 (60) Energy intake (kcal/kg/day) 649 ± 4 737 ± 50 Nitrogen balance (gm/kg/day) -11.2 ± 2.3 - 9.6 ± 2.5	0.24 (0.03-1.67)
2. Meredith 1990	32.4 ± 5.9	47.6 ± 8.7	NR	NR	NR	NR	Diarrhea 0/9 (0) 4/9 (44) Energy intake (kcal/kg/day) 26.2 ± 3.7 27.8 ± 3.0 Protein intake (gms/kg/day) 1.14 ± 0.17 1.15 ± 0.12	0.11 (0.01-1.80)
3. Mowatt-Larsen 1992	NR	NR	NR	NR	NR	NR	Diarrhea 6/21 (29) 6/20 (30) Elevated gastric residuals 8/21 (38) 7/20 (35) Energy intake (kcal/kg/day) 34.2 ± 11.3 32.4 ± 6.8 Protein intake (gm/kg/day) 1.5 ± 0.5 1.7 ± 0.3	0.95 (0.37-2.47) NR
4. Heimburger 1997	Peptide NR	Whole protein NR	Peptide NR	Whole protein NR	Peptide NR	Whole protein NR	Peptide Whole protein Diarrhea 10/26 (39) 4/24 (17)	2.31 (0.83-6.39)

C.Random: concealed randomization
ITT: intent to treat
NR : Not reported
MOF: multiorgan failure

± : mean ± standard deviation
† presumed ICU mortality unless otherwise specified
** RR= relative risk, CI= Confidence intervals

Figure 1.

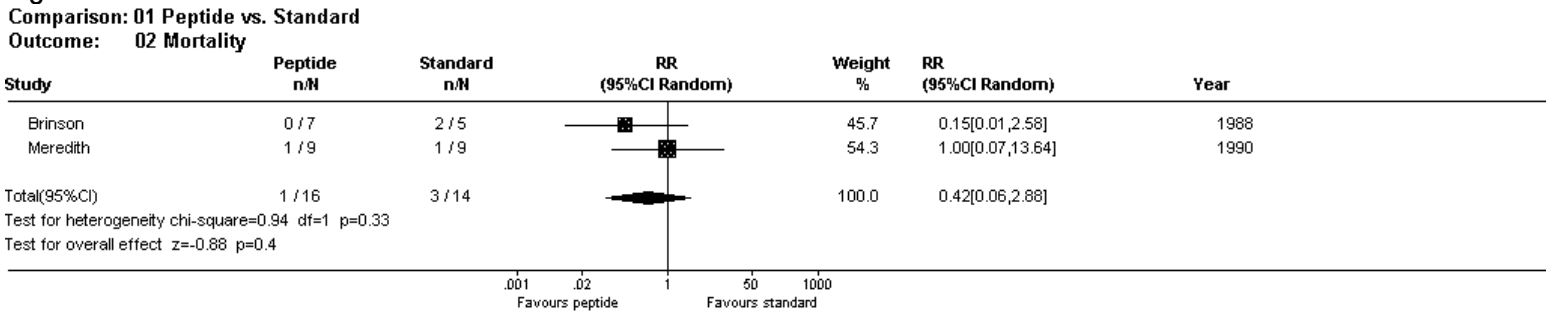


Figure 2.

