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Nutrition Support in Pancreatitis: Beyond Parenteral Nutrition

Andrea J. Yoder

Pancreatitis is a disease process that can present a nutritional challenge to clinicians. Conventional therapy includes withholding oral intake until the disease process has resolved. Traditionally, parenteral nutrition has been the standard nutrition therapy to support patients until oral nutrition can be resumed. However, parenteral nutrition has been found to be associated with higher rates of catheter-related sepsis, hyperglycemia, mortality, and is more costly than enteral nutrition. Recently, reports in the literature have shown enteral nutrition, distal to the ligament of Treitz, is possible while still minimizing pancreatic stimulation. The majority of these studies have used elemental or semi-elemental formulas based on the assumption that pancreatic insufficiency accompanies pancreatitis and these formulas cause less pancreatic stimulation. It has now been demonstrated that patients with pancreatitis, with or without pseudocysts, can tolerate standard formulas with added pancreatic enzymes if necessary. The following article will present the evolution from parenteral to enteral nutrition support in this patient population.

INTRODUCTION

Pancreatitis is caused by activation of pancreatic digestive enzymes within the pancreas leading to pain and inflammation (1). The inflammatory response to pancreatitis is similar to that of sepsis and can precipitate systemic inflammatory response syndrome (SIRS). SIRS can lead to multiple system organ failure, sepsis, hypermetabolism, hypercatabolism, and increased mortality in severe cases (2,3,4,5). The integrity of the gastrointestinal tract may also be affected by SIRS by increasing the intestinal permeability and altering the normal gut barrier with resultant bacterial translocation potential (2,3,6,7,8). Seventy to eighty percent of hospitalizations due to pancreatitis are mild cases resolving in 5–7 days with only conventional therapy that includes fluid resuscitation, pain management, antibiotic therapy, and withholding oral intake to avoid pain exacerbation (3,9,10,11).

Andrea J. Yoder, R.D., Clinical Nutritionist, Digestive Health Center of Excellence, University of Virginia Health System, Charlottesville, VA.

Nutrition support does not appear beneficial in mild cases of pancreatitis where oral nutrition can be resumed within 5–7 days. The remaining 20%–30% of patients progress to more severe cases associated with multi-system complications leading to increased mortality. As disease severity increases, however, and oral intake is not feasible, some form of nutrition support is necessary to fuel the acute stress state, prevent further nutrient depletion, and provide a means for nutrient repletion in malnourished patients (10,12).

Choosing a method of nutrition support to preserve mucosal health and gut function may also be important in attenuating the stress response to severe pancreatitis (2).

PARENTERAL NUTRITION

Historically, parenteral nutrition has been the standard nutrition therapy for patients with severe pancreatitis to minimize pancreatic stimulation and provide "gut rest." However, in comparison to other hospitalized patients on parenteral nutrition, patients with pancreatitis receiving parenteral nutrition have been found to have significantly higher rates of catheter-related sepsis and hyperglycemia (13,14,15,16). The cost of parenteral nutrition is significantly greater than enteral nutrition, not to mention the cost associated with treating any complications associated with it. Additionally, evidence is now available to support the use of enteral nutrition over parenteral nutrition in patients with pancreatitis (2,8,11,13,17,18,19,20,21).

ENTERAL NUTRITION

Enteral feeding is now accepted as the preferred means of nutrition support. Enteral presentation of nutrients is more physiologic, maintains gut integrity, is associated with fewer infectious complications, and is less expensive than parenteral nutrition (2,6,10,11,13,19). Until recently, enteral nutrition in patients with pancreatitis was not considered as a supportive modality based on the presumptive need to "rest the gut" until pancreatitis resolves. Contrary to original belief, studies have demonstrated that feeding into the jejunum *distal to the ligament of Treitz* minimizes digestive stimulation and can be tolerated in patients with pancreatitis (2,6,8,13,19,20,22,23,24). In comparative studies, parenteral nutrition is associated with twice the incidence of hyperglycemia, higher mortality, and more infectious complications than patients receiving enteral nutrition. Enterally fed patients with pancreatitis have had decreased length of hospital stay, shorter intensive care unit stays, and fewer infectious complications (11,13,19).

