The influence of early postoperative enteral feeding and promotility drugs on upper GI tract and gallbladder motility in the critical care setting

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Problem (I): Intolerance of enteral feeding

“In practice, however, the provision of adequate enteral nutrition is often limited by a variety of factors, including perceived intolerance of feeding in up to 30-50% of patients.”

Problem (II): Intolerance of enteral feeding

Nutrition support in the critically ill

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Delayed gastric emptying is the most common underlying reason for ‘feed intolerance’ and discontinuation of enteral feeding [26]. Using gastric scintigraphy, Chapman \textit{et al.} [29] have recently shown that gastric emptying was delayed in about 50\% of a mixed group of ICU patients.
Problem (III): Intolerance of enteral feeding

Intestinal motility disturbances in intensive care patients pathogenesis and clinical impact

The occurrence of GI motility disturbances in critically ill patients is well known. Abnormalities in gastric emptying affect 50% of mechanically ventilated patients and 80% of patients with increased cranial pressure after head injury [1, 2]. These
Problem (IV): Intolerance of enteral feeding

Gastrointestinal dysfunction relating to the provision of nutrition in the critically ill

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Impaired delivery and absorption are likely to influence clinical outcomes, particularly functional recovery,
Problem (V): Intolerance of enteral feeding

“There are many mechanisms that underlie upper GI motility disturbance in critically ill patients. These include impaired autonomic and enteric nervous system, smooth muscle disturbances, cytokine-mediated inflammation, medication effects, electrolyte disturbances, increased intracranial pressure, and hyperglycemia.”

Gastroparesis: evaluation

“A number of tests have been evaluate for gastroparesis, including radionuclide scintigraphy, ultrasonography, gastric impedance monitoring, gastric fluid chalenge, and the paracetamol absorption test (PAT).”


“The PAT is a simple, noninvasive, bedside test for assessing gastric emptying. It has not side effects, is widely available, ...”

Gastrointestinal promotility drugs

“Gastroparesis in critically ill patients may be corrected via the use of prokinetic agents. Prokinetic agents commonly used in the ICU include metoclopramide, cisapride, and erythromycin.”

Zaloga GP & Marik P. Crit Care Med 2000;28:2657
Metoclopramide

“Metoclopramide is well known prokinetic agent and is frequently used in the ICU. Its precise mechanism of action on the gastrointestinal tract is still unclear but it has been shown to facilitate the release of acetylcholine from gut cholinergic neurones, to antagonise dopamine`s inhibitory effects on gastrointestinal motility and to have a direct effect on lower oesophageal smooth muscle.”

Metoclopramide


* p < 0.05; + p < 0.01; # p < 0.001

PPC mg/L

Erythromycin

“Erytromycin is a macrolide antibiotic that increases gastric motility by acting on motilin receptors in the gut. ... Erytromycin also increases lower esophageal sphincter tone and esophageal peristalsis but has little effect on colonic motility.”

Zaloga GP & Marik P. Crit Care Med 2000;28:2657
Erythromycin

Figure 1. Success of feeding for patients given erythromycin (n = 10) vs. placebo (n = 10) at 1, 12, and 24 hrs after administration.

Cisapride

“Cisapride is a prokinetic agent that enhances the postganglionic release of acetylcholine from nerves in the enteric plexus.”

“Cisapride has been associated with serious and lethal cardiac arrythmias. ... is contraindicated in patients with prolonged QT intervals, renal failure, cardiac failure, ischemic heart disease, history of arrhythmias, respiratory failure, hypokalemia, and hypomagnesemia ...”

Zaloga GP & Marik P. Crit Care Med 2000;28:2657
Opioid antagonists

“... enterally administered naloxone, an opioid antagonist, significantly increased the volume of infused nutrition, reduced GRVs, and decreased the incidence of ventilator-associated pneumonia in patients taking opiate.”

“Orally and subcutaneously administered methylnaltrexone has been shown to improve oral-cecal transit time in patients taking opioids.”

Novel prokinetic agents

- Alvimopan and methylnaltrexone: peripheral $\mu$-opioid receptor antagonist
- Ghrelin: functionally related to motilin
- Tegaserod: peripherally acting partial 5-HT$_4$ receptor agonist and potent 5-HT$_{2B}$ receptor antagonist
- Dexloxioglumide: potent, specific, and competitive cholecystokinin 1 receptor antagonist
- Mitemcinal: motilin agonist

van der Meer YG, et al. Critical Care 2014;18:502
Acupuncture?

“... postoperative hypomotility of GB, with subsequent biliary stasis, is a well-known mechanism for formation of biliary sludge. Biliary sludge is a precursor of two relatively rare (< 2%), but extremely serious complications in cardiac and noncardiac surgery, namely acute acalculous cholecystitis and “idiopathic” pancreatitis. Moreover, it has been proved that biliary sludge has an impact on a later development of cholelithiasis and chronic cholecystitis ...”

