

7.0 Combination Parenteral Nutrition and Enteral Nutrition

June 28th, 2005

Recommendation:

Based on 5 level 2 studies, for critically ill patients starting on enteral nutrition we recommend that parenteral nutrition not be started at the same time as enteral nutrition. In the patient who is not tolerating adequate enteral nutrition, there are insufficient data to put forward a recommendation about when parenteral nutrition should be initiated. Practitioners will have to weigh the safety and benefits of initiating PN in patients not tolerating EN on an individual case-by-case basis. We recommend that PN not be started in critically ill patients until all strategies to maximize EN delivery (such as small bowel feeding tubes, motility agents) have been attempted.

Discussion: The committee noted that these data pertain to patients with an intact GI tract, not to those who have an absolute indication for parenteral nutrition. The committee reviewed the results of 5 level 2 studies that initiated PN at the same time as starting EN. When aggregated statistically these studies suggested no benefit. The committee noted that the study results were homogenous and that when the trials in which the combination EN + PN group received more calories than the EN group were compared to those trials that did not, there was no difference in mortality. Given the probability of harm from trials of PN vs. EN in critically ill patients (see section 1.0 En vs. PN) and excess costs associated with the addition of PN when initiating EN, a recommendation against its use was put forward. However, the committee noted the absence of data from randomized trials related to patients not tolerating adequate amounts of EN and when PN should be used in combination in this scenario.

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	2+
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	2+
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	3+
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	1+
Feasible	ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	2+
Cost	estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	1+

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Question: Does the use of parenteral nutrition in combination with enteral nutrition result in better outcomes in the critically ill adult patient?

Summary of evidence:

There were 5 level 2 studies that were reviewed and meta-analysed.

Mortality: All 5 studies reported on mortality. The meta-analysis shows that there was no effect on mortality with the use of combination EN + PN (RR 1.27, 95 % confidence interval 0.82-1.94, $p = 0.3$). When a sub group analysis was done comparing the trials that overfed to those that did not there was no difference in effect (see page 7-6).

Infections, LOS & ventilator days: 2 studies looked at infections, length of stay and ventilator days i.e. Chiarelli et al and Bauer et al. combination EN + PN was not associated with a higher incidence of infections (RR 1.14, 95 % confidence interval 0.66- 1.96, $p = 0.6$), no effect on hospital stay (standardized mean difference – 0.12, 95 % confidence interval – 0.45, 0.2, $p = 0.5$) and no effect on ventilator days based on these two studies (standardized mean difference 0.10, 95% confidence interval –0.23, 0.42, $p = 0.6$). See figure.

Other:

Cost: higher with combined group (Chiarelli/Bauer). Blood sugars were significantly higher in the EN + PN group when compared to the EN group but only on Day 7 in one study (Bauer et al) ($p < 0.05$). Chiarelli et al reported no difference in glycemia between the groups although no numbers were reported. None of the other studies reported on blood sugars.

Conclusions:

- 1) PN in combination with enteral nutrition in critically ill patients provides no added benefit compared to EN alone.
- 2) PN in combination with enteral nutrition is associated with a higher cost compared to EN alone.

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 combined EN + PN in critically ill patients

