

# Enteral nutrition and acute pancreatitis

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## INTRODUCTION

Acute pancreatitis (AP) is a common severe illness of the digestive tract with variable involvement of other regional tissues and/or remote organ systems<sup>[1-3]</sup>. Mild disease is associated with minimal organ dysfunction and rapid recovery, while severe disease is associated with multiple organ system failure and local complications such as necrosis, abscess, fistulas and pseudocyst formation<sup>[4-6]</sup>. Mild attacks account for 80% of hospital admissions for this condition and usually resolve in 5 to 7 days. Twenty percent of patients with severe acute pancreatitis (SAP) tend to have a more protracted hospital course with higher mortality, and are more likely to require a multidisciplinary treatment that includes Nutritional support<sup>[7-9]</sup>. Nutritional support in the patients with AP is both very critical and more complex. In the past years, parenteral Nutrition (PN) was recommended for patients with AP<sup>[10,11]</sup>, but recently, significant progress has been achieved in the field of enteral Nutrition (EN)<sup>[12,13]</sup>. Clinical research has shown that early delivery of Nutrition via the gastrointestinal tract after severe injury can reduce septic morbidity in critically injured patients<sup>[14-18]</sup>. Enteral diets have been reported to decrease Gut permeability and maintain mucosal immunity and Gut-associated lymphatic tissue (GALT)<sup>[19-21]</sup>. These observations provide new insights into the use of EN. Therefore, more and more clinicians have begun to use this technique for patients with AP. This review examines metabolic alterations of AP and effects on pancreatic secretion of EN, evaluates the indications, feeding access and formulas of EN, and assesses the clinical role of EN in AP.

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## METABOLIC ALTERATIONS AND AP

The metabolism of AP is very similar to sepsis, and is characterized by hyperdynamic changes, hypermetabolism, and catabolism. The hyperdynamic changes include increased cardiac output, decreased systemic vascular resistance, and an increase in oxygen consumption<sup>[22]</sup>. Hypermetabolism is seen in the majority of the patients<sup>[23]</sup> and is associated with increases in measured resting energy expenditure (REE) as high as 139% of that value predicted by the Harris-Benedict equation (HB). Bouffard *et al* demonstrated that total energy expenditure was 1.49 times of the predicted resting energy expenditure using the Harris-Benedict equation in patients with SAP<sup>[24]</sup>. A variety of factors affect the REE from one patient to the next, or even the same patient during his or her hospital course. Sepsis N complicating pancreatitis may independently raise energy expenditure further. In one study, development of sepsis led to an increase in mean measured REE from 105% to 120% of the HBREE<sup>[23]</sup>. However, this is not a uniform finding of the hypermetabolism across the entire patient population. Dickerson *et al*<sup>[23]</sup> found that 38% of a group of pancreatitis patients were normometabolic (measured REE = HBREE $\pm$ 10%), and 10% were actually hypometabolic (measured REE < 90% of the HBREE). With the variation of REE between patients with AP and with so many factors that can affect ultimate cumulative energy expenditure, indirect calorimetry may be useful to the clinician to measure caloric requirement accurately<sup>[23,24]</sup>. Catabolism is another important metabolic alteration in AP. Isotope techniques have been used to demonstrate that patients with SAP have a significantly higher urea production compared with controls, indicating both increased protein catabolism and diminished muscle protein synthesis. The resultant negative nitrogen balance is, therefore, a net effect of both of these changes<sup>[25]</sup>. Catabolism and proteolysis of skeletal muscle protein raises concentrations of aromatic amino acids, decreases levels of branched-chain amino acids, and accelerates ureagenesis. Nitrogen levels (from urea) in urine may increase up to 20-40 g·d<sup>-1</sup><sup>[26]</sup>. Overall, the circulating pool of amino acids decreases to as low as 40% of normal levels. Circulating glutamine levels in the serum may drop to as low as 55% of normal levels, while levels in skeletal muscle may drop to as low as 15% of normal levels<sup>[26]</sup>.

