3.3b Intentional Underfeeding: Hypocaloric Enteral Nutrition

March 2013

NEW SECTION in 2013

Recommendation: *There are insufficient data to make a recommendation on the use of hypocaloric enteral nutrition in critically ill patients.*

Discussion: The committee noted the single centre nature of the one study (Arabi 2011) and agreed that the targeted intervention related to underfeeding of calories (60-70% calories) represented usual care in critically ill patients as evidenced by recent audits of clinical practices. The delivery of additional protein via supplementation was also noted. Despite the significant reduction in hospital and 180 day mortality and the modest sample size of the trial, the committee agreed to wait for the multicentre trial to be completed before putting forward a recommendation on the use of intentional underfeeding (i.e. hypocaloric enteral nutrition).

Semi Quantitative Scoring

Values	Definition	2013 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	2 (mortality)
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	n/a
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)	1
Low cost	Estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	3
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	2

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Question: Does the use of hypocaloric enteral nutrition vs full feeding result in better outcomes in the critically ill adult patient?

Summary of evidence: There was 1 level 2 study reviewed that compared starting at 60-70% goal rate (underfed group) plus protein supplements to 90-100% goal rate feeds (Arabi 2011). The actual amounts of calories received in the underfed group vs goal rate were 59% ± 16.1% vs 71.4% ± 22.8% ($p<0.0001$) while protein intakes were similar: 65.2% ± 25.7% vs 63.7% ± 25.0% ($p=0.63$). This is in contrast to the Taylor study that compared starting at full rate enteral nutrition to gradual introduction, in which the full rate group compared to the gradual introduction received 59% vs 37% calories and 69 vs 38% nitrogen in the first week post injury (refer to section 3.2 Achieving target dose of EN for more details). The Arabi study also compared intensive insulin therapy to control in a 2 X 2 factorial design, refer to section 10.4 Insulin therapy data pertaining to these groups.

Mortality: Hypocaloric enteral nutrition had no effect on ICU mortality (RR 0.81, 95% CI 0.48, 1.35, $p=0.42$*) or 28 days mortality (RR 0.79, 95% CI 0.48, 1.29, $p=0.34$*), but was associated with a significant reduction in hospital mortality (RR 0.71, 95% CI 0.50, 1.00, $p=0.05$*), and associated with a trend towards a reduction in 180-day mortality (RR 0.73, 95% CI 0.52, 1.02, $p=0.06$*).

Infections: Hypocaloric enteral nutrition had no effect on the overall incidence of ICU-acquired infections per 1000 ICU days ($p=0.89$) or on the incidence of VAP per 1000 ventilator days ($p=0.34$).

LOS & ventilator days: Hypocaloric enteral nutrition was associated with a trend towards a reduction in both ICU LOS (WMD -2.80, 95% CI -5.93, 0.33, $p=0.08$*) and in ventilator days (WMD -2.60, 95% CI -5.64, 0.44, $p=0.09$*), but had no effect on hospital LOS (WMD 3.00, 95% CI -22.42, 28.42, $p=0.82$*).

Other: Due to the study design, the hypocaloric enteral nutrition group received significantly fewer calories than the full feeds group ($p=0.0001$).

Conclusions:

1. The use of hypocaloric enteral nutrition vs full feeds is associated with a reduction in hospital mortality and a trend towards a reduction in 180 day nortality in critically ill patients.
2. The use of hypocaloric enteral nutrition vs full feeds is associated with a trend towards a reduction in ICU length of stay and ventilator days.

*Risk ratios, mean differences, confidence intervals and p-values indicated above were calculated using Review Manager 5.1. P-values reported in the published article are: hospital mortality p=0.04, ICU mortality p=0.42, 28-day mortality p=0.34, 180-day mortality p=0.07, ICU LOS p=0.09, hospital LOS p=0.81, ventilator days p=0.10

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 hypocaloric vs. full feeding in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
				Trophic Feeds	Full Feeds	Trophic Feeds	Full Feeds
1) Arabi 2011*	ICU patients ~30% brain trauma 40% Type 2 diabetes N=240 BMI (kg/m^2) Trophic feeds pts: 28.5±7.4 Full feeds pts: 28.5±8.4 Age Trophic feeds pts: 50.3±21.3 Full feeds pts: 51.9±22.1	C.Random: Yes ITT: Yes Blinding: No (9)	Underfed: 60-70% goal + protein supplements vs. 90-100% goal Calories actually received 59.0% vs 71.4% Protein actually received 65.2% vs 63.7% Isonitrogenous, non-isocaloric	ICU 21/120 (18) 28 Day 22/120 (18) Hospital 36/120 (30) 180 Day 38/120 (32)	ICU 26/120 (22) 28 Day 28/120 (23) Hospital 51/120 (43) 180 Day 52/120 (43)	All Infections/1000 days 54.7 VAP/1000 vent days 14 Sepsis 53/120 (44)	All infections/1000 days 53.6 VAP/1000 vent days 10 Sepsis 56/120 (47)

Table 2. Randomized studies evaluating hypocaloric vs full feeding in critically ill patients

Study	LOS days		Ventilator days		Cost		Other	
	Trophic Feeds	Full Feeds	Trophic Feeds	Full Feeds	Trophic Feeds	Full Feeds	Trophic Feeds	Full Feeds
1) Arabi 2011*	ICU 11.7 ± 8.1 (120) Hospital 70.2 ± 106.9 (120)	ICU 14.5 ± 15.5 (120) Hospital 67.2 ± 93.6(120)	10.6 ± 7.6 (120)	13.2 ± 15.2 (120)	NR	NR	Kcal/day 1067 ± 306 p=0.0001	1252 ± 432

C.Random: concealed randomization
† presumed hospital mortality unless otherwise specified
± ( ) : mean ± Standard deviation (number)
ITT: intent to treat; NA: not available
‡ refers to the # of patients with infections unless specified

* Data shown here for underfed group and full fed groups include patients randomized to the intensive insulin and conventional insulin therapy within these 2 groups. Refer to the intensive insulin therapy section for data on intensive insulin vs conventional groups.
** Includes 272 patients that also randomized to an experimental arm of omega 3fatty acids arm.