8.0 Parenteral Nutrition vs. Standard care January 31st 2009

Recommendation:

Based on 5 level 2 studies, in critically ill patients with an intact gastrointestinal tract, we recommend that parenteral nutrition not be used routinely.

Discussion: The committee noted that the differences in these aggregated results compared to other meta-analyses (Simpson 2005, Peter 2005, Braunshweig 2001, Koretz 2001) were largely due to the difference in the population studied i.e. inclusion of elective surgery and other hospitalized patients. The current aggregated results in critically ill patients suggest no effect on mortality but that PN may be associated with an increase in infectious complications. Given the concerns about the possibility of harm and higher cost associated with PN when compared to standard treatment, the committee decided to put forward a recommendation against its use in patients with an intact GI tract. It is worthy to emphasize that this recommendation applies to the average critically ill patient with an intact GI tract only and does not pertain to patients with a compromised GI tract in whom PN maybe indicated. The committee noted that although the results of the meta-analysis do not support the use of PN in critically ill patients, prolonged periods of starvation (> 2weeks) is associated with poor outcomes (Sandstrom 1993).

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 (mortality) 0 2 (complications)
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 (mortality) 1 (complications)
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	2
Adequacy of control group	Extent to which the control group presented standard of care (large dissimilarities=1, minor dissimilarities=2, usual care=3)	1
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)	2
Low cost	Estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	1
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	1

8.0 Parenteral Nutrition vs. Standard care January 31st 2009

Question: Compared to standard care (IV fluids, oral diet, etc.), does parenteral nutrition (PN) result in improved clinical outcomes in critically ill patients with an intact GI tract?

Summary of Evidence: From on a recent meta-analysis of PN vs. standard care in critically ill and surgical patients (Heyland et al, JAMA 1998 Dec 16;280(23):2013-9), there were 6 out of 26 studies that included patients that would routinely be admitted to the ICU as part of their management. Two of these trials evaluated the use of combination EN + PN and hence were excluded from this section and incorporated into section 7.0 (combination EN + PN). There were 4 level 2 studies that were reviewed and one level 2 study additional study published since the meta-analysis.

Mortality: When the 5 studies from this review were aggregated, PN had no effect on mortality (RR 0.82, 0.42,1.61, p = 0.56) (figure 1).

Infections: Only one study (Sax 1987) reported the number of patients with infectious complications and parenteral nutrition was associated with an increase in infectious complications (14.0 vs. 4.0%, p=0.36).

LOS and Ventilator days: Based on 4 studies that reported hospital length of stay, the use of parenteral nutrition had no effect on hospital stay (Weighted mean difference, WMD 0.51, -6.93, 7.95, p = 0.89) (figure 2). Two studies reported on ventilator days and found no differences between the groups.

Other: An improvement in nitrogen balance in the PN groups was noted in some studies (Abel, Sax, Reilly). Two studies reported higher costs associated with the use of parenteral nutrition. The use of PN was also associated with a higher incidence of other complications (pneumonia, respiratory failure, acute renal failure and catheter related sepsis).

Conclusions:

1) Parenteral nutrition has no effect on mortality in critically ill patients
2) Parenteral nutrition may be associated with an increase in complications in critically ill patients.
3) Parenteral nutrition has no effect on hospital stay.

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 parenteral nutrition vs. standard care in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
				PN	control	PN	control
1) Abel 1976	Malnourished cardiac surgery patients N = 44	C.Random: not sure ITT: no Blinding: no (4)	PN without lipids after surgery vs D5W	4/20 (20)	3/24 (12.5)	NA	NA
2) Sax 1987	Acute pancreatitis N = 54	C.Random: not sure ITT: yes Blinding: no (8)	PN with lipids after admission vs. IV fluids	1/29 (3)	1/26 (4)	4/29 (14)	1/26 (4)
3) Reilly 1990	Liver transplant patients malnourished N = 18	C.Random: not sure ITT: yes Blinding: no (7)	PN with lipids after transplant vs D5W	0/8 (0)	2/10 (20)	NA	NA
4) Sandstrom 1993	Major surgery, trauma, 20% malnourished N = 300	C.Random: yes ITT: yes Blinding: no (10)	PN with lipids after surgery vs. D5W	12/150 (8)	10/150 (7)	NA	NA
5) Xian-Li 2005*	Severe acute pancreatitis N = 69	C.Random: yes ITT: yes Blinding: no	PN with lipids vs. IV fluids	3/21 (14)	10/23 (44)	Number of infectious complications** 11	21

Table 1. Randomized studies evaluating parenteral nutrition vs. standard care in critically ill patients

Study	LOS days		Ventilator days		Cost		Other	
	PN	control	PN	control	PN	control	PN	control
1) Abel 1976	Hospital 19 ± 6	Hospital 18 ± 6	5.25 ± 4.8	3.46 ± 2.5	$ 12,290 ± 1395	$ 9630 ± 1562	Post-op complications 16/20 (80)	6/24 (25)
2) Sax 1987	Hospital 15 ± 4	Hospital 10 ± 3	NA	NA	NA	NA	Infected catheters per group 28	13
3) Reilly 1990	Hospital 67.3 ± 29 ICU 3.8 ± 1.0	Hospital 47.2 ± 19 ICU 6 ± 2.3	2.3 ± 0.9	3.6 ± 2.7	NA	NA	NA	
4)Sandstrom 1993	NA	NA	NA	NA	NA	NA	NA	
5) Xian-Li 2005*	28.6 ± 6.9	39.1 ± 10.6	NA	NA	NA	NA	NA	

