10.2 Strategies to Optimize Parenteral Nutrition and Minimize Risks: Use of lipids January 8th 2007

Recommendation:
Based on 2 level 2 studies, in critically ill patients who are not malnourished, are tolerating some EN, or when parenteral nutrition is indicated for short term use (< 10 days), withholding lipids high in soybean oil should be considered. There are insufficient data to make a recommendation about withholding lipids high in soybean oil in critically ill patients who are malnourished or those requiring PN for long term (> 10 days). Practitioners will have to weigh the safety and benefits of withholding lipids high in soybean oil on an individual case-by-case basis in these latter patient populations.

Discussion: The committee noted a large reduction in infectious complications associated with withholding lipids albeit this effect maybe due to reduced calories or the absence of lipids. The feasibility and cost favoured withholding lipids. One of the studies excluded malnourished patients (McCowen) while the other excluded patients with essential fatty acid deficiency (Batistella). The committee expressed concerns over the effects of long term fat free parenteral nutrition and the paucity of data in malnourished patients. The committee decided that while the concerns regarding withholding lipids (i.e. hypocaloric nutrition and essential fatty acid deficiency) were probably minimal for those patients tolerating some EN and requiring PN for short term (< 10 days), this cannot be extrapolated to those who have an absolute contraindication to EN and need PN for a longer duration. Given the emerging evidence around the potential benefits of omega 3 fatty acids, it was agreed that this recommendation be made specific to withholding lipid emulsions that were high in soybean oil.

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	3+ for infections
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	2+
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+
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	2+

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Question: Does the presence of lipids in parenteral nutrition affect outcomes in the critically ill adult patient?

Summary of evidence: There were 2 level 2 studies reviewed that compared the use of lipids high in soybean oil to no lipids in parenteral nutrition (Battistella, McCowen).

Mortality: Battistella and McCowen reported no difference in mortality between the groups. McCowen. A meta-analysis confirmed this (RR 1.29,CI 0.16-10.7, p = 0.8)

Infections:
A significant reduction in pneumonia (p =0.05), line sepsis (p= 0.04) and total number of infectious complications was seen in trauma patients not receiving lipids compared to those receiving lipids (Battistella). In the McCowen study, the group that received no lipids (hypocaloric group) showed a trend towards a reduction in infections (p =0.2). Combining these studies, the meta-analysis done showed a significant reduction in infections in the group that received no lipids (RR 0.63,CI 0.42-0.93, p =0.02)

LOS and Ventilator days:
A significantly shorter ICU stay (p = 0.02), hospital stay (p = 0.03) and significantly fewer ventilated days (p = 0.01) were observed in trauma patients not receiving lipids compared to those receiving lipids (Battistella). No difference in LOS was seen in the McCowen study (did not report on ventilator days)

Other complications: Incidence of hyperglycemia was similar in the hypocaloric and standard groups (McCowen).

Conclusions:

Withholding lipids high in soybean oil does not reduce mortality but is associated with a significant reduction in infections in critically ill patients and may reduce LOS and duration of ventilation in trauma patients.

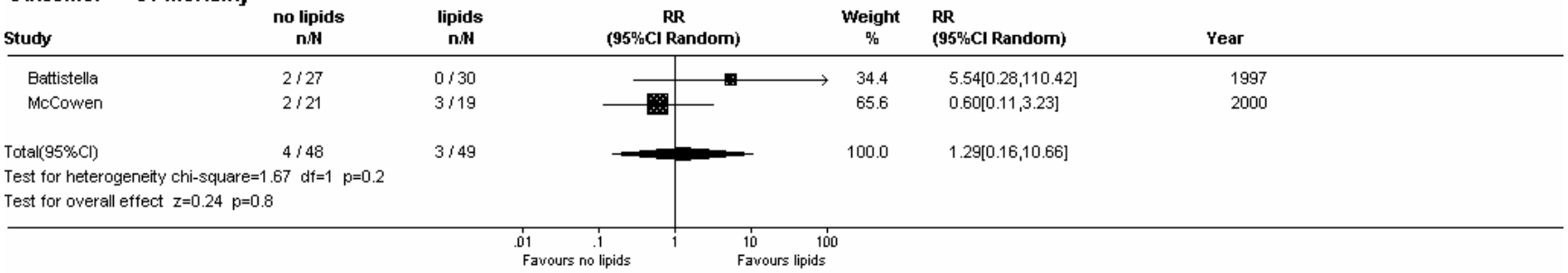
Level 1 study: if all of the following are fulfilled: concealed randomization, blinded outcome adjudication and an intention to treat analysis.
Level 2 study: If any one of the above characteristics are unfulfilled.

