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Original article

A randomised controlled feasibility and proof-of-concept trial in delayed gastric emptying when metoclopramide fails: We should revisit nasointestinal feeding versus dual prokinetic treatment Achieving goal nutrition in critical illness and delayed gastric emptying: Trial of nasointestinal feeding versus nasogastric feeding plus prokinetics

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SUMMARY

Background & aims: Delayed gastric emptying (DGE) commonly limits the use of enteral nutrition (EN) and may increase ventilator-associated pneumonia. Nasointestinal feeding has not been tested against dual prokinetic treatment (Metoclopramide and Erythromycin) in DGE refractory to metoclopramide. This trial tests the feasibility of recruiting this 'treatment-failed' population and the proof of concept that nasointestinal (NI) feeding can increase the amount of feed tolerated (% goal) when compared to nasogastric (NG) feeding plus metoclopramide and erythromycin treatment.

Methods: Eligible patients were those who were mechanically ventilated and over 20 years old, with delayed gastric emptying (DGE), defined as a gastric residual volume ≥250 ml or vomiting, and who failed to respond to first-line prokinetic treatment of 3 doses of 10 mg IV metoclopramide over 24 h. When assent was obtained, patients were randomised to receive immediate nasointestinal tube placement and feeding or nasogastric feeding plus metoclopramide and erythromycin (prokinetic) treatment.

Results: Of 208 patients with DGE, 77 were eligible, 2 refused assent, 25 had contraindications to intervention, almost exclusively prokinetic treatment, and it was feasible to recruit 50. Compared to patients receiving prokinetics (n = 25) those randomised to nasointestinal feeding (n = 25) tolerated more of their feed goal over 5 days (87–95% vs 50–89%) and had a greater area under the curve (median [IQR] 432 [253–464]% vs 350 [213–381]%, p = 0.026) demonstrating proof of concept. However, nasointestinally fed patients also had a larger gastric loss (not feed) associated with the NI route but not with the fluid volume or energy delivered.

Conclusions: This is first study showing that in DGE refractory to metoclopramide NI feeding can increase the feed goal tolerated when compared to dual prokinetic treatment. Future studies should investigate the effect on clinical outcomes.

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Glossary

CRRT	continuous renal replacement therapy
DGE	delayed gastric emptying
EN	enteral nutrition
GRV	gastric residual volumes
NG	nasogastric
NI	nasointestinal
PN	parenteral nutrition
SAE	serious adverse events
SAR	serious adverse reactions
TPN	total parenteral nutrition
VAP	ventilator-associated pneumonia

Take home message

Under-nutrition in ICU is associated with poor outcome and commonly caused by delayed gastric emptying (DGE). In patients with DGE refractory to metoclopramide treatment, a higher percentage of goal nutrition is tolerated via intestinal feeding than gastric feeding plus dual metoclopramide and erythromycin treatment.

Tweet

Goal nutrition is better tolerated via intestinal feeding than with gastric feeding plus dual metoclopramide and erythromycin treatment.

1. Introduction

Attempting to meet goal requirements using enteral nutrition (EN) may be associated with reductions in mortality, infection, hospital stay and nutritional deficit [1]. However, delayed gastric emptying (DGE) limits the use of EN and may be associated with increased risk of ventilator-associated pneumonia (VAP) [2]. NI feeding and total parenteral nutrition (TPN) can overcome DGE and may reduce VAP-risk but nasointestinal (NI) EN is cheaper and reduces infection risk [1] by maintaining gut immunocompetence [3].

Delayed gastric emptying (DGE) presents in 30.5% of ICU patients [4]. DGE is associated with increased mortality and time to discharge alive, lower energy and protein input and fewer ventilator-free days after adjustment for age, sex and APACHE score, particularly when it persists >1d or relapses [4]. Cumulative 24 h gastric residual volumes (GRVs) of even 150 mL are associated with objectively measured DGE [5]. However, while DGE is associated with increased retrograde intestinal peristalsis [6] prokinetic drugs such as metoclopramide and erythromycin improve gastric emptying and reduce intolerance due to large GRVs and vomiting [7]. And, the improved intestinal nutrient delivery following erythromycin increases glucose absorption [8] and is tolerated without ileus in most patients on full rate NI feeding [9].

Evidence on whether prokinetics or NI feeding are more effective in over-coming DGE is equivocal. When NI feeding is delayed, nasogastric (NG) feeding delivers more EN during erythromycin treatment [10] and achieved similar EN delivery and clinical outcomes during metoclopramide and erythromycin treatment [11]. Conversely, rapid NI tube placement was associated with greater tolerance (%goal), a smaller cumulative deficit and reduced prokinetic drug use and treatment cost [9].

Treatments are not risk-free. It has been recommended that gastric feeding is not interrupted when the GRV is less than 500 ml but that prokinetic drugs are initiated when GRVs are 200–500 ml [12]. However, prokinetic use is associated with early tachyphylaxis (metoclopramide: 2–3 days; metoclopramide + erythromycin: 6 days) [13] and side-effects (metoclopramide: neurological [14], erythromycin: cardiac and potential bacterial resistance). Conversely, additional 'blind' NI tube placement adds a 1.5% risk of misplacing the tube in the respiratory tract and 0.5% risk of pneumothorax or pneumonia [15].

This is the first trial to test the feasibility of recruiting patients with proven DGE where first-line prokinetic (metoclopramide) treatment has failed. We study the proof-of-concept of whether NI feeding immediately post-randomisation increases the feed goal (%) tolerated compared to NG feeding plus metoclopramide and erythromycin prokinetic treatment. Earlier studies recruited patients 'at risk' of DGE and only confirmed intestinal feeding 15 h after tube placement [11].

2. Methods

This was a randomised, feasibility and proof-of-concept study. Ethical (NRES Committee South Central – Southampton A, REC reference: 12/SC/0530) and Medicines and Healthcare products Regulatory Agency (MHRA) (18524/0221/001-0001) approval was obtained prior to commencement. Intervention blinding was not possible because the research team placed the enteral tubes whilst sham tubes are both discernible and an inherent complication risk.

The study was undertaken at Frenchay Hospital ICU admitting approximately 600 patients per year, 66% non-surgical, a mean APACHE II score of 16 ± 7.2 and overall predicted mortality of 33%. Mechanically ventilated adults receiving EN were eligible at any point post-ICU admission if they had DGE (vomiting or 1 GRV exceeded 250 mL) after first-line prokinetic treatment of three 10 mg doses of IV metoclopramide over 24 h [9]. Based on scintigraphy in critically patients, a GRV of 250 mL in 24 h approximates the lowest threshold at which only patients with DGE will be captured and therefore permits earlier treatment of DGE compared to higher thresholds [5]. Mechanical ventilation was defined as presence of an endotracheal tube or tracheostomy excluding those on CPAP alone or breathing spontaneously. Patients were excluded if prokinetics were contraindicated (erythromycin: on macrolides, metoclopramide: <20y) [1], EN had become contraindicated because the GI tract was not accessible or functional including ileus, active GI bleeding, intestinal obstruction and potential GI ischaemia, EN was considered ineffective when moribund or anticipated EN requirement was for ≤48 h, if the EN goal was unattainable including those with severe malnutrition, short bowel syndrome, substrate intolerance, renal failure (serum creatinine >190uM) and not on continuous renal replacement therapy and hepatic encephalopathy necessitating protein restriction, or where an NI tube was contraindicated due to abnormal anatomy or surgery or was already in situ.

2.1. Recruitment and randomisation

Assent was obtained from relatives or a non-research ICU consultant for study admission until informed patient consent was possible. Researchers numbered each recruit then email requested