* Only data comparing the groups receiving standard PN and IV fluids reported here.
** Not included in meta-analysis as not reported as number of patients with infections.
C.Random: concealed randomization ‡ refers to the # of patients with infections unless specified
ITT: intent to treat † hospital mortality unless otherwise specified
NA: not available ± ( ) : mean ± Standard deviation (number)

Figure 1.

Review: Parenteral Nutrition v. Standard care
Comparison: 01 Parenteral Nutrition vs. Standard care
Outcome: 01 Mortality

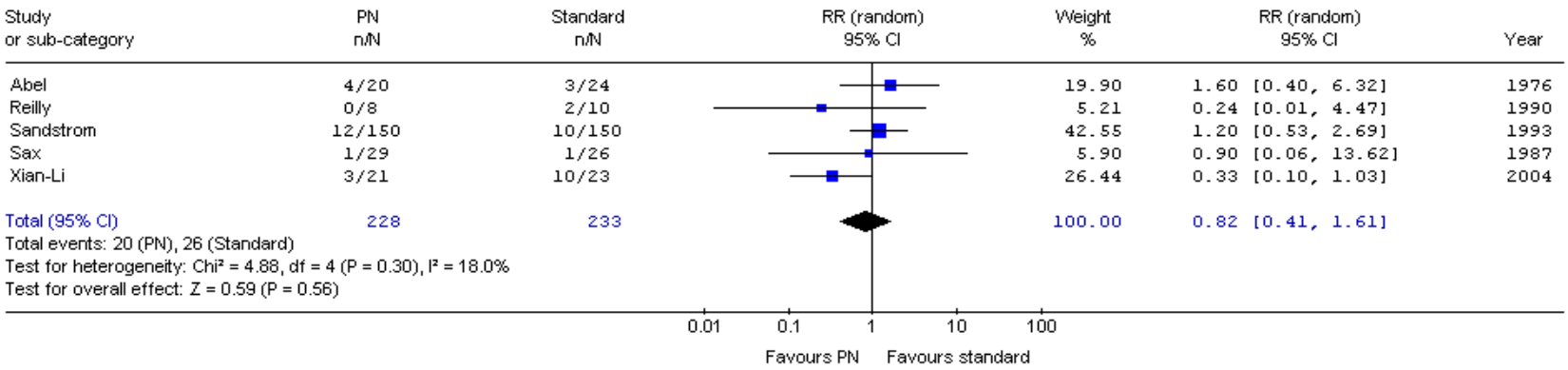
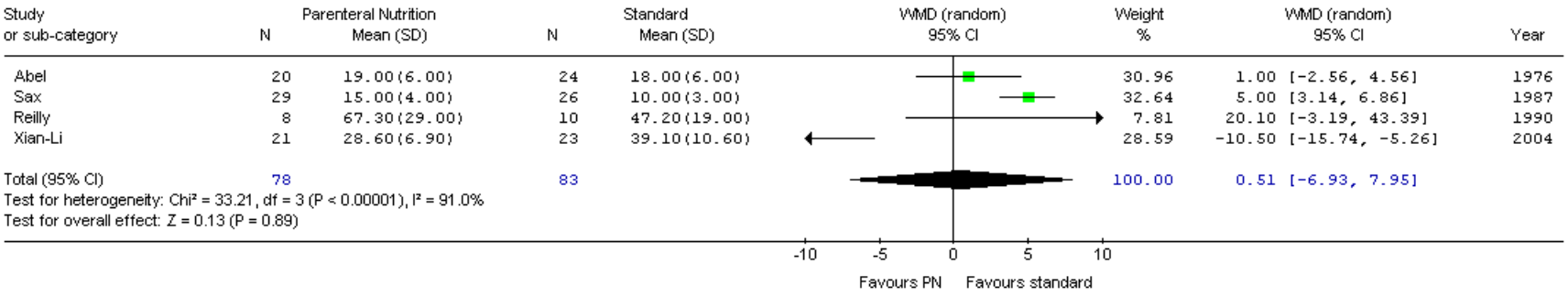


Figure 2.