Study	Population	Methods (score)	Intervention (both interventions started at same time)	Mortality # (%)†		Infections # (%)‡	
				EN + PN	EN	EN + PN	EN
1) ID # 83 Herndon 1987	Burns > 50 % TBSA N = 28	C.Random: not sure ITT: yes Blinding: no (6)	EN + PN vs EN EN + PN group received significantly more calories than EN group	8/13 (62)	8/15 (53)	NA	NA
2) ID # 62 Herndon 1989	Burn patients N = 39	C.Randomization: not sure ITT: yes Blinding: no (7)	EN+ PN vs EN EN + PN group received significantly more calories than EN group	10/16 (63) > Day 14	6/23 (26) > Day 14	NA	NA
3) ID # 59 Dunham 1994*	Blunt trauma N = 37	C.Random: not sure ITT: no Blinding: no (8)	EN+ PN vs EN EN + PN group given same calories as EN	3/10 (30)	1/12 (8.3)	NA	NA
4) ID # 60 Chiarelli 1996	ICU patients medical and surgical N = 24	C.Random: not sure ITT: yes Blinding: no (8)	EN+ PN vs EN EN + PN were given 33 kcal/kg/day, EN were given 31 kcal/kg/day	3/12 (25)	4/12 (33)	6/12 (50)	3/12 (25)
5) ID # 61 Bauer 2000	ICU patients N =120 (all degrees of malnutrition)	C.Random: not sure ITT: yes Blinding: double (12)	EN+ PN vs EN + placebo. EN + PN received 24.6 ± 4.9 kcal/kg/day vs. EN group 14.2 ± 6.5 kcal/kg/day (p< 0.0001)	3/60 (5) before day 4 17/60 (28) Day 90	4/60 (6.7) before day 4 18/60 (30) Day 90	39/60 (65)	39/60 (65)

Table 2. Randomized studies evaluating combination parenteral nutrition and enteral nutrition in critically ill patients

Study	LOS days		Ventilator days		Cost		Other	
	EN + PN	EN	EN + PN	EN	EN + PN	EN	EN + PN	EN
1) ID # 83 Herndon 1987	NA	NA	NA	NA	NA	NA	NA	
2) ID # 62 Herndon 1989	NA	NA	NA	NA	NA	NA	NA	
3) ID # 59 Dunham 1994	NA	NA	NA	NA	NA	NA	Nutrition related complications 5/10 (50) 3/12 (25)	
4) ID # 60 Chiarelli 1996	37 ± 13 (12) hospital	41 ± 23 (12) hospital	19 ± 6 (12)	19 ± 2 (12)	50,000 lira/year more than EN	...	NA	NA
5) ID # 61 Bauer 2000	31.2 ± 18.5 (60) hospital 16.9 ± 11.8 (60) ICU	33.7 ± 27.7 (60) hospital 17.3 ± 12.8 (60) ICU	11 ± 9	10 ± 8	204 ± 119 Euro/pt/week	106 ± 47 Euro/pt/week	Glycemia on Day 7 (g/L) 1.16 ± 0.36 1.31 ± 0.49	

C.Random: concealed randomization

* Dunham: only looked at data pertaining to EN+PN vs EN (not EN +PN vs PN)

± () : mean ± Standard deviation (number)

ITT: intent to treat; NA: not available

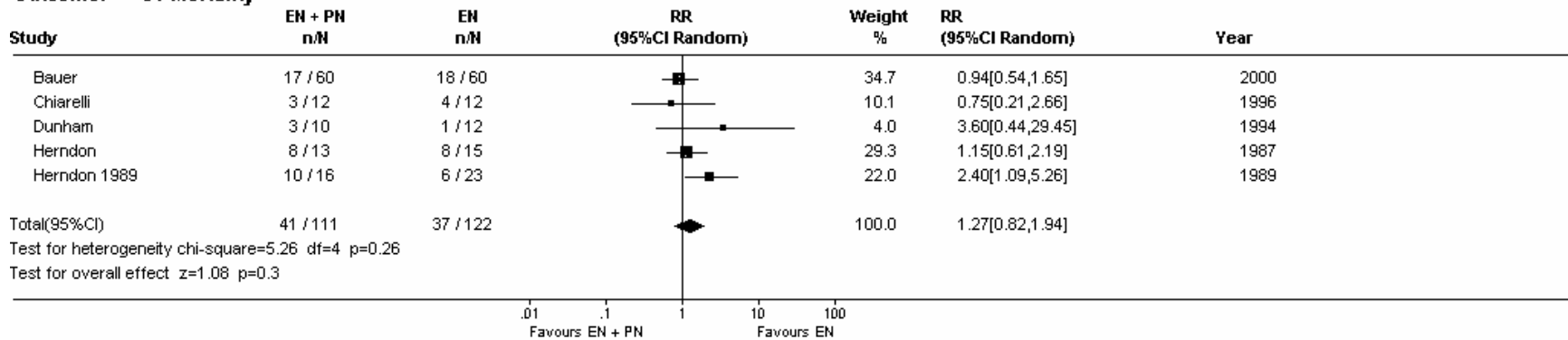
† presumed hospital mortality unless otherwise specified