Errors in carbohydrate and fat metabolism also occur with AP, and may or may not be associated with underlying chronic pancreatitis. This may result from increased cortisol and catecholamine

secretion in the stressed state (which leads to an increase in the glucagon/insulin ratio), impaired beta-cell function, and insulin resistance. Gluconeogenesis is increased, while glucose clearance and oxidation are diminished. In AP, glucose intolerance occurs in 40%-90% of cases, and insulin is required in as many as 81% of patients. Isotope techniques have been used to demonstrate that patients with severe disease have an impaired ability to oxidize glucose compared with controls. Exogenous glucose infusion causes almost complete suppression of gluconeogenesis from protein in normal subjects, but not in patients with AP. These changes are consistent with a state of hepatic insulin resistance, and are similar to those observed in patients with sepsis<sup>[27,28]</sup>. Micronutrient and vitamin deficiencies (such as hypocalcemia, hypomagnesemia, lower zinc levels, and thiamine and folate deficiencies), may also be present on admission or develop during hospitalization. Hypocalcemia occurs most often in as many as 25% of patients, presumably related to decreased parathyroid hormone secretion, increased stimulation of calcitonin, hypomagnesemia, and hypoalbuminemia<sup>[22-31]</sup>. The effects of increased metabolic demands are compounded by an inability or reluctance to maintain an adequate oral intake, so that patients become malnourished during the course of their illness. Malnutrition may be especially apparent in those who have an acute outbreak of chronic pancreatitis, because some patients with chronic alcoholic pancreatitis may also have suffered nutrient deficiencies.

In recent studies, the disease and its complications and metabolic changes have been associated with the release of cytokines and other mediators of inflammation, such as interleukin-1 (IL-1), IL-6, IL-8, tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) and platelet-activating factor<sup>[32-36]</sup>. In addition, researchers have reported activation of the complement cascade, release of oxygen-derived free radicals and nitric oxide, and generation of prostaglandin E<sub>2</sub> and thromboxane A<sub>2</sub> from the metabolism of arachidonic acid<sup>[37,38]</sup>. These cytokines and mediators may cause systemic inflammatory response syndrome (SIRS), which in turn promotes a series of metabolic alterations and multiple organ failure<sup>[39]</sup>. If prolonged and combined with starvation, these changes can lead to a rapid loss of lean body mass, associated morbidity, and death<sup>[40]</sup>. Increased intestinal permeability in animals<sup>[41-44]</sup> and humans<sup>[45]</sup>, along with an associated impaired Gut barrier function, may lead to translocation of bacteria and endotoxins from the Gut lumen into systemic circulation<sup>[46]</sup>, which contributes to the release of cytokines and systemic inflammatory responses. Experimental animal work has indicated that EN may prevent bacterial translocation in AP<sup>[47]</sup>.

#### EFFECTS OF EN ON PANCREATIC SECRETION

The key pathological mechanism of AP is

autodigestion of the pancreas and peripancreatic tissues by pancreatic enzymes. Oral and nasogastric feeding increases pancreatic secretion by stimulation of the cephalic and gastric phase, and it is suggested that early oral feeding may lead to recurrence of symptoms, elevations of serum amylase and lipase, and delayed complications<sup>[48,49]</sup>. In a study of 8 patients with AP, it was found that the interdigestive secretions of the exocrine pancreas were not different, within 72 h of the onset of mild to moderate disease, from those in 26 normal controls. Based on this evidence, the authors propose early inhibition of pancreatic secretion with somatostatin in the acute phase of the illness<sup>[50]</sup>. Animal studies<sup>[51,52]</sup> show that "pancreatic rest" reduces pancreatic synthetic activity and basal proteolytic and bicarbonate secretions, but evidence from human studies is less certain. A retrospective study suggests that early oral feeding predisposes patients to major peripancreatic infections, while prolonged nasogastric suction reduces the incidence of these infections<sup>[53]</sup>. However, randomized controlled studies<sup>[54]</sup> in patients with mild to moderate AP have, failed to establish the value and efficacy of putting the pancreas to rest by avoiding exocrine secretion. The definition of the pancreatic rest is variable. There are three main fluid volumes of pancreas juice: protein enzymes, and bicarbonate, which have different functions and reactions to stimulations. Of them, protein enzyme output is thought to be responsible for the autodigestion of the gland and perpetuation of the inflammatory process. One study showed that reducing the protein enzyme output from pancreas while stimulating fluid volume and bicarbonate output put the pancreas to rest. From the available studies, in spite of some controversies, the reduction of pancreatic secretion or "putting the pancreas to rest" is necessary when dealing with the patients with AP in clinical practice.

