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Randomized control trials

Early nasogastric tube feeding versus nil per os in mild to moderate acute pancreatitis: A randomized controlled trial

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SUMMARY

Background & aims: Nasojejunal tube feeding is a standard of care in patients with predicted severe acute pancreatitis (AP) and several recent trials suggested that nasogastric tube feeding (NGT) is as safe and efficient as nasojejunal tube feeding in these patients. The aim was to investigate whether NGT presents any benefit to patients with mild to moderate AP.

Methods: The study design was a randomized controlled trial. The patients in the intervention group received NGT within 24 h of hospital admission. The patients in the control group were on nil per os (NPO). The severity of acute pancreatitis was determined according to the new international multidisciplinary classification.

Results: There were 17 patients randomly allocated to the NGT group and 18 to the NPO group. The visual analogue pain score decreased to a significantly greater extent in the NGT group (from median 9 (range 7–9) at baseline to 1 (0–3) at 72 h after randomization) compared with the NPO group (from 7 (5–9) to 3 (1–4) ($p = 0.036$). The number of patients not requiring opiates at 48 h after randomization was significantly different ($p = 0.024$) between NGT (9/17) and NPO (3/18). Oral food intolerance was observed in 1/17 patient in the NGT group and 9/18 patients in the NPO group ($p = 0.004$). The overall hospital stay in the NGT group was 9 (5–12) days as compared with 8.5 (6–13) days in the NPO group ($p = 0.91$).

Conclusions: NGT commenced within 24 h of hospital admission is well tolerated in patients with mild to moderate acute pancreatitis. Further, when compared with NPO, it significantly reduces the intensity and duration of abdominal pain, need for opiates, and risk of oral food intolerance, but not overall hospital stay (ClinicalTrials.gov number, NCT01128478).

1. Introduction

Acute pancreatitis (AP) is a common digestive disease and the most frequent disorder of the pancreas. There has been a steady increase in the hospitalization rate for AP in the USA and Western Europe over the last several decades.[1,2] A recent US nation-wide study of hospital admissions for AP identified 226,000 admissions for a population incidence rate of 0.78 per 1000 in 2003.[3] The direct cost of these hospitalizations was estimated to be $2.2 billion.[4] Given that two-thirds of the actual cost of treatment in AP is attributable to hospitalization, the consumption of healthcare resources could be significantly reduced by shortening the duration of the hospital stay.[5] Currently, most of the research efforts in AP have been directed towards the important, although relatively small subgroup of patients with severe form of AP. However, efforts to reduce the length of hospital stay in patients with non-severe AP might prove to be particularly cost-effective as they represent up to 85% of all patients with AP.

The usual criteria for hospital discharge of patients with non-severe AP are the resolution of pain and tolerance of oral refeeding. The conventional management of AP involves a nil per os (NPO) regimen until the symptoms (pain) and signs (ileus) of AP have resolved.[6,7] It is customary to commence oral intake with the resumption of clear oral fluids. If this is tolerated the patients are then offered oral food. However, this practice of staged re-introduction of feeding after a sustained period of NPO for AP is reported to be associated with pain relapses and prolonged hospitalization in at least a quarter of patients.[8–11] It is suggested that this is sub-optimal, with considerable room for improvement.

To date, the only strategy to prevent pain relapse after introduction of oral food in patients with AP that has been studied is the use of a long-acting somatostatin analogue.[12,13] In an uncontrolled pilot study, only one of 23 (4.3%) patients treated with one intramuscular injection of lanreotide 30 mg on the day before oral refeeding had

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a recurrence of pain from AP.[12] However, a subsequent randomized placebo-controlled trial did not confirm a beneficial effect of lanreotide on either the incidence of the pain relapse or the total length of hospital stay.[13]

Another possible approach to prevent pain relapse after introduction of oral food is early nasogastric tube feeding (NGT).[8] A randomized controlled trial (RCT) from the UK provided some evidence of a potentially favourable effect of NGT on pain by demonstrating no difference in pain and analgesic requirement between nasogastric and nasojejunal tube feeding in patients with predicted severe AP.[14] Notably, it showed that pain measured by visual analogue score (VAS) decreased markedly from 7 on the first day to 0 on the third day of tube feeding in both groups. However, this has not been studied to patients with non-severe AP, pain relapse has not been the trial endpoint, and the absolute effect of NGT (i.e. in comparison with no nutrition) has not been determined.