Review: Parenteral Nutrition v. Standard care
Comparison: 01 Parenteral Nutrition vs. Standard care
Outcome: 03 Hospital Length of Stay



TOPIC: 8.0 Parenteral Nutrition vs. Standard care

Article inclusion log

Criteria for study selection

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

	Author	Journal	I	E	Why rejected
1	Abel	Arch Surg 1976	√		
2	Heim	TumorDiagnostik & Therapie 1985		√	Cancer pts
3	Cardona	J Clin Nutr Gastroenterol 1986		√	Cancer pts
4	Sax	American Journal of Surgery 1987	√		
5	Reilly	JPEN 1990	√		
6	Buzby	World J Surgery 1993		√	Surgery pts
7	Sandstrom	Annals of Surgery 1993	√		
8	Gil	Nutrition 1997		√	Cancer pts
9	Heyland*	JAMA 1998	√		
10	Hu	Spine 1998		√	Surgery pts
11	Bozzetti	JPEN 2000		√	Elective surgery pts
12	Heyland	Proceedigns of the Nutrition Society 2000		√	Systematic review, ICU studies included
13	Braunschweig	Am J Clin Nutr 2001		√	Not all ICU patients, ICU studies included
14	Koretz	Gastroenterology 2001		√	Not all ICU patients, not PN vs standard
15	Xian-Li	Clin Nut Suppl 2004	√		
16	Peter	CC Medicine 2005		√	Not all studies of ICU patients
17	Simpson	Intensive Care Med 2005		√	Not all studies of ICU patients

I = included, E = excluded

*individual studies pertaining to critically ill patients included in this meta-analysis were reviewed

Reference List

1. Abel RM, Fischer JE, Buckley MJ, Barnett GO, Austen WG. Malnutrition in cardiac surgical patients. Results of a prospective, randomized evaluation of early postoperative parenteral nutrition. Arch Surg. 1976 Jan;111(1):45-50.

2. Heim ME, Leweling H, Edler L, Queiber W. Adjuvant parenteral nutrition in patients with colorectal cancer receiving polychemotherapy: a randomized clinical trial. TumorDiagnostik & Therapie. 1985 6:129-133

3. Cardona D, Del Moral V, Salvador R, Andreu MA, Trias R, Bonal J. Early postoperative total parenteral nutrition in gastric cancer: a cost-effectiveness study. J Clin Nutr Gastroenterol. 1986 1:267-270

4. Sax HC, Warner BW, Talamini MA, Hamilton FN, Bell RH Jr, Fischer JE, Bower RH. Early total parenteral nutrition in acute pancreatitis: lack of beneficial effects. Am J Surg. 1987 Jan;153(1):117-24.

5. Reilly J, Mehta R, Teperman L, Cemaj S, Tzakis A, Yanaga K, Ritter P, Rezak A, Makowka L. Nutritional support after liver transplantation: a randomized prospective study. JPEN J Parenter Enteral Nutr. 1990 Jul-Aug;14(4):386-91.

6. Buzby GP. Overview of randomized clinical trials of total parenteral nutrition for malnourished surgical patients. World J Surg. 1993 Mar-Apr;17(2):173-7.

7. Sandström R, Drott C, Hyltander A, Arfvidsson B, Scherstén T, Wickström I, Lundholm K. The effect of postoperative intravenous feeding (TPN) on outcome following major surgery evaluated in a randomized study. Ann Surg. 1993 Feb;217(2):185-95.

8. Gil MJ, Franch G, Guirao X, Oliva A, Herms R, Salas E, Girvent M, Sitges-Serra A. Response of severely malnourished patients to preoperative parenteral nutrition: a randomized clinical trial of water and sodium restriction. Nutrition. 1997 Jan;13(1):26-31.

9. Heyland DK, MacDonald S, Keefe L, Drover JW. Total parenteral nutrition in the critically ill patient: a meta-analysis. JAMA. 1998 16;280(23):2013-9.

10. Hu SS, Fontaine F, Kelly B, Bradford DS. Nutritional depletion in staged spinal reconstructive surgery. The effect of total parenteral nutrition. Spine. 1998 Jun 15;23(12):1401-5.

11. Bozzetti F, Gavazzi C, Miceli R, Rossi N, Mariani L, Cozzaglio L, Bonfanti G, Piacenza S. Perioperative total parenteral nutrition in malnourished, gastrointestinal cancer patients: a randomized, clinical trial. JPEN J Parenter Enteral Nutr. 2000 Jan-Feb;24(1):7-14.

12. Heyland DK. Parenteral nutrition in the critically-ill patient: more harm than good? Proc Nutr Soc. 2000 Aug;59(3):457-66.

13. Braunschweig CL, Levy P, Sheean PM, Wang X. Enteral compared with parenteral nutrition: a meta-analysis. Am J Clin Nutr. 2001 Oct;74(4):534-42.

14. Koretz RL, Lipman TO, Klein S; American Gastroenterological Association. AGA technical review on parenteral nutrition. Gastroenterology. 2001 Oct;121(4):970-1001.

15. Xian-Li He et al. Effect of total parenteral nutrition (TPN) with and without glutamine dipeptide supplementation on outcome in severe acute pancreatitis (SAP). Clinical Nutrition Supplements 2004(1):43.

16. Peter JV, Moran JL, Phillips-Hughes J. A metaanalysis of treatment outcomes of early enteral versus early parenteral nutrition in hospitalized patients. Crit Care Med. 2005 Jan;33(1):213-20; discussion 260-1.

17. Simpson F, Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. Intensive Care Med. 2005 Jan;31(1):12-23. Epub 2004 Dec 9.