

4.3 Composition of Enteral Nutrition: Protein/peptides

June 28th, 2005

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, +, ++, +++ |
|---------------------|---|----------------------|
| 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 | similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials | 1+ |
| Safe | 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+ |
| Feasible | ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU | 3+ |
| Cost | estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU | 2+ |

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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) (see page 4.3-5)

Infections: Based on the two studies that reported on infections, there were no difference between the groups (Heimbürger, Mowatt-Larsen) (RR 0.85, 95 % confidence intervals 0.64, 1.13, p = 0.3) (See page 4.3-5).

LOS: One study found a trend towards fewer hospital days (p =0.17) in the peptide based group (Meredith) (See page 4.3-6)

Ventilator days: Not reported.

Other complications: A trend towards an increase in diarrhea with the use of peptides was seen in one study (Heimbürger 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

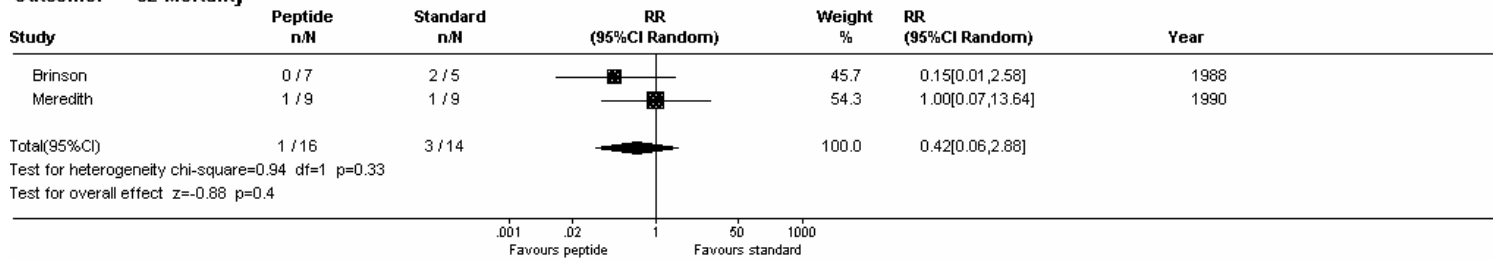
| Study | Population | Methods (score) | Intervention | Mortality # (%)† | | Infections # (%) | |
|-------------------------------------|--|--|---|------------------|---------------------|-----------------------|-----------------------------|
| | | | | peptide | Whole protein | peptide | Whole protein |
| 1) ID # 33 Heimburger 1997 | ICU patients N = 50 | C.Random: not sure ITT: no Blinding: no (7) | Small peptide formula vs whole protein formula | peptide NA | Whole protein NA | peptide 17/26 (65) | Whole protein 18/24 (75) |
| 2) ID # 34 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 | NA | NA | 12/21 (60) | 14/20 (70) |
| 3) ID # 74 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) | NA | NA |
| 4) ID # 94 Brinson 1988 | Mixed ICU's patients with MOF, hypoalbuminemia, malnutrition 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) | NA | NA |

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

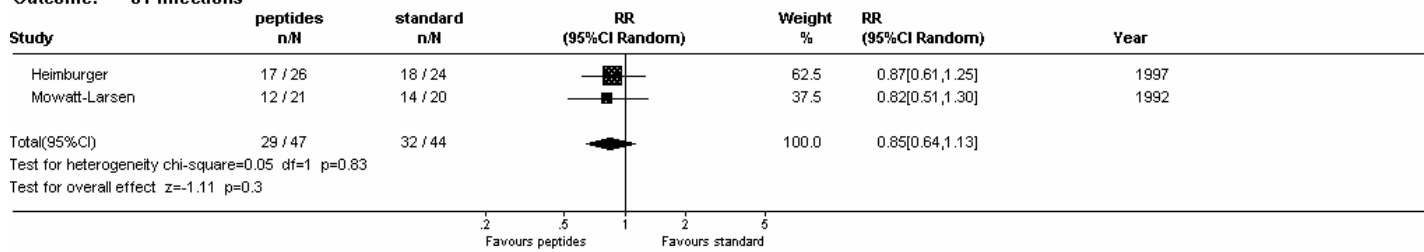
| Study | LOS days | | Ventilator days | | Cost | | Other | | RR (CI) ** |
|----------------------------------|------------|---------------|-----------------|---------------|---------|---------------|---|-----------------------|------------------|
| | peptide | Whole protein | peptide | Whole protein | peptide | Whole protein | Peptide | Whole protein | |
| ID # 33 Heimburger 1997 | NA | NA | NA | NA | NA | NA | Diarrhea 10/26 (39) | Diarrhea 4/24 (17) | 2.31 (0.83-6.39) |
| ID # 34 Mowatt-Larsen 1992 | NA | NA | NA | NA | NA | NA | Diarrhea 6/21 (29) | Diarrhea 6/20 (30) | 0.95 (0.37-2.47) |
| | | | | | | | elevated gastric residuals 8/21 (38) | 7/20 (35) | NA |
| | | | | | | | 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 | |
| ID # 74 Meredith 1990 | 32.4 ± 5.9 | 47.6 ± 8.7 | NA | NA | NA | NA | Diarrhea 0/9 (0) | Diarrhea 4/9 (44) | 0.11 (0.01-1.80) |
| | | | | | | | 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 | |
| ID # 94 Brinson 1988 | NA | NA | NA | NA | NA | NA | Diarrhea 1/7 (14) | Diarrhea 3/5 (60) | 0.24 (0.03-1.67) |
| | | | | | | | energy intake (kcal/kg/day) 649 ± 4 | 737 ± 50 | |
| | | | | | | | Nitrogen balance (gm/kg/day) -11.2 ± 2.3 | -9.6 ± 2.5 | |

