**ORIGINAL ARTICLE**

**Early Nasogastric Enteral Nutrition in Acute Pancreatitis**

Ahmed Nurus Sami, Naseer Khan, Hamid Rasheed Goreja

**ABSTRACT**

**Objective:** To evaluate the effectiveness and safety of early Nasogastric Enteral Nutrition in patients with Acute Pancreatitis

**Study Design:** Randomized controlled trial.

**Place and Duration of Study:** The study was conducted at IIMC Hospital Islamabad, and Railways Hospital Rawalpindi from June 2008 to April 2011.

**Materials and Methods:** A total of 26 patients were studied over the course of 34 months who were admitted with the diagnosis of acute pancreatitis. Patients were divided randomly in two equal groups by consecutive sampling method. One group was given enteral nutrition (EN) through nasogastric tube beginning within 24 hours of admission (group-I), and the other group was provided nutrition through parenteral route (PN) only (Group-II). Outcome in the two groups such as length of hospital and ICU stay, infective complications, nutrition related complications, metabolic and catheter related complications were compared.

**Results:** Baseline of the study regarding infective complications and mortality were comparable. Average hospital stay was shorter by 22.3% in enteral-ly fed group. ICU stay was also shorter in group-I patients. Significant difference was seen in relief of abdominal pain amongst the two groups, enteral-ly fed (group-I) patients had earlier relief of pain starting on the 3rd day, compared to 5th day in group-II. Majority of the patients in group-I (84.5%) had pain relief between 4th and 9th day, while in group-II, 76.8% had pain relief between 7th and 12th day. Mean pain relief in enteral-ly fed patients was in 7.5 days and in parenteral nutrition group in 10.2 days. Nutrition related complication of diarrhoea was noted in 2 enterally fed patients. Metabolic complications (hyperglycaemia), and catheter related septic complications were seen only in parenterally fed patients. Acute pseudocyst formation occurred in one patient of enterally fed group as noted on follow up.

**Conclusion:** Early enteral nutrition is safe and effective in the management of acute pancreatitis. Enteral-ly fed patients show advantage of shorter hospital and ICU stay, and earlier relief of symptoms compared to patients managed on parenteral nutrition. Our study considers early enteral nutrition feasible and desirable.

**Key Words:** Acute pancreatitis, Early enteral nutrition, Total parental nutrition.

**Introduction**

Acute pancreatitis (AP) ranges from a mild and self-limiting disease (80%) which usually resolves spontaneously within days, to a rapidly progressive fulminant illness with significant morbidity and mortality.\(^1,2\)

The clinical course of an attack of acute pancreatitis varies from a short period of hospitalization with supportive care to prolonged hospitalization and admission to an Intensive Care Unit (ICU) due to the development of systemic inflammatory response syndrome (SIRS), multi-organ failure (MOF), and septic complications. Acute malnutrition is expected to increase morbidity and mortality due to impaired immune function, increased risk of sepsis, poor wound healing, and multiple organ failure.\(^3\) Nutritional management for acute pancreatitis is an important issue and has always been regarded as a vital part of treatment.

Traditional teaching has been that the management of acute pancreatitis begins with “pancreatic rest,” due to the assumption that stimulation of pancreas by food intake during acute phase would exacerbate the inflammatory process by releasing more enzymes. Avoidance of oral intake to prevent inappropriate stimulation of pancreas was therefore considered necessary. The validity of this concept of “pancreatic rest” is heavily debated.\(^4,5,6\)

Pancreatic inflammation is followed by the
absorption of endotoxins from the intestine due to bacterial translocation, which over stimulates the already primed immune system, excessive absorption of endotoxins occurs in acute pancreatitis.\textsuperscript{7,8,9} These \textcite{SamaH, UedaT, Take yaway et al} found a significant positive correlation between intestinal mucosal permeability and changes in endotoxins and tumor necrosis factor-$f_{IL}$, also that the severity of disease and septic complications were positively associated with the severity of gut mucosal damage.\textsuperscript{10} Intestinal permeability was seen to be increased in severe acute pancreatitis, intestinal permeability correlated with endotoxins absorption and bacterial translocation.\textsuperscript{9} The current hypothesis is that the gut-derived bacteria translocate due to a combination of pathophysiological events which are disturbed gastrointestinal motility, bacterial overgrowth, reduction of arterial blood flow, increased permeability of the gastrointestinal mucosal barrier and bacterial translocation, leading to distant systemic infections, including infection of peripancreatic area and infectious pancreatic necrosis.\textsuperscript{12,13}