The issue of whether or not the EN can successfully put the pancreas to rest is considerably more complex and controversial. In an early study in dogs, Ragins *et al*<sup>[55]</sup> demonstrated that intragastric delivery of nutrients (Vivonex) caused an increase in the volume, and protein content, and bicarbonate content of pancreatic secretions compared with those in saline-infused controls. Intraduodenal feeding only increases the volume of pancreatic secretions, but does not affect protein or bicarbonate secretion. In contrast, jejunal infusion showed no increase in any of the three components of pancreatic secretion. Other studies of dogs<sup>[56,57]</sup> also show that the intraduodenal delivery of elemental diets or pure amino acid solutions significantly increases pancreatic secretions, suggesting that the amino acid content of elemental diets is responsible for the stimulatory effects. In contrast, intrajejunal administration of nutrients is not associated with a significant change in the volume, protein content, or bicarbonate content of pancreatic secretions compared with controls.

Keith<sup>[58]</sup>, in a study of two patients with chronic pancreatitis, reported changes in volume and amylase output in response to the intrajejunal infusion of an elemental formula. Keith concluded that bypassing the stomach, thereby minimizing acid secretion, played an important role in keeping the pancreas at rest. In direct contrast, other studies showed stimulation of pancreatic enzyme secretion in response to jejunal feeds<sup>[59,60]</sup>.

Another factor affecting pancreatic secretion is the kind of feeding formulas. A study<sup>[59]</sup> on volunteers fed either an elemental diet or a food homogenate (via a nasoenteral tube placed at the duodenojejunal flexure) indicates that the latter has a greater stimulatory effect on the secretion of pancreatic lipase and chymotrypsin than the former. The authors suggest that this difference might be related to the greater nitrogen content of the food homogenate. Grant *et al*<sup>[61]</sup> demonstrated the effect of jejunal infusion of a formula with long-chain fat in a postoperative patient with an isolated duodenal fistula. Infusion of Osmolite into the jejunum resulted in a significant increase in lipase output, but no changes in amylase, bicarbonate, or fluid volume. Infusion of either Vinonex or Criticare, which are nearly fat-free, showed no significant increase in any component of pancreatic secretion. Similarly, Cassim and Allardyce<sup>[62]</sup>, using a dog model, showed that an intact protein blended diet infused into the jejunum increased volume enzyme output, while an elemental formula increased only volume and bicarbonate with no change in protein enzyme output. Bodoky *et al*<sup>[63]</sup> randomized 12 patients undergoing pylorus-preserving pancreaticoduodenectomy for chronic pancreatitis. The patients received either EN via a needle catheter feeding jejunostomy (7 patients) or PN (5 patients). A catheter placed during operation in the pancreatic duct was used to collect pancreatic secretions. The authors found that evidence of the disease was mainly apparent in the pancreatic head and that the function of the pancreatic remnant was near normal. They did not find any difference in the volume of pancreatic secretions or the content of bicarbonate, protein, chymotrypsin or protein amylase between the two groups. Recently, a study<sup>[64]</sup> compared the effects of an elemental diet with an immune-enhancing formula administered by a jejunal route on pancreatic secretions after Whipple pancreaticoduodenectomy. The authors found a small but significant increase in pancreatic enzyme and bicarbonate secretion after jejunal feeding compared with the fasting state, but there was no significant difference in pancreatic enzyme output when the effects of the elemental and immune-enhancing feeds were compared.

Summarizing available evidence from both human and animal studies, one may conclude that oral, intragastric and intraduodenal feeding produce a significant stimulation of pancreatic secretions. In contrast, intrajejunal feeding has a smaller stimulatory effect. Elemental formulas (with

individual amino acids and nearly fat-free) clearly cause less stimulation than standard formula with intact protein and long-chain fat. Therefore, intrajejunal feeding is the rational route of EN for patients with AP.