‡ refers to the # of patients with infections unless specified

Overall Mortality

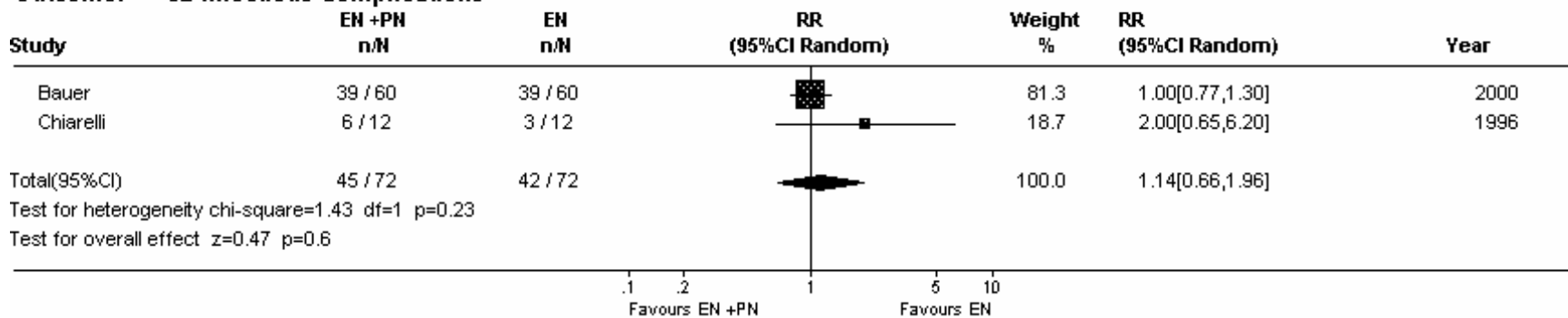
Comparison: 01 Combination EN +PN

Outcome: 01 Mortality



Comparison: 01 Combination EN +PN

Outcome: 02 Infectious Complications

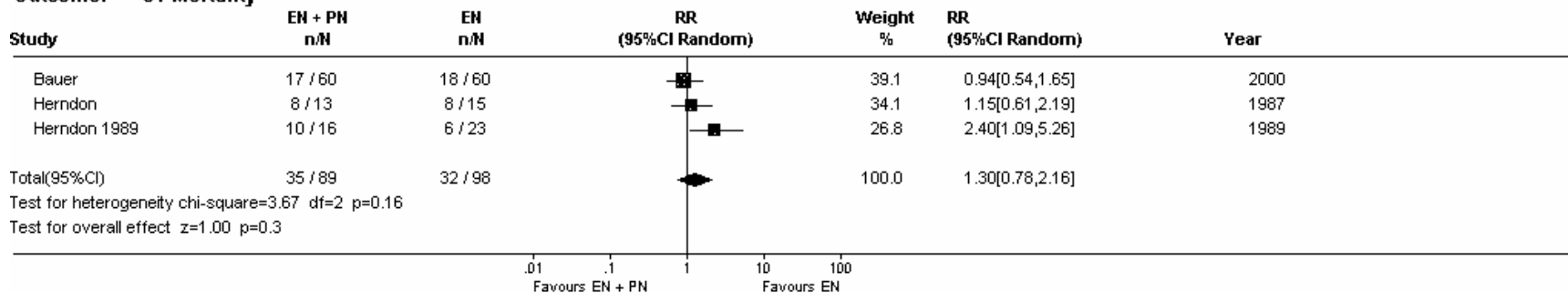


Sub group analysis:

Mortality in non-isocaloric trials (where the comb EN + PN group received significantly more calories than the EN group)

Comparison: 01 Combination EN +PN

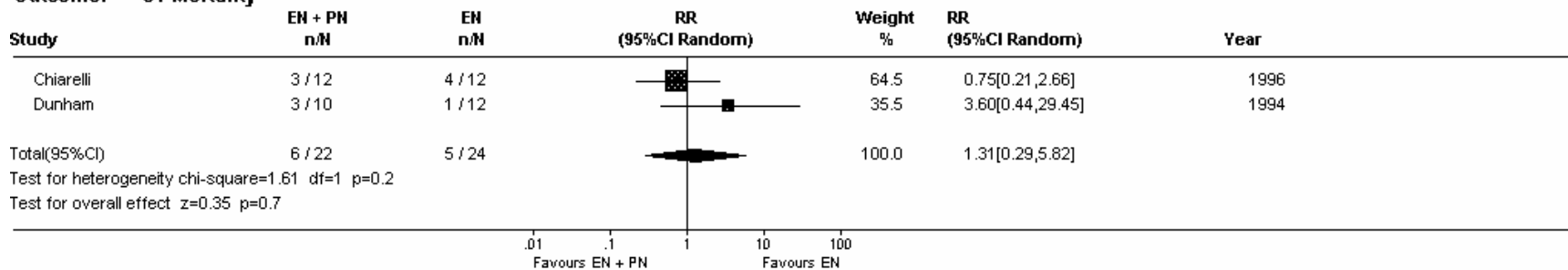
Outcome: 01 Mortality



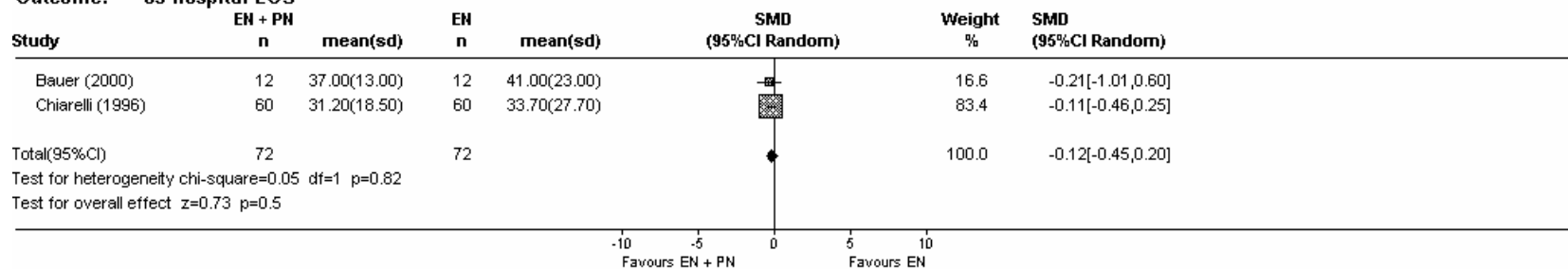
Mortality in the isocaloric trials (where the comb EN + PN received similar calories to the EN group)