Integrity of the mucosal barrier depends not only on a good blood supply, but also gastrointestinal hormones and presence of nutrients in the lumen. As the mucosal cells derive almost all their nutrients from the gut lumen wide spread mucosal atrophy occurs in patients on total parenteral nutrition due to lack of hormones and nutrients in the lumen.\textsuperscript{14,15} These trials concluded that enteral nutrition was associated with fewer infectious complications and lower cost than parenteral nutrition.\textsuperscript{16,17,18,19} TPN has its own problems although it is very effective in maintaining nutrition in almost any critically ill patient, it can cause serious complications in particular, catheter related sepsis and hyperglycemia.\textsuperscript{20}

Initially it was suggested that to ensure full pancreatic rest, nutrition tubes should be placed in the jejunum.\textsuperscript{21,22} In the past few years, it has been proposed that enteral nutrition through nasogastric tubes may be a simple, safe and equally valid alternative to nasojejunal tubes, with the potential advantage of earlier administration of nutrients.\textsuperscript{23,24}

The purpose of our study was to evaluate the effectiveness and safety of early enteral nutrition within 24hrs of admission in patients of acute pancreatitis as compared to the current practice of total parenteral nutrition for 72 hrs. Nasogastric intubation was preferred to nasojejunal intubation because it was considered just as safe in earlier studies and simpler to place without the involvement of endoscopy or fluoroscopy.\textsuperscript{23}

**Materials and Methods**

A total of 26 patients were studied over the course of 34 months from June 2008 to April 2011 at IIMC hospital Islamabad, and Railways Hospital Rawalpindi, admitted with a diagnosis of acute pancreatitis and who fulfilled the inclusion criteria of the study. The patients were divided randomly into two groups in equal numbers by consecutive sampling method. On admission detailed history taking and physical examination was done. Complete blood count, serum lipase, serum amylase, triglyceride, abdominal ultrasound and contrast enhanced spiral CT abdomen was done to detect pancreatic oedema, necrosis and possible abscess formation. Ranson score was calculated. Patients with score $<3$ were considered to have mild pancreatitis, score $3-5$ moderate pancreatitis. While those with Ranson score $>5$ were classified as severe acute pancreatitis. Patents were
monitored and reassessed every day thereafter by clinical examination and necessary blood tests.

Inclusion criteria were diagnosis of acute pancreatitis if at least 2 of the 3 following features were present: 1) Upper abdominal pain, 2) Serum lipase or Amylase levels three times above the upper level of normal and 3) Characteristic findings of acute pancreatitis on abdominal CT.

Exclusion criteria were 1) History of acute or chronic pancreatitis. 2) Diagnosis of pancreatitis > 24 hours after admission. 3) Onset of symptoms > 96 hours (4 days) before admission. 4) Acute pancreatitis due to malignancy 5) Post-ERCP pancreatitis. 6) Acute pancreatitis post surgery. 7) Pregnancy.

All patients received prophylactic antibiotics, fluid and electrolyte management, in addition to analgesics. ERCP was done where required for biliary pancreatitis. Blood sugar was monitored and adjusted by insulin on sliding scale.

Patients in group-I were given enteral nutrition (EN) through nasogastric tube beginning within 24 hours after admission, with a target of approximately 1.5 g protein/Kg/day, and 20 Kcal energy/Kg/day by hourly feeding. Feeding was commenced at 20ml/hr and increased progressively to goal rates. 'Ensure powder' from Abbot Laboratories was used as a supplement which provided 1Kcal energy/ml and proteins 15.9gms/100ml. In addition clear fluids such as water, tea, green tea and fruit juices were permitted orally if patient desired.

Patients in group-II were kept nil by mouth and on total parenteral nutrition (TPN) through central venous line, and oral diet was started 72 hours after admission if tolerated, and no complication had occurred.

Time of pain relief was measured by visual analogue scoring system 1-10. Pain was considered severe for score 6-10, moderate 3-5, and mild for score less than 3. Pain was considered relieved if patient scored 0-1.

Outcome in the two groups were compared regarding mean time of hospital stay, mean time of ICU stay, infective complications such as intra abdominal sepsis and infective pancreatic necrosis. Catheter and nutrition related complications such as diarrhea, and metabolic complications such as hyperglycemia were noted. Pseudocyst formation if any was noted on follow up (Table I).