#### EN NECESSITY AND AP

Eighty percent of patients admitted for AP exhibit mild signs of symptoms of the disease, which usually has a self-limiting hospital course and is managed by intravenous fluid resuscitation and analgesia. These patients are likely to return to an oral diet within 7 days. The remaining 20% of patients admitted with SAP tend to have a more protracted hospital course, these patients have a more prolonged gastroduodenal atony, an increased risk for complications, and require surgical operations. This latter group is more likely to require Nutritional support by the enteral and/or parenteral route. Thus, it is necessary to identify the severity of AP before recommending enteral feeding. A variety of scoring systems has been devised to determine severity of AP and may actually be more accurate than clinical assessment. The Acute Physiology and Chronic Health Evaluation (APACHE) II scoring system<sup>[65]</sup> and Ranson criteria<sup>[66,67]</sup> are two of the more useful scoring systems. Patients with a Ranson score of 2 or less or an APACHE II score of 9 or less are identified as having mild pancreatitis. In these cases, Nutritional support is considered unnecessary unless complications develop or the score begins to increase. In contrast, patients who score 3 or greater on the Ranson criteria scale or 10 or greater on the APACHE II scale, may be identified as having SAP and should be considered for Nutritional support particularly if the score increase in the first 48 h. The intrajejunal route of enteral feeding is the best, unless patients present with shock, massive bleeding of the gastrointestinal tract, intestinal obstruction, jejunum fistula or severe enteroparalysis.

#### ENTERAL ACCESS AND AP

There are three main categories of enteral access for patients with AP: ① nasojejunal tube, ② percutaneous gastrostomy/jejunostomy tube and ③ surgical jejunostomy with gastrostomy<sup>[68,69]</sup>. The choice of the route depends upon the phase of the disease and available expertise. During the early phase, resuscitation is the priority, and obtaining the access at this time must be weighed against the risk. Once the patient is believed to be stable, initial attempts at enteral feeding are probably reasonable. The first choice should be placement of a nasojejunal tube, because this technique is not invasive and easy to perform. The tube can be placed by using blind, pH, fluoroscopic and endoscopic-assisted techniques<sup>[70]</sup>. However, the endoscopic technique is a more popular method in clinical practice. One distinct advantage of endoscopic placement is that it can be performed at the bedside. An endoscopic placement method for

long nasojejunal tubes was described by Berger and Papapietro<sup>[71]</sup>. In 24 patients with AP, 28 tubes were placed using this method. In 15 patients with brain damage, traditional nasojejunal feeding tubes were placed without endoscopy. The position of both types of tubes was determined by fluoroscopy with the aid of contrast media. The results showed that the endoscopic placement method was simple and the tube was placed beyond the ligament of Treitz in all patients. No traditional tube was placed in the jejunum and contrast media filled the duodenum in all cases. The authors suggest that nasojejunal tubes can be easily placed beyond the ligament of Treitz with endoscopic aid and can be used for enteral feeding in patients with AP. Recently, Salasidis *et al*<sup>[72]</sup> introduced an air insufflation technique for placing the nasojejunal tube, reporting successful placement in 32 patients. This technique can also be used at patients' bedside<sup>[73]</sup>.

Patients with gastroparesis and high nasogastric tube outputs may be good candidates for a combined gastric decompression / nasojejunal feeding tube. However, this kind of tube is more difficult to place and can be easily dislodged.

Patients who develop complications (pneumonia, ARDS) with protracted needs for enteral support may be candidates for percutaneous enteral access. For most patients with AP, a combination of percutaneous endoscopic gastrostomy and jejunostomy should be used for simultaneous gastric decompression and jejunal feeding<sup>[74]</sup>. The percutaneous gastrojejunostomy can also be performed by radiologically-guided method, which has a higher success rate and fewer complications<sup>[75]</sup>. In some patients, a direct percutaneous endoscopic jejunostomy technique<sup>[76]</sup>, which allows placement of tubes directly in the jejunum with a success rate of around 85% and a minimal complications, is also a choice for enteral feeding.

Surgical jejunostomy is indicated for the patients requiring operations. There are many techniques used for jejunostomy: Witzel, Stamm, Marwedel, open gastrojejunostomy, needle catheter technique, and laparoscopy<sup>[12,77]</sup>. Among them, needle catheter jejunostomy is attractive for short-term (<4-6 wk) use. Myers JG *et al*<sup>[78]</sup> studied this technique in 2022 cases and reported a rate of 1.55% for technique complications. For long-term use, the Witzel or Marwedel jejunostomy with 14, 16 or 18F catheters is the most (it more than 3) popular technique. One advantage of the large-bore tube is the easy administration of both enteral feedings and medications. Also, once the tube has been in place for approximately a week, it can be easily replaced should it become occluded or inadvertently dislodged<sup>[21]</sup>. No matter which kind of jejunostomy technique is used, it is necessary to perform a gastrostomy, allowing simultaneous gastric decompression and jejunal feedings.

