4.2a Composition of Enteral Nutrition: (Carbohydrate/fat): High fat/low CHO May 2015

There were no new randomized controlled trials since the 2009 and 2013 updates and hence there are no changes to the following Summary of Evidence.

Recommendation: *There are insufficient data to recommend high fat/low CHO diets for critically ill patients.*

Discussion: The committee noted that the with respect to ventilator days, the evidence from two small studies showed only a small treatment effect and wide confidence intervals and the presence of heterogeneity between the two studies. The significant improvement in a surrogate endpoint i.e. glycemic control in the group receiving the higher fat/lower CHO formula in one study was noted. Concerns were expressed about the safety of high fat diets and the committee noted the higher cost of high fat formulas compared to standard. The feasibility was not felt to be a great concern

Semi Quantitative Scoring

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	1
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	1
Adequacy of control group	Extent to which the control group represented standard of care (large dissimilarities = 1, minor dissimilarities=2, usual care=3)	3
Biological plausibility	Consistent with understanding of mechanistic and previous clinical work (large inconsistencies =1, minimal inconsistencies =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, heterogeneous patients, diverse practice settings =3.	1
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	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	2

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Question: Does a high fat/low CHO enteral formula affect outcomes in the critically ill adult patient?

Summary of evidence: There were three level 2 studies that compared a high fat, low CHO formula to a standard formula. Two studies compared Pulmocare (55% fat, 28 % CHO) and one compared Novasource Diabetic Plus (40% fat, 40 % CHO) to standard formula (29-30 % fat, 49-53% CHO).

Mortality: Two studies reported on mortality and found no differences between the groups (Al Saady 1994, Mesejo 2003).

Infections: One study reported infectious complications and found no differences between the two groups (Mesejo 2003)

LOS: Only one study reported on ICU length of stay and found no differences between the two groups (Mesejo 2003)

Ventilator days: Were significantly lower in the high fat group in one study (Al Saady 1994 $p<0.001$), no difference found in the van de Berg 1994 study or the Mesejo 2003 study.

Other complications: In the one study that reported on glycemic control, glucose levels and the dose of insulin needed were significantly lower in the group receiving the higher fat, lower CHO formula.

Conclusions:

1) A high fat, low CHO enteral formula may be associated with a reduction in ventilated days in medical ICU patients with respiratory failure and better glycemic control in critically ill patients with hyperglycemia.
2) No difference in mortality, infections or LOS found between the critically ill patients receiving high fat/low CHO formula or standard.

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 High Fat/Low CHO Enteral Nutrition In Critically ill Patients

Study	Population	Methods (score)	Intervention	Mortality # (%)		RR (CI)**	Infections # (%)		RR (CI)**
1. van den Berg 1994	Medical ICU patients with COPD Chronically ventilated N=32	C.Random: not sure ITT: yes Blinding: no (5)	55% fat, 28 % CHO (Pulmocare) vs 30 % fat, 53 % CHO (standard, Ensure Plus)	High fat/low CHO NR	Standard NR	NR	High fat/low CHO NR	Standard NR	NR
2. Al Saady 1994	Ventilated patients Acute respiratory failure N=40	C.Random: not sure ITT: no Blinding: double (9)	55% fat, 28 % CHO (Pulmocare) vs 30 % fat, 53 % CHO (standard, Ensure Plus)	3/9 (33)	3/11 (27)	1.22 (0.32-4.65)	NR	NR	NR
3. Mesejo 2003	Critically ill pts with Diabetes or hyperglycemia from 2 different centers N=50	C.Random: not sure ITT: yes Blinding: single (9)	40% fat, 40 % CHO (Novasource Diab Plus) vs. 29 % fat, 49 % CHO (Standard, Isosource Protein)	8/26 (31)	7/24 (29)	1.05 (0.45, 2.47)	10/26 (38.5)	8/24 (33)	1.15 (0.55, 2.43)

Table 1. Randomized Studies Evaluating High Fat/Low CHO Enteral Nutrition In Critically ill Patients (continued)

Study	LOS days		Ventilator days		Cost		Other	
1. van den Berg 1994	High fat/low CHO NR	Standard NR	High fat/low CHO 4 (median)	Standard 6 (median)	High fat/low CHO NR	Standard NR	High fat/low CHO Gastric retention 1/15 (7)	Standard 1/17 (6)

2. Al Saady 1994	NR	NR	3.6 ± 0.7	6.2 ± 1.5	NR	NR	Diarrhea 3/9 (33) 3/11 (27)
3. Mesejo 2003	ICU 14.8 ± 9.4	ICU 14.8 ± 8.8	8.7 ± 6.2	9.4 ± 6.0	NR	NR	Plasma Glucose Levels (mmol/L) 9.8 ± 2.4 12.4 ± 2.6

C.Random: concealed randomization
ITT: intent to treat
NR: Not reported

± : Mean ± Standard deviation
** RR= relative risk, CI= Confidence intervals