Table I: Characteristics of 26 patients included in the study

<table>
<thead>
<tr>
<th>Demography</th>
<th>Group-I (Enteral feeding)</th>
<th>Group-II (Parenteral feeding)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male/Female</td>
<td>Male/Female</td>
</tr>
<tr>
<td>Age (Year)</td>
<td>128</td>
<td>146</td>
</tr>
<tr>
<td>Multimorbid pancreatitis</td>
<td>10 (38.5%)</td>
<td>9 (35.2%)</td>
</tr>
<tr>
<td>Severe pancreatitis</td>
<td>3 (23.0%)</td>
<td>4 (30.7%)</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Biliary</td>
<td>9 (69.2%)</td>
<td>17 (76.9%)</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>3 (23.0%)</td>
<td>2 (15.8%)</td>
</tr>
<tr>
<td>Amylase on admission average</td>
<td>410 U/L, 382 U/L</td>
<td></td>
</tr>
<tr>
<td>Lipase on admission average</td>
<td>965 U/L, 890 U/L</td>
<td></td>
</tr>
</tbody>
</table>

Results

A total of 26 patients were studied randomly divided into two groups as shown in Table I. Group-I receiving enteral nutrition (EN) through NG tube starting within 24 hours of admission, and Group-II received total parenteral nutrition (TPN) for at least 72 hours after admission

Baseline of each trial was comparable. There was no significant difference in mortality and morbidity between the group fed enterally by nasogastric tube soon after admission (group-I) and the group on TPN for 72 hours after admission (group-II) (Table II).

Average hospital stay was 9.8 days in group-I, and 12.6 days in group-II. In group-I, 9 patients were nursed in ICU, and the mean
day. Mean pain relief in group-I was in 7.5 days, while in group-II it was in 10.2 days.

Discussion

Acute pancreatitis is a life threatening catabolic condition secondary to marked inflammatory response. Over the years several strategies were found ineffective in improving the outcome for patients with severe pancreatitis.\textsuperscript{23,24} In the absence of a known specific therapy that can counteract pancreatic inflammatory cascade, ICU management and nutritional support have emerged as the two vital measures in first few weeks of disease.

Optimal nutritional support can help improve the associated comorbidities.\textsuperscript{25,26} Nutritional support in severe acute pancreatitis can be achieved by parenteral or enteral routes. Early enteral nutrition has been regarded in the past as an unsafe nutritional support route in view of the pancreatic-rest theory in the management of acute pancreatitis due to the simple belief that stimulation of pancreas by food intake during acute phase would exacerbate the inflammatory process by releasing more enzymes. Parenteral nutrition was therefore proposed as the modality of choice. PN however resulted in increased infectious and metabolic complications as confirmed by various randomized clinical trials comparing EN with PN.\textsuperscript{26,27} These trials concluded that EN was associated with fewer complications.\textsuperscript{28} EN was found to be the only strategy effective in preventing complications in acute pancreatitis.\textsuperscript{29}

<table>
<thead>
<tr>
<th>Table II: Comparison of clinical features and complications of 26 patients included in the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Features and Complications</td>
</tr>
<tr>
<td>-------------------------------------</td>
</tr>
<tr>
<td>Hospital stay mean days</td>
</tr>
<tr>
<td>ICU stay mean days (number of patients admitted in ICU)</td>
</tr>
<tr>
<td>Relief of pain mean days</td>
</tr>
<tr>
<td>Intra abdominal sepsis</td>
</tr>
<tr>
<td>Infective pancreatic necrosis</td>
</tr>
<tr>
<td>Acute Pseudocyst formation</td>
</tr>
<tr>
<td>Hypoglycemia &gt;200 mg/dL</td>
</tr>
<tr>
<td>Diarrhoea</td>
</tr>
<tr>
<td>Catheter related sepsis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table III: Time required for pain relief in both study groups (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time taken for pain relief (days)</td>
</tr>
<tr>
<td>----------------------------------</td>
</tr>
<tr>
<td>Up to 3</td>
</tr>
<tr>
<td>4-6</td>
</tr>
<tr>
<td>7-9</td>
</tr>
<tr>
<td>10-12</td>
</tr>
<tr>
<td>12-14</td>
</tr>
</tbody>
</table>

stay time was 7 days, while in group-II, 8 patients were admitted in ICU for a mean of 9 days.

There was no death in either group. Rate of infective complications was similar in the two groups; 2 patients from group-II and 1 patient from group-I developed intra abdominal sepsis in the peripancreatic area as found on CT examination. Infective pancreatic necrosis did not occur in any patient in either group.

Diet related complication (diarrhoea) occurred in 2 patients who were on enteral nutrition (group-I), this complication was not seen in group-II. In two patients in enteral fed group who developed an ileus, temporary reduction in the volume of oral feed was done for two to three days because of fullness and nausea.

In group-II, 3 patients developed hyperglycemia >200mg/dL, and 1 patient had catheter related sepsis, these complications were not seen in group-I.