Most of the studies reported in the literature have used elemental or semi-elemental formulas in patients with pancreatitis (Table 1). The assumption that elemental or semi-elemental formulas will be better tolerated in patients with pancreatitis is two-fold: 1—standard enteral nutrition formulas containing fat will stimulate the pancreas and 2—that maldigestion accompanies pancreatitis. Table 2 lists the characteristics and costs of some of the commericially available elemental formulas. More recently, several authors have reported use of standard, polymeric formulas in patients with pancreatitis with success (2,7,18,20). A recently published retrospective analysis of patients with pancreatitis with pseudocysts receiving home enteral nutrition demonstrated 97% of patients received a standard, polymeric formula. Patients with *Clostridium Difficile* negative diarrhea who were suspected to have pancreatic insufficiency were empirically treated with pancreatic enzyme powder added directly to a standard formula. In this retrospective review, only 6% of patients had documented pancreatic insufficiency, although 42% of patients were prescribed pancreatic enzymes, leaving 58% of patients without enzymes. Of note, only 12% of all patients with or without pancreatic enzymes reported diarrhea in the home setting (18). If pancreatic insufficiency does parallel pancreatitis, a greater incidence of diarrhea would have been expected as over half of the patients were receiving standard formulas without enzymes. In a study by Erskine, et al (25) patients with cystic fibrosis and pancreatic insufficiency participated in feeding trials of elemental and polymeric formulas with and without pancreatic enzymes to compare the absorption of nutrients. No benefit in absorption was seen with an elemental formula over a polymeric formula with pancreatic enzymes. This suggests patients with pancreatic insufficiency can utilize standard, polymeric formulas as opposed to elemental formulas, with pancreatic enzyme supplementation as needed.

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Table 1. Summary of literature reports of enteral nutrition in patients with pancreatitis
(EN= enteral nutrition; PN= parenteral nutrition)

Author	*Design*	*Forumla Type/ Route of Delivery*	*Results*
Abou-Assi, et al (11) (2002)	Prospective randomized comparison of EN (n=26) vs PN (n=27)	Elemental; Nasojejunal	EN group had: Less hyperglycemia ($p<0.03$) Fewer septic complications ($p<0.01$) Decreased days of nutrition support ($p<0.03$) Fewer hospital costs ($p<0.0001$)
Bodocky, et al (24) (1991)	Prospective randomized comparison of EN (n=7) to PN (n=5)	Elemental; Jejunostomy	Pancreatic exocrine stimulation patterns are the same for patients fed enterally in the jejunum as compared to parenteral feeding
Kalfarentzos, et al (13) (1997)	Prospective randomized comparison of EN (n=18) vs PN (n=20)	Semi-Elemental; Nasojejunal	Both EN & PN were well-tolerated Decreased morbidity in EN group ($p<0.05$) Fewer septic complications in EN group
Kudsk, et al (23) (1990)	Retrospective review of Post-op EN support (n=11)	Elemental; Surgical Jejunostomy	n=9 supported for 31 +/- 6.8 days without exacerbation of disease
McClave, et al (19) (1997)	Prospective randomized comparison of EN (n=16) vs PN (n=16)	Elemental; Nasojejunal	4x greater cost of therapy for PN compared to EN Decreased incidence of hyperglycemia in EN group Similar resolution of clinical symptoms in both groups
Nakad, et al (6) (1997)	Prospective study of EN (n=21)	Elemental; Nasojejunal	EN tolerated in all patients without exacerbation of disease
Olah, et al (8) (2002)	Prospective comparison of EN (n=41) vs PN (n=48)	Elemental; Nasojejunal	Fewer infectious complications, decreased multiple organ failure, and decreased mortality in EN vs PN
Powell, et al (7) (2000)	Prospective randomized comparison of EN (n=13) vs conventional therapy (n=14)	Standard polymeric; Nasojejunal	No significant effect of EN on markers of inflammatory response (CRP, IL-6, TNF Receptor 1) (EN only met 21 % of estimated needs, and oral intake resumed within 10 days)
Pupelis, et al (20) (2001)	Prospective randomized comparison of EN (n=21) vs IV fluids (n=30)	Standard polymeric; Nasojejunal	Decreased mortality in the EN group ($p=0.05$)