Table 1. Randomized studies evaluating lipids (PN) in critically ill patients

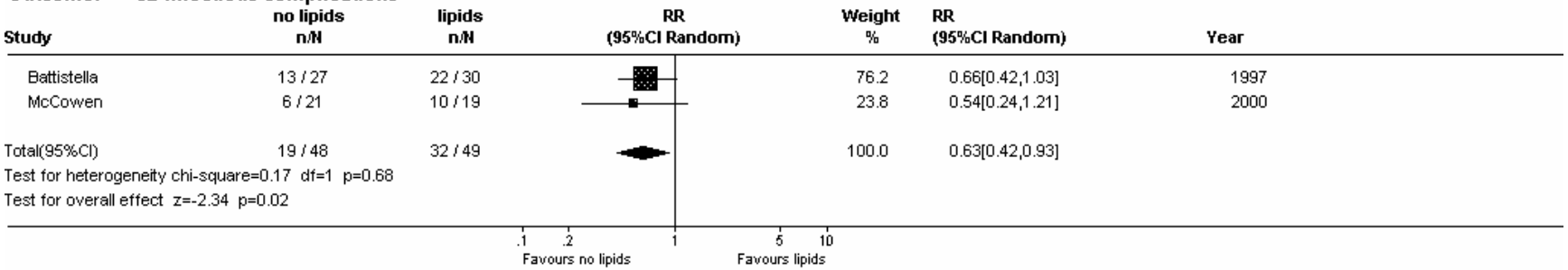
Study	Population	Methods (score)	Intervention	Mortality # (%)†		RR (CI)**	Infections # (%)‡		RR (CI)**
1)Battistella 1997	Polytrauma patients N = 60	C.Random: not sure ITT: no Blinding: no (8)	PN without lipids (1.5 g/kg protein, no lipids) vs. PN with lipids (30 kcal/kg/day + 1.6 gm/kg/d protein, 25 % calories from fat)	No lipids 2/27 (7)	Lipids 0/30 (0)	0.18 (0.01-3.60)	No lipids Lipids Pneumonia 13/27 (48) 22/30 (73) line sepsis 5/27 (19) 13/30 (43) total # infections per group 39/27 72/30		1.52 (0.97-2.38) 2.34 (0.96-5.70) NA
2) McCowen 2000	Probable ICU patients (mostly ventilated) n= 48	C.Random: not sure ITT: no Blinding: no (6)	Hypocaloric PN (no lipids), Pro 70g/d CHO 1000kcal/d vs standard PN (with lipids) ,Pro1.5g/kg/d, 25kcal/kg/d + lipids	Hypocaloric PN 2/21 (10)	Standard PN 3/19 (16)	0.60 (0.11-3.23)	Hypocaloric PN 6/21 (29)	Standard PN 10/19 (53)	0.54 (0.24-1.21)

Study	LOS days		Ventilator days		Cost		Other
1) Battistella 1997	No Lipids 18± 12 (27) ICU 27 ± 16 (27) hospital	Lipids 29 ± 22 (30) ICU 39 ± 24 (30) hospital	No lipids 15 ± 12 (27)	Lipids 27 ± 21 (30)	No lipids NA	Lipids NA	No lipids Lipids NA NA Calories received kcal/kg/day 21 ± 2 28 ± 2 Protein received gm/kg/day 1.6 ± 0.1 1.6 ± 0.2
2) McCowen 2000	Hypocaloric PN 19 ± 14 (21)	Standard PN 17 ± 15 (19)	Hypocaloric PN NA	Standard PN NA	Hypocaloric PN NA	Standard PN NA	Hypocaloric PN Standard PN Calories received kcal/kg/day 14 ± 3 18 ± 4 Protein received gm/kg/day 1.1 ± 0.2 1.3 ± 0.2 Hyperglycemia 20 % 26 %

Comparison: 01 lipids vs no lipids (parenteral)
Outcome: 01 mortality



Comparison: 01 lipids vs no lipids (parenteral)
Outcome: 02 Infectious complications



TOPIC: 10.1 Use of lipids

(Reviewers: Ulrich Suchner, Minto Jain, John Drover and Brian Jurewitsch)

Article inclusion log

Criteria for study selection

Type of study: RCT or Meta-analysis
Population: critically ill human patients (no elective surgical patients)
Intervention :TPN and /or 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.	Battistella (lipids vs no lipids)	J Trauma 1997	√		
2.	McCowen	CCMedicine 2000	√		
3.	De Chalain	J Surg Res 1992			
4.	Suchner	CC Med 2001		√	No significant outcomes
5.	Lenssen	Am J Clin Nutr 1998		√	Not ICU patients
6.	Tappy	CC Med 1998		√	Not RCT, no significant outcomes
7.	Venus	CC Med 1988		√	Not RCT, no significant outcomes

I = included, E = excluded

References

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3. De Chalain TM, Michell WL, O'Keefe SJ, Ogden JM. The effect of fuel source on amino acid metabolism in critically ill patients. Surg Res. 1992 Feb; 52(2): 167-76.

4. Suchner U, Katz DP, Furst P, Beck K, Felbinger TW, Senftleben U, Thiel M, Goetz AE, Peter K. Effects of intravenous fat emulsions on lung function in patients with acute respiratory distress syndrome or sepsis. Crit Care Med. 2001 Aug; 29(8): 1569-74.

5. Lenssen P, Bruemmer BA, Bowden RA, Gooley T, Aker SN, Mattson D. Intravenous lipid dose and incidence of bacteremia and fungemia in patients undergoing bone marrow transplantation. Am J Clin Nutr. 1998 May; 67(5): 927-33.

6. Tappy L, Schwarz JM, Schneiter P, Cayeux C, Revelly JP, Fagerquist CK, Jequier E, Chiolero R. Effects of isoenergetic glucose-based or lipid-based parenteral nutrition on glucose metabolism, de novo lipogenesis, and respiratory gas exchanges in critically ill patients. Crit Care Med. 1998 May; 26(5): 860-7.

7. Venus B, Prager R, Patel CB, Sandoval E, Sloan P, Smith RA. Cardiopulmonary effects of Intralipid infusion in critically ill patients. Crit Care Med. 1988 Jun; 16(6): 587-90.