

5.2 Strategies to Optimize Delivery and Minimize risks of EN: Motility agents

June 28th, 2005

Recommendation:

Based on a systematic review of the literature and 1 level 2 study in critically ill patients who experience feed intolerance (high gastric residuals, emesis), the use of metoclopramide as a motility agent should be considered.

Discussion: The committee noted the lack of treatment effect on clinical outcomes from a recent systematic review (1) and one randomized trial. However the committee felt that the beneficial effects of motility agents on gastrointestinal motility and feed intolerance from these 2 sources should be recognized. Due to the concerns re: bacterial resistance and the potential for cardiac toxicity with the use of erythromycin, it was agreed that the recommendation be made for metoclopramide. Given the low probability of harm, the favourable feasibility and cost considerations and the benefits of motility agents in improving nutrient intake, particularly when initiating early EN, the committee decided that motility agents be considered as a strategy to optimize nutrient intake.

(1) Booth CM, Heyland DK, Paterson WG. Gastrointestinal promotility drugs in the critical care setting: a systematic review of the evidence. Crit Care Med. 2002 Jul;30(7):1429-35

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	1+ (surrogate)
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	similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials	1+
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+
Feasible	ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	3+
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+

5.2 Topic: Strategies to optimize delivery and minimize risks of Enteral Nutrition: Motility Agents

June 28th, 2005

Question: Compared to standard practice (placebo), does the routine use of motility agents improve clinical outcomes in critically ill patients?

Summary of Evidence: There was one systematic review that was reviewed. Only studies pertaining to critically ill patients (not elective surgery) were included. Studies on tube placement were excluded. From this review, only one study (Yavagal et al) evaluated the effects of a pro-motility agent (metoclopramide) on clinical outcomes in the critical care setting. Another study (Berne et al) studied the use of erythromycin on gastric emptying and clinical outcomes. Four other studies on metoclopramide, three studies on cisapride (no longer available on the market) and three studies on erythromycin looked at surrogate outcomes (not clinically important).

Mortality: In the two studies that reported on mortality, there was no significant difference in mortality between the groups.

Infections: In the one study that reported on infections, there was no significant difference in the incidence of pneumonia between the groups.

LOS, Ventilator days: Not reported.

Other: The time to development of pneumonia was statistically different in the one study (Yavagal) (5.95 days versus 4.46 days, $p=0.006$), however, the clinical significance of this difference is negligible. One study (Berne) demonstrated positive effects on measures of gastric emptying (confirm this) and feeding tolerance.

Conclusion:

- 1) Motility agents have no effect on mortality or infectious complications in critically ill patients.
- 2) Motility agents may be associated with an increase gastric emptying and a reduction in feeding intolerance in critically ill patients.

Table 1. Randomized Studies Motility Agents In Critically Ill Patients

Study	Population n	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡		Nutritional Indices	
				Experimental	Control	Experimental	Control	Experimental	Control
1) Yavagal 2000	Mixed ICU N = 305	C.Random: not sure ITT: yes Blinding: (10)	Metoclopramide 10 mg NG vs. placebo	73/ 131 (56)	92/174 (53)	22/131 (17)	24/174 (14)	N/A	N/A
2) Berne 2002	Critically injured patients n= 48	C.Random: not sure ITT: no Blinding: no (6)	Erythromycin 250 mg IV q 6 hrs vs. 5% dextrose IV q 6 hrs	2/32 (6)	2/36 (6)	pneumonia 13/32 per group*	pneumonia 18/36 per group*	Feeds tolerated at 48 hrs 58 %	44 % Feeds tolerated for the study 65 %

* infections reported as per group, not # patients with infections

TOPIC: 5.2. Motility Agents

(Reviewers: Jan Greenwood & 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
	1.	Yavagal	CCMedicine 2000	√	
	2.	Berne	J Trauma 2002	√	
48.	3.	Booth*	CCMedicine 2002		√ Review
	4.	Reigner	CC Medicine 2002		√ No significant outcomes
	5.	Ritz	CC Medicine 2001		√ Not RCT
	6.	Griffith	CC Medicine 2003		√ No significant outcomes
	7.	Marino	Br J Neurosx 2003		√ No significant outcomes

I = included, E = excluded

References

1. Yavagal DR, Karnad DR, Oak JL: Metoclopramide for preventing pneumonia in critically ill patients receiving enteral tube feeding: A randomized controlled trial. *Crit Care Med.* May;28(5):1408-11, 2000.
2. Berne JD, Norwood SH, McAuley CE, Vallina VL, Villareal D, Weston J, McClarty J. Erythromycin reduces delayed gastric emptying in critically ill trauma patients: a randomized, controlled trial. *J Trauma.* 2002 Sep; 53(3): 422-5.
3. Booth CM, Heyland DK, Paterson WG. Gastrointestinal promotility drugs in the critical care setting: A systematic review of the evidence. *Crit Care Med.* Jul;30(7):1429-35, 2002.
4. Reignier J, Bensaid S, Perrin-Gachadoat D, Burdin M, Boiteau R, Tenailon A. Erythromycin and early enteral nutrition in mechanically ventilated patients. *Crit Care Med.* 2002 Jun; 30(6): 1237-41.
5. Ritz MA, Fraser R, Edwards N, Di Matteo AC, Chapman M, Butler R, Cmielewski P, Tournadre JP, Davidson G, Dent J. Delayed gastric emptying in ventilated critically ill patients: measurement by ¹³C-octanoic acid breath test. *Crit Care Med.* 2001 Sep; 29(9): 1744-9.
6. Griffith DP, McNally AT, Battey CH, Forte SS, Cacciatore AM, Szeszycki EE, Bergman GF, Furr CE, Murphy FB, Galloway JR, Ziegler TR. Intravenous erythromycin facilitates bedside placement of postpyloric feeding tubes in critically ill adults: a double-blind, randomized, placebo-controlled study. *Crit Care Med.* 2003 Jan; 31(1): 39-44.
7. Marino LV, Kiratu EM, French S, Nathoo N. To determine the effect of metoclopramide on gastric emptying in severe head injuries: a prospective, randomized, controlled clinical trial. *Br J Neurosurg.* 2003 Feb; 17(1): 24-8.