Table 1. Summary of literature reports of enteral nutrition in patients with pancreatitis (continued)
(EN= enteral nutrition; PN= parenteral nutrition)

Author	*Design*	*Forumla Type/ Route of Delivery*	*Results*
Windsor, et al (2) (1998)	Prospective randomized comparison of EN (n=16) vs PN (n=18)	Standard plymeric; Nasojejunal	Significant reduction in C-reactive protein & APACHEII scores in EN group (no change in PN) Serum IgM Endo Cab Antibodies increased in PN group (no change in EN group $p< 0.05$) Increased Antioxidant capacity in EN group
Yoder, et al (18) (2002)	Retrospective review of home course of EN support (n=33)	Standard polymeric (97%), Elemental (3%); Percutaneous gastrostomy with jejunal extension (PEG-J)	EN was well-tolerated 77% of patients achieved nutrition goals Reported GI complications did not hinder EN delivery 61% of patients maintained or gained weight

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Table 2. Nutrition Information of Various Elemental Products

Product	*Source*	*Calories per mL*	*% Free H20*	*CHO g/L*	*Pro g/L*	*Fat g/L*	*MCT:LCT (1)*	*Price/1000 kcal*
AlitraQ	Ross	1.00	85	165	52.5	15.5	53:47	$29.16
Criticare HN	Mead J	1.06	84	207.5	35.8	5	No MCT	$25.70
Optimental	Ross	1.00	84	139	51.3	28.4	45:55	$24.60
Peptamen	Nestle	1.00	85	127	40	39	70:30	$21.66
Peptamen 1.5	Nestle	1.50	77	191	60	58.5	70:30	$14.44
Perative	Ross	1.30	79	177.2	66.6	37.4	40:60	$8.80
Reabilan HN	Nestle	1.33	85	131.5	31.5	40.5	50:50	$23.56
Tolerex	Novartis	1.00	86	230	21	1.5	No MCT	$16.61
Vital HN	Ross	1.00	87	185	41.7	10.8	45:55	$20.28
Vivonex TEN	Novartis	1.00	85	210	38	2.8	No MCT	$18.28
Vivonex Plus	Novartis	1.00	85	190	45	6.7	No MCT	$21.20

Note: None of these products contain fiber
1: Medium chain triglyceride (MCT): Long chain triglyceride (LCT)
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Table 3. Cost Comparison of Elemental Formulas Versus Standard Formulas with Pancreatic Enzymes

Formula	*Cost per 1000 calories**
Elemental	
Criticare HN	$26.90
Peptamen, unflavored	$21.65
Vital HN	$20.28
Vivonex TEN	$17.72
Standard with Pancreatic Enzymes**	
Nutren 1.5, unflavored	$4.36
Deliver 2.0	$4.93
Promote with Fiber	$7.60
Probalance	$7.60