## ENTERAL FORMULAS AND AP

Numerous enteral formulas are available today to meet various needs. They are generally classified as elemental (monomeric), semi-elemental (oligomeric), polymeric or specialized formulas<sup>[12]</sup>. All of these formulas contain varying concentrations of proteins, carbohydrates, and fats, depending on the patient's disease state. A number of factors such as paralytic ileus, glucose intolerance, fat intolerance with hypertriglyceridemia, and pancreatic enzyme deficiency, should be considered when selecting the enteral products for the patients with AP. In view of the metabolic features of AP, elemental diets (so-called chemically defined diets) should be considered as the first option. Although there is some variation among products, most elemental diets are lactose-free, are nearly fat-free (only 2%-3% of calories are derived from long-chain fat), and contain protein almost entirely in the form of individual amino acids. Examples include Precision HN (Sandoz, 1.3% calories as fat), Criticare HN (Mead Johnson, 3% calories as fat), and Vivonex High Nitrogen (Norwich Eaton, 0.87% calories as fat). These diets cause less stimulation of pancreatic exocrine secretion than standard formulas, and can lower pancreatic activity, which is beneficial for treatment of the AP.

There is rationale for use of a second category of formulas for patients with AP, that of semielemental diets. One advantage of these diets is that the nutrients are more easily absorbed in the absence of digestive enzymes. An animal study on a ligated model of the pancreatic duct<sup>[79]</sup> and a human study with cystic fibrosis patients<sup>[80]</sup> have shown that protein in the form of small peptide chains may be absorbed more efficiently than individual amino acids. Although semielemental formulas usually contain a higher percentage of fat calories than the elemental diets, only a small percentage is composed of long-chain fat. Most of the fat is in the form of medium-chain triglycerides (MCT), which can be directly absorbed across the small intestinal mucosa into the portal vein in the absence of lipase or bile salts. The enteral products such as Criticare HN (Mead Johnson, 5% of calories as fat, MCT), Pepti-2000 (Nutricia, 10% of calories as fat, MCT), and Vital HN (Ross, 11% of calories as fat, MCT) are all semielemental formulas, and can be used effectively in clinical practice<sup>[12]</sup>.

Another category of formulas is polymeric diets, which contain 50% to 55% carbohydrates, 15% to 20% intact proteins, and 30% fats. These diets are frequently used in patients with functional gastrointestinal tracts. Many polymeric diets have recently been added to the novel nutrient substrates, such as glutamine, arginine,  $\omega$ -3 fatty acids, nucleotides, and fiber, which play important roles in some critically ill patients in the maintenance of mucosal integrity and immune status<sup>[12,81-83]</sup>. A recent study reported that, an average critically ill

patients who received a glutamine-enhanced enteral feed required a shorter stay in the hospital than patients who were fed a standard isocaloric isonitrogenous enteral feed<sup>[84]</sup>. The authors also documented a significant reduction in postintervention costs; the cost per survivor was 30% less in the glutamine fed group. The beneficial effects of immune-enhancing formulas have also been observed in critically ill patients<sup>[12,21,85-89]</sup>. Randomized, controlled studies reported that patients who received immune-enhancing enteral feeds containing arginine, nucleotides and  $\omega$ -3 fatty acids (fish oil) after operation and trauma had a lower rate of postoperative infections and wound complications compared with patients receiving isocaloric, isonitrogenous control feeds<sup>[88,89]</sup>. Two recent meta-analyses of randomized controlled trials<sup>[86,87]</sup> comparing patients receiving standard EN with those receiving commercially available immune-enhancing feeds reported that, although immuno Nutrition has no effect on mortality rate, there is a significant reduction in infection rates, ventilator duration and length of hospital stay in these patients. At present, there are no available reports on the clinical effects of immune-enhancing diets on patients with AP. But recently, there was a case report<sup>[90]</sup> comparing the pancreatic output with respect to different feeding regimens in a patient who underwent a partial pancreatectomy for carcinoma. There was no difference in pancreatic exocrine secretion when the patient was fed jejunally with a polymeric immune-enhancing formula or supported with two different formulations of TPN. The authors suggest that jejunal feeding of polymeric immune-enhancing diet may be safe to administer patients with AP. Therefore, considering the above advantages, polymeric diets, particularly those containing glutamine, arginine,  $\omega$ -3 fatty acids, nucleotides, and fiber, may be used in AP patients, but the beneficial effects require further study.