Prokinetic agents and gall bladder (II)

“No contraction of the gallbladder was demonstrated, even though metoclopramide has been shown to contact intestinal smooth muscle.”


“Erythromycin improves fasting and postprandial gallbladder emptying.”

Prokinetic agents and gall bladder: metoclopramide


p = NS

GBEF %

Prokinetic agents and gall bladder: erythromycin

Is the enteral nutrition an promotility agent “per se”?  

“..., it has been demonstrated that early enteral feeding after multiple injury diminishes gastric intolerance towards food and promotes speedier establishment of motility in gastroduodenal segment of digestive tract.”

Is the enteral nutrition an promotility agent “per se”?

“..., we have shown that early postoperative gastric supply with liquid isoosmolar enteral formula probably improves gastric emptying...”

Is the enteral nutrition an promotility agent “per se”? 

Is the enteral nutrition an promotility agent “per se”?

“..., we conclude that early postoperative enteral feeding moderately stimulates GB motility ...”

GUIDELINES

Perioperative fasting in adults and children: guidelines from the European Society of Anaesthesiology
Ian Smith, Peter Kranke, Isabelle Murat, Andrew Smith, Geraldine O'Sullivan, Eldar Søreide, Claudia Spies and Bas in't Veld

This guideline aims to provide an overview of the present knowledge on aspects of perioperative fasting with assessment of the quality of the evidence. A systematic search was conducted in electronic databases to identify trials published between 1950 and late 2009 concerned with perioperative fasting, early resumption of oral intake and the effects of oral carbohydrate mixtures on gastric emptying and postoperative recovery. One study on perioperative fasting which had not been included in previous reviews and a further 13 studies published since the most recent review were identified. The searches also identified 20 potentially relevant studies of oral carbohydrates and 53 on early resumption of oral intake. Publications were classified in terms of their evidence level, scientific validity and clinical relevance. The Scottish Intercollegiate Guidelines Network scoring system for assessing level of evidence and grade of recommendations was used. The key recommendations are that adults and children should be encouraged to drink clear fluids up to 2 h before elective surgery (including caesarean section) and all but one member of the guidelines group consider that tea or coffee with milk added (up to about one fifth of the total volume) are still clear fluids. Solid food should be prohibited for 6 h before elective surgery in adults and children, although patients should not have their operation cancelled or delayed just because they are chewing gum, sucking a boiled sweet or smoking immediately prior to induction of anaesthesia. These recommendations also apply to patients with obesity, gastro-oesophageal reflux and diabetes and pregnant women not in labour. There is insufficient evidence to recommend the routine use of antacids, metoclopramide or H2-receptor antagonists before elective surgery in non-obstetric patients, but an H2-receptor antagonist should be given before elective caesarean section, with an intravenous H2-receptor antagonist given prior to emergency caesarean section, supplemented with 30 ml of 0.3 mol l−1 sodium citrate if general anaesthesia is planned. Infants should be fed before elective surgery. Breast milk is safe up to 4 h and other milks up to 6 h. Thereafter, clear fluids should be given as in adults. The guidelines also consider the safety and possible benefits of preoperative carbohydrates and offer advice on the postoperative resumption of oral intake.


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Preoperative feeding and gastric emptying!

5. Preoperative carbohydrates: gastric emptying and potential benefits
Recommendation
It is safe for patients (including diabetics) to drink carbohydrate-rich drinks up to 2 h before elective surgery (evidence level 1++, recommendation grade A).
Preoperative feeding and gastric emptying!

“... we have shown that preoperative feeding ... with carbohydrate-enriched drink before spinal anesthesia does not affect the gastric emptying ...”


Fig. 1. Plasma concentrations of paracetamol (mg/l) at given time points after administration of paracetamol tablets. Group 1, patients fed preoperatively; Group 2, control group.
“... in patients after laparoscopic resection of colorectal cancer preoperative enteral nutrition has accelerated postoperative normalization of gastric emptying.”

“In this model, preoperative CHO loading improved food intake, and intestinal barrier function. Moreover, the biomarkers citrulline and 3-MeHis returned to normal levels. These are distinct parameters reflecting different aspects of intestinal function and well-being.”

Preoperative feeding and postoperative gastric emptying!

Conclusion

“Present evidence strongly suggest that enteral nutrition should be preferred to parenteral nutrition whenever possible, ..., enteral feeding should begin as early as possible, ...”

“... gastrointestinal motility agents appear to have ... benefit ... this leads to improved tolerance to feeds and nutritional indexes and decreased infectious morbidity.”

“..., it seems that overnight fasting should be avoided as much as possible and preoperative fluid administration up to 2 h before induction of anaesthesia is recommended.”
Conclusions

“EN appears to be superior to both PN and standard therapy with no nutritional support across diverse patient populations. When EN is not feasible, aggressive nutritional support may have to be held for 7 to 10 days following an injury or an acute event. These patients, despite critical illness, sepsis, and multiple organ dysfunction, are better managed by standard therapy with no PN support over this initial period.”