*Cost information obtained from company using toll-free number (2001 prices)
**Cost based on 1/2 teaspoon enzymes added per can of formula
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Another issue with using enteral nutrition in this population is gastrointestinal tolerance. Some of the gastointestinal symptoms frequently used to evaluate tolerance of enteral nutrition include nausea, vomiting, abdominal distention, and diarrhea. Several studies have reported on tolerance of enteral nutrition in patients with pancreatitis. Windsor, et al (2) reported nausea and abdominal distention attributed to an ileus early in the course. However, symptoms resolved and enteral nutrition was resumed after two to four days. No patients in the Windsor study experienced diarrhea. Nakad (6) also observed only four cases of mild diarrhea out of 21 patients. Enterally fed patients in the Powell, et al (7) study had higher nausea scores, although the difference in comparison to the conventional therapy group was not statistically significant. In addition, Powell did not observe any major complications with enteral feeding. In a retrospective review of patients with pancreatitis who received enteral nutrition in the home setting, enteral nutrition support was achieved without any major incidents of gastrointestinal events (18). The most commonly reported event was short-lived nausea and vomiting (42% of patients). Similar to previous studies of hospitalized patients, other symptoms with less incidence observed in the study included diarrhea and distention. Despite these reported gastrointestinal symptoms, nutrition goals were met in 77% of patients. Although enteral nutrition may be related to gastrointestinal symptoms, other aspects of the disease may also contribute to symptoms regardless of enteral nutrition.

Another benefit of enteral nutrition over parenteral nutrition is cost of therapy. Parenteral nutrition is considerably more expensive than enteral nutrition. Abou-Assi (11) reported that, for patients with acute pancreatitis, $291,110 was spent on parenteral nutrition in one year, whereas $2,981 was spent for enteral nutrition during the same year. Had all patients received enteral nutrition, the institution would have appreciated a considerable cost savings. As previously reported, further savings can be fostered by choosing standard formulas over more expensive elemental formulas. Despite the addition of pancreatic enzymes to the formula, the combined cost of enzymes and standard formulas still offers a significant savings (Table 3).

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Table 4. Post PEG-J Placement Protocol for Patients with Pancreatitis at The University of Virginia Health System

- NPO except 8 ounces of ice chips per day
- Enteral nutrition to start via the J-port upon return to the unit per Nutrition Support Team recommendations
- G-port to gravity for the first 24 hours after PEG-J placed
  - If <500 cc's drainage, clamp G-port and monitor for nausea/vomiting
  - If >500 cc's drainage, continue gravity drainage and assess need for jejunal reinfusion
- Start liquid PPI via J-port
- Check gastric pH (via G-port) Day #2 after PEG-J placed
- Check qualitative fecal fat Day #2 after PEG-J placed and appreciable amounts of enteral nutrition have been received

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There is only one published study reporting the use of enteral feedings with resolving pancreatitis in the home setting (18). Previous studies of patients with pancreatitis receiving enteral nutrition report the placement of a nasojejunal feeding tube for nutrition support, but do not include clinical response beyond the hospital setting. At the current author's institution, it is now standard practice to place percutaneous endoscopic gastrostomy feeding tubes with a jejunal extension (PEG-J) in patients with pancreatitis with pseudocysts who are expected to require nutrition support for greater than four weeks. Patients are discharged home on enteral nutrition and followed up in outpatient clinic with serial computed tomography scans to evaluate the resolution of pancreatitis and pseudocysts. A liquid proton pump inhibitor (PPI) is ordered and administered via the J-port. The rationale for liquid PPI is threefold: 1—to decrease acid secretion which is a potent stimulator of pancreatic secretions, 2—to reduce the total volume of gastric secretions in patients who require gastric venting, 3—secretions reinfused into the jejunum will not be an acidic medium for which the intestinal mucosa is not intended. A gastric pH is checked 2–3 days after PEG-J placement to ensure adequate acid suppression therapy, and a qualitative fecal fat is checked after the patient has reached his goal nutrition delivery to evaluate for pancreatic insufficiency. If a patient has *Clostridium Difficile* negative diarrhea and/or a positive qualitative fecal fat after initiating enteral nutrition, pancreatic enzymes are added to the feedings. One half teaspoon pancreatic enzyme powder per can is mixed in warm tap water and added to the formula. See Table 4 for a summary of this protocol.

Nutrition support practices in patients with pancreatitis have evolved in recent years. No longer is parenteral nutrition thought to be the standard nutrition therapy for patients with pancreatitis should they require nutrition support. Further investigation is necessary to clearly demonstrate the efficacy of enteral nutrition and the use of standard enteral formulas in this patient population. ■

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