#### CLINICAL EXPERIENCES WITH EN

The use EN as therapy for patients with AP goes back to the 1970s when Voitek *et al*<sup>[91]</sup> demonstrated the beneficial effects of an elemental diet in 6 patients with complicated pancreatitis, reporting both positive nitrogen balance and weight gain. Since then a number of reports in the literature described successful use of enteral feeding in patients with pancreatitis without exacerbating the disease process. Most of the studies describe patients within whom the inflammatory process had peaked and begun to resolve, and the enteral feeding were used as transitional feedings.

Since the end of the 1980s, there is now renewed interest in early enteral feeding for AP. One large series<sup>[92]</sup> described the early use of EN within 48 hours of onset of AP. Among 83 patients with no evidence of ileus on admission for AP, 92%

tolerated their enteral infusion well. Kudsk *et al*<sup>[93]</sup> reviewed an experience of feeding jejunostomies in 11 patients who underwent exploratory laparotomy for complications of pancreatitis. Two died, but the remaining 9 patients gradually improved on enteral feeding with none showing exacerbation of their diseases. No catheters were lost and mild diarrhoea was encountered only during the first week of therapy. This study indicates that prolonged jejunal feeding may be provided safely in patients with SAP without aggravating the disease. Parekh *et al*<sup>[94]</sup> showed similar beneficial effects of EN in 9 patients with AP in whom enteral feeding was commenced at a mean of 11 days after admission and continued for a mean of 16 days. This not only improved Nutritional status but was also accompanied by successful resolution of complications in 7 of the 9 patients. The authors suggest that stable patients who are unable to benefit from EN. Simpson *et al*<sup>[95]</sup> retrospectively reviewed nasoenteral feeding in 5 patients with acute alcoholic pancreatitis with a mean Ranson score of 1.8. None needed PN and the disease and its complications resolved in all 5. Nakad *et al*<sup>[96]</sup> described a study of early EN with SAP patients using double-lumen nasogastrojejunal tube within 60 h after admission. Severity was established by a mean Ranson score of 3.57. No patient developed a relapse, hypertriglyceridaemia or abnormalities of liver function, indicating that jejunal feeding can be used safely in SAP patients without reactivation of the inflammatory process.

Pupelis *et al*<sup>[97]</sup> reported 29 patients who had been operated on for SAP. They were randomized to receive either EN and conventional intravenous fluids postoperatively ( $n = 11$ ) or conventional intravenous fluid alone ( $n = 18$ ). Seventeen additional patients who had major abdominal operations for other conditions were also given EN and intravenous fluids and comprised the control group. Nutritional intake, duration of stay in the intensive care unit (ICU), hospital morbidity, mortality, and outcome were observed. Ten of the 11 patients given EN combined with conventional intravenous fluids survived, whereas 5 of the 18 given fluids alone died. The pattern of bowel transit in the fed group did not differ from that in the control group. The authors suggest that postoperative EN seems to be safe and effective in patients with SAP and may improve survival. However, another randomized, controlled study of EN vs conventional therapy (i.e. no Nutritional support) in patients with SAP provided no evidence of improved outcome in patients receiving Nutritional support in terms of organ dysfunction score or inflammatory markers such as antiendotoxin core antibody, IL-6, TNF receptor 1 and CRP<sup>[98]</sup>. Patients receiving enteral feeding had significantly worse abnormal intestinal permeability on the 4th day of therapy. However, this trial involved a total of only 27 patients and a median of 1.8 MJ/day was delivered over the first 4 d by EN,

which constituted 21% of daily caloric requirements. So, the results may be deliberated. Chen and Zhu<sup>[99]</sup> compared the effect of early EN and late EN. Thirty-eight patients were divided into an early group (start EN 3 to 4 days after operation) and a late group (start EN 7 days after operation). All patients received PN at first, and then were transferred to EN. The results indicated that patients tolerated the therapy well in both groups. In addition, early correction of hypoalbuminemia with more quickly improved serum albumin was observed in the group of early enteral feeding.