Acute pancreatic pseudocyst developed in 1 patient in group-I as found on the fifth week during follow up. (Table II)

Early relief of abdominal pain was noted in group-I (Table III). Pain relief began on the third day in enterally fed patients (7.6%), while in patients on PN pain relief began on the 5th day. In group-I, 11 patients (84.5%) had pain relief between 4th and 9th day, while in group-II relief was obtained by majority of patients i.e. 10 (76.8%) between 7th and 12th
Windsor et al demonstrated that acute phase response and high serum antibody levels noted in PN managed patients were suppressed in enterally fed external nutrition patients.\textsuperscript{32} Integrity of the mucosal barrier depends not only on a good blood supply, but also gastrointestinal hormones and presence of nutrients in the lumen. Since mucosal cells derive almost all its nutrients from the gut contents, wide spread atrophy of mucosal cells occurs in patients on TPN.\textsuperscript{14,15} Interestingly, a study by Rahman et al found that severe acute pancreatitis was associated with decrease in both intestinal mucosal blood flow and the intestinal beneficial bacteria \textit{Lactobacilli} and \textit{Bifidobacteria}.\textsuperscript{73} Whether the protective effects of enteral nutrition in patients with severe acute pancreatitis are related to its effects on intestinal mucosal blood flow and/or intestinal bacterial flora remains unknown. It is most likely due to the ability of enteral nutrition to maintain gut function that it prevents bacterial overgrowth as well as endotoxins production and absorption, resulting in reduction of parenteral nutrition associated complications.

Eatock et al first introduced early nasogastric feeding into nutritional management of severe acute pancreatitis.\textsuperscript{34} Then Pandey et al experimented oral feeding in patients with severe acute pancreatitis, suggesting that nasogastric feeding is feasible in up to 80\% cases.\textsuperscript{35} Current literature suggests that enteral nutrition is superior to parenteral nutrition in decreasing infectious complications, length of hospital stay, and mortality.\textsuperscript{36} Enteral nutrition is preferred to parenteral nutrition for improving patient outcomes,\textsuperscript{37} and has largely replaced the parenteral route.\textsuperscript{38}

This study was intended to find the feasibility and safety of early nasogastric enteral nutrition compared to total parenteral nutrition in the management of acute pancreatitis. We have found early enteral nutrition not only feasible and safe, but having favorable outcome in certain aspects compared to management on parenteral nutrition.

In our study hospital stay of patients on enteral nutrition (group-I) was significantly less (22.3\%) than those on TPN (group-II) which also translates into reduced expenses incurred on treatment, although the cost figure was not calculated not being an objective of this study. This is consistent with the study of kalfarentzos et al who found that hospital stay of patients on enteral nutrition was shorter than those on TPN.\textsuperscript{39} Mean ICU stay in group-I was shorter by 2 days (7 days) compared to group-II (9 days).

There was no significant difference in infective complications. Incidence of intra-abdominal sepsis was similar in either group (Table II). There was no mortality, and no case of infective pancreatic necrosis occurred in either group.

Acute pancreatic pseudocyst occurred in one patient of group-I and none in group-II. This is consistent with the findings of Eckerwall GE et al, who has concluded that incidence of some late complications may be higher in early nasogastric enteral nutrition group.\textsuperscript{40}

In this study we found patients on enteral nutrition to have significant advantage on patients on TPN regarding earlier pain relief. Relief of abdominal pain as noted by visual analogue scale was in mean 7.5 days in group-I patients, while it occurred in mean 10.2 days in group-II.

Main adverse effect of enteral nutrition support was diarrhea, which was noted in 2
enterally fed patients (group-I). It was easily managed by reducing oral intake for two to three days; none of the patients in group-II had this complication. Hyperglycemia >200 mg/dl was seen in 3 patients in group-II. Catheter related sepsis was also seen in one patient with centeral venous line in group-II. Metabolic and catheter related complications were not seen in any group-I patient. Early nasogastric enteral nutrition was found to be safe and practical in our study. None of the patients had to be shifted to TPN from enteral nutrition, although in some cases the quantity of NG intake had to be reduced for a few days due to diarrhoea, ileus and nausea.

Conclusion
This study found early enteral nutrition effective and safe in patients of acute pancreatitis. Early initiation of enteral nutrition was found to be associated with earlier relief of abdominal pain, shorter length of hospital stay, and shorter ICU stay. We conclude that it is superior to PN for improving patient outcomes and is clinically beneficial.

References
2. Pandol SJ, Saluja AK, Imrie CW, Banks PA. Acute pancreatitis bench to the bedside Gastroenterology. 2007; 132; 1127-51
17. McClave SA, Greene LM, Snider HL. Comparison of the safety of early enteral vs parenteral in mild acute pancreatitis. JPN J


25. Bai Y, Gao J, Zou DW, Li ZS: Prophylactic Antibiotics Cannot Reduce Infected Pancreatic Necrosis and Mortality in Acute Necrotizing