Comparison: 01 Combination EN +PN

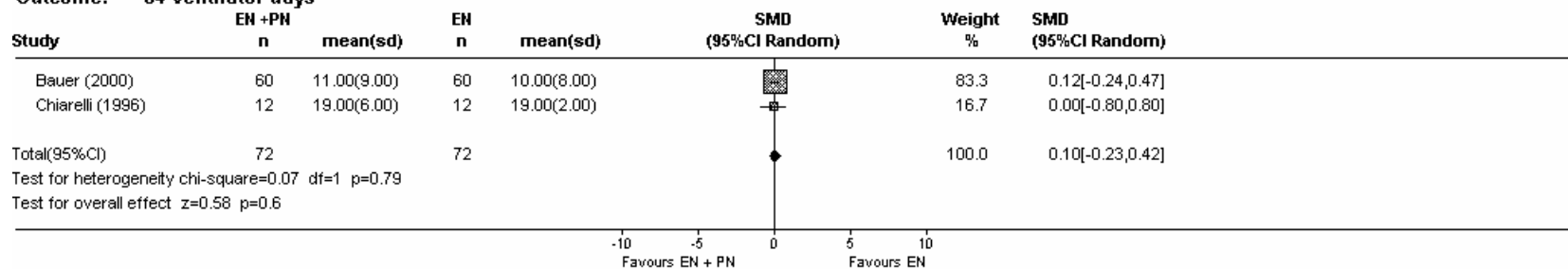
Outcome: 01 Mortality



Comparison: 01 Supplemental PN (EN + PN) vs EN
Outcome: 03 hospital LOS



Comparison: 01 Supplemental PN (EN + PN) vs EN
Outcome: 04 ventilator days



TOPIC: 7.0 Combination EN + PN

(Reviewers: Brian Jurewitsch & Darlene Harrietha)

Article inclusion log

Criteria for study selection

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	
59.	1.	Dunham	J Trauma 1994	√		
60.	2.	Chiarelli	Minerva Anaesth '96	√		
61.	3.	Bauer	Int Care Med 2000	√		
62.	4.	Herndon	J Burn Care Rehab 1989	√		
83.	5.	Herndon	J Trauma 1987	√		
	6.	Deegan	Clin Int Care 1999		√	Not RCT
	7.	Hausmann	Int. Care Med 1985		√	Excluded as compares EN + PN to PN, not to EN
	8.	Marik	Crit Care Med 2001		√	Not RCT
	9.	Marik	Crit Care Shcok 2001		√	Not RCT

I = included, E = excluded

References

1. Hausmann D, Mosebach KO, Caspari R, Rommelsheim K (1985) Combined enteral-parenteral nutrition versus total parenteral nutrition in brain-injured patients. A comparative study. *Intensive Care Med* 11:80-84
2. Herndon DN, Stein MD, Rutan TC, Abston S, Linares H (1987) Failure of TPN Supplementation to improve liver function, immunity, and mortality in thermally injured patients. *J Trauma* 27:195-204
3. Herndon DN, Barrow RE, Stein M, Linares H, Rutan TC, Rutan R, Abston S (1989) Increased mortality with intravenous supplemental feeding in severely burned patients. *J Burn Care Rehabil* 10:309-13
4. Dunham CM, Frankenfield D, Belzberg H, Wiles C, Cushing B, Grant Z (1994) Gut failure- predictor of or contributor to mortality in mechanically ventilated blunt trauma patients? *J Trauma* 37:30-4
5. Chiarelli AG, Ferrarello S, Piccioli A, Abate A, Chini G, Berioli MB, Peris A, Lippi R (1996) Total enteral nutrition versus mixed enteral and parenteral nutrition in patients in an intensive care unit. *Minerva Anestesiol* 62:1-7
6. Bauer P, Charpentier C, Bouchet C, Nace L, Raffy F, Gaconnet N (2000) Parenteral with enteral nutrition in the critically ill. *Intensive Care Med* 26:893-900
7. Deegan H, Dent S, Keefe L, Drover JW, Heyland DK (1999) Supplemental parenteral nutrition in the critically ill patient: a retrospective study. *Clinical Intensive Care* 10:131-136
8. Huang YC, Yen CE, Cheng CH, Jih KS, Kan MN (2000) Nutritional status of mechanically ventilated critically ill patients: comparison of different types of nutritional support. *Clin Nutr* 19:101-7
9. Marik P, Karnack C, Varon J (2001) The effect of enteral nutrition, parenteral nutrition and parenteral nutrition together with “trickle” feeds on mortality in critically ill ICU patients. *Critical Care Medicine* 29 :A126
10. Marik P, Karnack C, Varon J (2002) The addition of trickle feeds reduces the complications associated with parenteral nutrition. *Critical Care Shock* 5:1-10