#### EN VS PN AND AP

Although there have been a number of studies comparing the clinical effects of EN and PN in postoperative, injured, burned, cancer, or critically ill patients<sup>[16-18,100-106]</sup>, only three articles have been published that compare EN with PN in AP patients<sup>[107-109]</sup>. McClave *et al*<sup>[107]</sup> performed the first prospective, randomized trial comparing early EN with PN in 30 patients with mild, or acute chronic pancreatitis. EN was via nasojunal tube and PN was via a central or peripheral line, both within 48h of admission. Efficacy was measured by the percentage of goal energy intake ( $25\text{kcal}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ ) achieved, days to oral diet and length of hospital stay. Although enterally fed patients lagged 1 day behind the other group in achieving energy goals, this difference disappeared by the fourth day. Mean Ranson, APACHE III and multiple organ failure scores decreased in the EN group and increased in the PN group, but these differences were not statistically significant. Patients in the latter group had significantly higher stress-induced hyperglycaemia over the first 5 days. There was a statistically insignificant trend towards earlier normalization of serum amylase, progression to oral diet, and decrease in hospital and intensive therapy unit stay in the EN group compared with the PN group. The mean cost of parenteral feeding was 4 times higher than that of enteral feeding. The authors suggest that EN for AP is not only safe and effective, but also significantly less costly than PN. Compared with PN, EN may promote more rapid resolution of the toxicity and stress response to pancreatitis. In another prospective randomized trial<sup>[108]</sup>, comparing parenteral with enteral feeding in 38 consecutive patients with severe necrotizing pancreatitis, there was no statistically significant difference between the two groups with regard to intensive therapy unit support, use of antibiotics, hospital stay and number of days of Nutritional support. Nitrogen balance improved equally in both groups, but severe hyperglycaemia requiring insulin therapy was twice as frequent in the PN group compared with the EN group. Total complications and septic complications were significantly more common in the PN group, suggesting that EN should be the preferred method for Nutritional support in patients with SAP.

Windsor *et al*<sup>[109]</sup> recently published a randomized controlled trial of EN versus PN in 34 consecutive patients with AP who had a mean Glasgow score of 2 and APACHE II score of 8. After 7 d of Nutritional support, the EN group became better than the PN group with respect to CRP concentrations and APACHE II scores. Furthermore, the serum level of immunoglobulin M and endotoxin core antibodies increased in the PN group whereas it remained unchanged in the EN group. The total antioxidant capacity also fell in the former group and increased in the latter. There was a reduction in the requirement for intensive care, incidence of intra-abdominal sepsis, multiple organ failure, need for operative intervention, and mortality rate in the enterally fed group compared with the parenterally fed group. There was, however, no difference in hospital stay. The authors conclude that EN is not only feasible, but may modulate the inflammatory and sepsis response, reduce disease severity and improve clinical outcome and physiological parameters compared with PN. Erstad<sup>[110]</sup> reviewed the literature of both PN and EN in patients with AP from 1966 to 1999. The results show that the duration of AP and time to oral feedings is similar whether patients receive EN (i.e., jejunal tube feedings) or PN. Additionally, complications, length of stay, and costs are either similar or decreased with EN versus PN, suggesting that the EN rather than PN should be used to provide Nutrition to patients with AP. PN should be reserved for patients in whom nasojunal feeding is not possible.

#### CONCLUSIONS

Patients with AP have a hypermetabolic and hypercatabolic state, resulting in mal Nutrition. Nutritional support for patients with AP is needed, particularly in SAP patients. Jejunal feeding is well tolerated and, unlike gastric and duodenal feeding, does not stimulate pancreatic secretions. EN by the jejunal route is feasible and safe, even in the early stage of AP. The elemental or semi-elemental formulas should usually be used. Although there is no definite evidence that EN support alters clinical outcome or the natural history in most patients with AP, at present, the beneficial effects of EN towards improving the Nutritional condition, protecting Gut barrier function, reducing translocation of bacteria and endotoxins, modulating the inflammatory and septic response, and decreasing the cost have been observed. Therefore, the EN rather than PN should be used to provide nutritional support for patients with AP. PN should be reserved for the patients in whom jejunal feeding is not possible. Furthermore, larger sample multi-center trials are needed to identify the effects of EN on clinical outcome and the natural history in patients with AP, and the beneficial effects of formulas containing the novel nutrient substrates also require further study in the patients with AP.

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