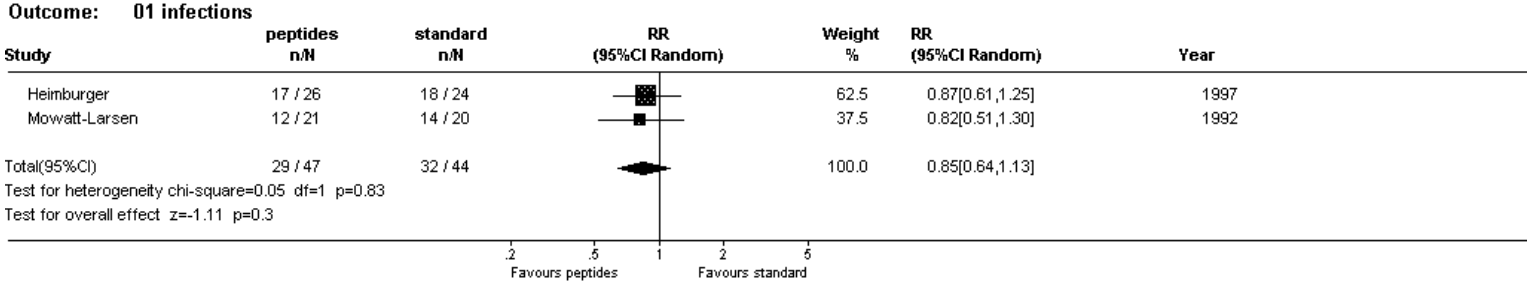
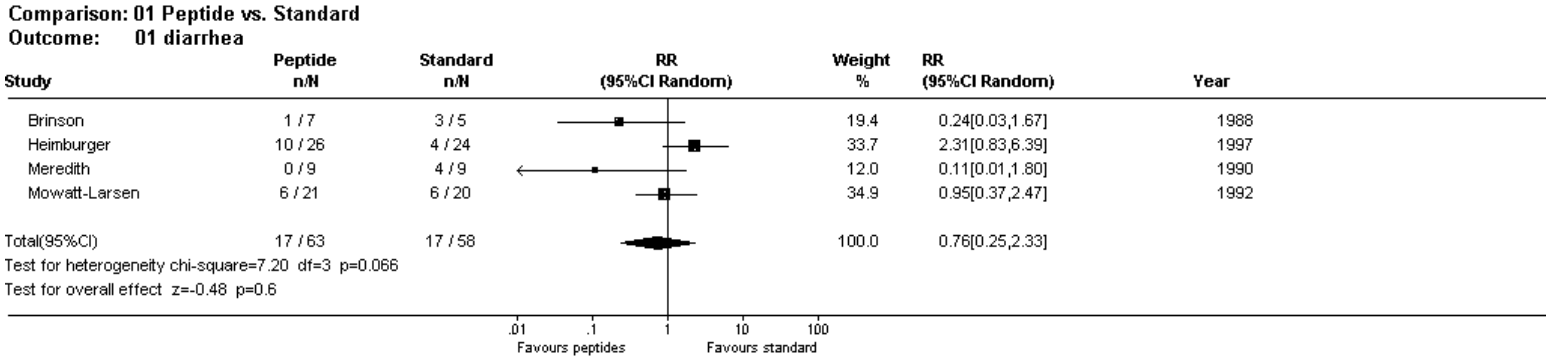


Figure 3.



TOPIC: 4.3 Composition of EN: Protein/peptides

Article inclusion log

Criteria for study selection

Type of study: RCT or Meta-analysis
Population: critically ill, ventilated patients (no elective surgery patients)
Intervention: EN
Outcomes: mortality, LOS, QOL, functional recovery, complications, cost. Exclude studies with only biochemical, metabolic or nutritional outcomes.

	Author	Journal	I	E	Why Rejected
1	Wolfe	Ann Surg 1982		√	Crossover study
2	Cerra	Surgery 1985		√	Elective surgery patients
3	Brinson	Crit Care Med 1988	√		
4	Meredith	J Trauma 1990	√		
5	Borlase	Surg Gynecol Obstet 1992		√	Elective surgery patients
6	Mowatt-Larsen	JPEN 1992	√		
7	Heimburger	JPEN 1997	√		
8	Dietscher	JADA 1998		√	No clinical outcomes
9	Tiengou	JPEN 2006		√	Not ICU pts

I = included, E = excluded

Reference List

1. Cerra FB, Shronts EP, Konstantinides NN et al. Enteral feeding in sepsis: a prospective, randomized, double-blind trial. Surgery 1985;98(4):632-9.

2. Brinson RR, Kolts BE. Diarrhea associated with severe hypoalbuminemia: a comparison of a peptide-based chemically defined diet and standard enteral alimentation. Crit Care Med. 1988 Feb;16(2):130-6.

3. Meredith JW, Ditesheim JA, Zaloga GP. Visceral protein levels in trauma patients are greater with peptide diet than with intact protein diet. J Trauma. 1990 Jul;30(7):825-8; discussion 828-9.

4. Borlase BC, Bell SJ, Lewis EJ et al. Tolerance to enteral tube feeding diets in hypoalbuminemic critically ill, geriatric patients. Surg Gynecol Obstet1992;174:181-188.

5. Mowatt-Larssen CA, Brown RO, Wojtysiak SL, Kudsk KA. Comparison of tolerance and nutritional outcome between a peptide and a standard enteral formula in critically ill, hypoalbuminemic patients. JPEN J Parenter Enteral Nutr. 1992 ;16(1):20-4.

6. Heimburger DC, Geels VJ, Bilbrey J, Redden DT, Keeney C. Effects of small-peptide and whole-protein enteral feedings on serum proteins and diarrhea in critically ill patients: a randomized trial. JPEN 1997;21(3):162-7.

7. Dietscher JE, Foulks CJ, Smith RW. Nutritional response of patients in an intensive care unit to an elemental formula vs a standard enteral formula. JADA 1998;98(3):335-336.

8. Tiengou LE, Gloro R, Pouzoulet J, Bouhier K, Read MH, Arnaud-Battandier F, Plaze JM, Blaizot X, Dao T, Piquet MA. Semi-elemental formula or polymeric formula: is there a better choice for enteral nutrition in acute pancreatitis? Randomized comparative study. JPEN J Parenter Enteral Nutr. 2006 Jan-Feb;30(1):1-5.