C.Random: concealed randomization
 ITT: intent to treat
 NA: not available
 ± : mean ± standard deviation
 † presumed ICU mortality unless otherwise specified
 ** RR= relative risk, CI= Confidence intervals
 MOF: multiorgan failure

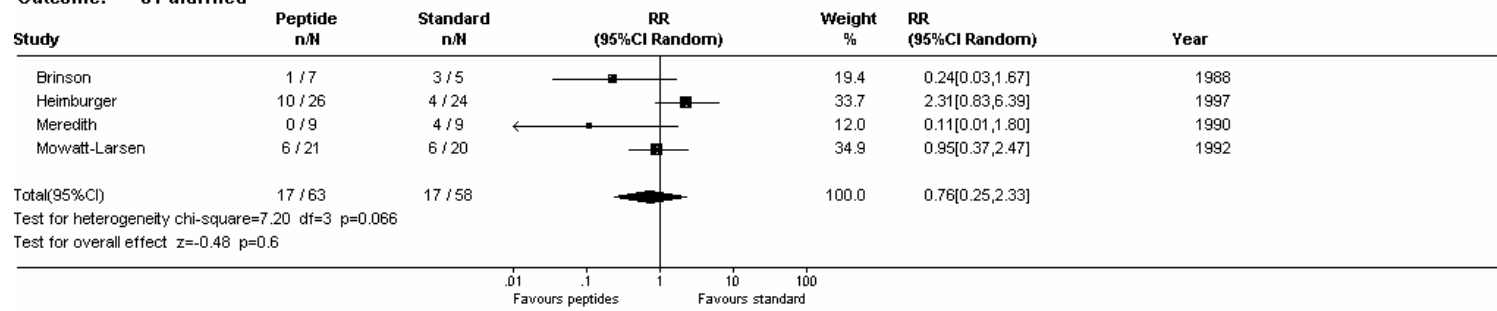
Comparison: 01 Peptide vs. Standard
Outcome: 02 Mortality



Comparison: 01 peptides vs standard
Outcome: 01 infections



Comparison: 01 Peptide vs. Standard
Outcome: 01 diarrhea



TOPIC: 4.3 Composition of EN: Protein/peptides

(Reviewers: Voula Christofilos & Rupinder Dhaliwal)

Article inclusion log

Criteria for study selection

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

| ID # | Author | Journal | I | E | why rejected |
|------|--|-----------------------------|---|---|-------------------------------------|
| 33. | 1. Heimburger (standard vs elemental) | JPEN 1997 | √ | | |
| 34. | 2. Mowatt-Larsen (standard vs elemental) | JPEN 1992 | √ | | |
| 35. | 3. <i>Dietscher</i> (standard vs elemental) | JADA 1998 | | √ | Excluded as no significant outcomes |
| | 4. Van den Berg | Clin Nut 1998 | | √ | No RCT |
| | 5. Borlase | Surgery, Gyne, Obst 1992 | | √ | Surgery patients |
| 74. | 6. Meredith (standard vs elemental) | J Trauma 1990 | √ | | |
| 94 | 7. Brinson | CCMed 1988 | √ | | |
| | 8. Cerra (BCAA vs std) | Surgery 1985 | | √ | Elective surgery patients |
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I = included, E = excluded