The aim of this study was to determine the tolerance and efficacy of NGT versus NPO in patients with mild to moderate AP.

2. Methods

2.1. Study design

This was a prospective randomized controlled trial called the MIMOSA trial (MIld to MOderate acute pancreatitis: early naSogastric tube feeding compared with pAncreas rest). The trial was conducted at a tertiary centre (Auckland City Hospital, Auckland, New Zealand) between May 2010 and April 2011. The New Zealand Northern X Human Ethics Committee approved the study protocol (NTX/08/11/107). The study protocol was also registered at www.ClinicalTrials.gov (NCT01128478).

The inclusion criteria were:

- diagnosis of AP;
- age >18 years;
- written informed consent.

Diagnosis of AP required at least two of the following three criteria:

- abdominal pain suggestive of AP;
- serum amylase and/or pancreatic amylase activity at least three times the upper limit of normal;
- findings of AP on CT (e.g. diffuse or segmental enlargement of the pancreas and/or peripancreatic necrosis and/or pancreatic encrosis).[6]

Patients were excluded if they had:

- symptoms for more than 96 h;
- severe or critical AP;
- chronic pancreatitis (pancreatic calcifications and/or duct abnormalities);
- post-ERCP pancreatitis;
- intraoperative diagnosis;
- pregnancy;
- malignancy;
- received nutrition before randomization (either artificial nutrition or oral feeding);
- previously enrolled into the trial.

Severe or critical AP was defined according to the international multidisciplinary classification of acute pancreatitis severity as the presence of organ failure and/or pancreatic infection at the time of randomization.[15] Organ failure was defined in accordance with the SOFA score as a score ≥2 for at least one of three organ systems, i.e., respiratory, renal without pre-existing renal disease, and cardiovascular.[16] Pancreatic infection was defined as one of the following: gas bubbles within (peri)pancreatic necrosis on CT, or a positive culture from (peri)pancreatic necrosis material obtained by image-guided FNA or during the first drainage and/or necrosectomy.[15]

2.2. Study groups

There were two study groups:

i) Intervention: The patients in the intervention group were initially NPO but received nasogastric feeding that commenced within 24 h of hospital admission via a 10 Fr 109 cm (43″) tube placed into the stomach (CORFLO® – ULTRA, Corpak Medsystems, Wheeling, IL, USA). A commercially available semi elemental tube feed (Peptisorb®, Nutricia Clinical NZ) was used. Enteral nutrition was started at a rate of 25 mL/h and increased stepwise until 100 mL/h was reached over 24–48 h. It was continued until the decision of the treating teams to introduce oral feeding.
ii) Control: The patients in the control group were on an NPO regimen until the decision of the treating teams to introduce oral feeding.

2.3. General patient management

All the patients were managed according to the same clinical care pathway. All clinical decisions were the responsibility of the treating teams. The teams were independent of the principal investigator of the study. In particular, the transition from tube feeding or NPO was their decision alone. In both groups, intravenous fluids and parenteral narcotics were administered at a rate and frequency decided by the treating teams. The treating teams were also responsible for charting all the medications, including analgesia, in which case they were supported by a dedicated hospital pain team. The treating teams were advised that in order to be discharged each patient should meet three criteria for at least 24 h: tolerance of oral food; no abdominal pain; and no use of opioid analgesics.

2.4. Endpoints

The primary endpoint was the total length of hospital stay.
The secondary endpoints were:

- presence of oral food intolerance;
- time from admission until tolerance of oral food;
- time from oral refeeding until hospital discharge;
- time from admission until minimal or no pain;
- opiate requirements;
- change in pain intensity;
- progression of AP severity;
- number and type of interventions during hospital stay;
- in-hospital mortality;
- hospital readmission.

2.5. Definitions

The symptoms of patients were monitored until discharge by means of a detailed daily patient diary. Oral food intolerance was defined as putting the patient onto an NPO regimen because of pain relapse, nausea, or vomiting after introduction of oral food.[17,18]