



ESPEN Guidelines on Parenteral Nutrition: Pancreas

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SUMMARY

Assessment of the severity of acute pancreatitis (AP), together with the patient's nutritional status is crucial in the decision making process that determines the need for artificial nutrition. Both should be done on admission and at frequent intervals thereafter. The indication for nutritional support in AP is actual or anticipated inadequate oral intake for 5–7 days. This period may be shorter in those with pre-existing malnutrition. Substrate metabolism in severe AP is similar to that in severe sepsis or trauma. Parenteral amino acids, glucose and lipid infusion do not affect pancreatic secretion and function. If lipids are administered, serum triglycerides must be monitored regularly. The use of intravenous lipids as part of parenteral nutrition (PN) is safe and feasible when hypertriglyceridemia is avoided.

PN is indicated only in those patients who are unable to tolerate targeted requirements by the enteral route. As rates of EN tolerance increase then volumes of PN should be decreased.

When PN is administered, particular attention should be given to avoid overfeeding. When PN is indicated, a parenteral glutamine supplementation should be considered.

In chronic pancreatitis PN may, on rare occasions, be indicated in patients with gastric outlet obstruction secondary to duodenal stenosis or those with complex fistulation, and in occasional malnourished patients prior to surgery.

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Preliminary remarks

Most of the principles of nutritional support in acute and chronic pancreatitis were published in the ESPEN guidelines on enteral nutrition.¹ The aim of this chapter is to focus on specific issues related to the proper use of parenteral nutrition (PN) in pancreatic diseases. Thus, these guidelines are an extension of the previously published ESPEN guidelines on enteral nutrition.¹

1. Acute pancreatitis

Introduction

The management, treatment and outcome of acute pancreatitis (AP) are determined by disease severity. Approximately 75% of the patients have mild disease with mortality below 1%.² Mortality increases up to 20% if the disease progresses to its severe

necrotizing form^{3–8} and in the most severe cases mortality can range from 30 to 40%.^{7,8}

Although the impact of the nutritional status on outcome in patients with severe AP has not been fully elucidated it is probable that severe malnutrition will adversely affect outcomes⁹ as occurs in other critical diseases.¹⁰ Malnutrition is known to occur in 50–80% of chronic alcoholics and alcohol is a major etiological factor in acute pancreatitis.¹¹ Morbid obesity is also associated with poorer prognosis.¹²

Assessment of the severity of AP, together with the patient's nutritional status is crucial in the decision making process that determines the need or otherwise for artificial nutrition. Both should be done on admission and at frequent intervals thereafter.

The indication for nutritional support in AP is an actual or anticipated inadequate oral intake for 5–7 days. This period may be shorter in those with pre-existing malnutrition. Assessment of disease severity assists in this decision because identification of a likely severe course (by whatever assessment criteria used) alerts the clinician to the likely need for nutritional support. However, it is

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Summary of statements: Pancreas

Subject	Recommendations	Grade	Number
Metabolism	Substrate metabolism in severe acute pancreatitis (AP) is similar to that in response to severe sepsis or trauma. There is increased protein catabolism, characterized by an inability of exogenous glucose to inhibit gluconeogenesis, increased energy expenditure, increased insulin resistance and increased dependence on fatty acid oxidation to provide energy substrates.	A	1.1
	Energy needs may differ and change substantially according to severity and stage of the disease, the patient's associated diseases, and specific complications occurring during the clinical course of AP.	B	
Amino acids	Severe AP is characterized by substantial protein catabolism and increased energy requirements.	A	1.2
	Parenteral amino acid infusion does not affect pancreatic secretion or function.	A	
	When PN is indicated, parenteral glutamine supplementation (>0.30 g/kg Ala-Gln dipeptide) should be considered.	B	1.3
Carbohydrates	Glucose should be the preferred carbohydrate energy source for several reasons: it is cheap, readily available and easy to monitor. Moreover its administration may counteract gluconeogenesis, but meticulous attention is required to avoid hyperglycemia.	A	1.4
	In case of hyperglycemia exogenous insulin is recommended to maintain blood glucose as close as possible to the normal range.	B	
	Parenteral carbohydrate infusion does not affect pancreatic secretion and function.	A	
Lipids	Lipids provide an efficient source of calories. The use of intravenous lipids in pancreatitis is safe if hypertriglyceridemia is avoided.	C	1.6
	Triglyceride values below 12 mmol/L are recommended but ideally serum levels should be kept within normal ranges.	C	
	Current best practice recommendations are to ensure appropriate infusion rates for fat emulsions (from 0.8 to 1.5 g/kg per day) and temporarily to discontinue infusion if persistent (>72 h) hypertriglyceridemia occurs (>12 mmol/L).	C	
Micronutrients	As in all critically ill patients, a daily dose of multivitamins and trace elements is recommended. Despite patients with severe AP having demonstrable deficits in plasma and tissue levels of several micronutrients, at present there are insufficient data to support supranormal doses.	C	1.7
Indications	In cases of mild disease, oral feeding can be resumed after a short period of starvation if pain has ceased.	A	1.8
	In mild AP spontaneous recovery with resumption of oral intake generally occurs within 3–7 days, and therefore, there is no need for special nutritional treatment (neither PN nor EN) unless such patients are malnourished prior to the initial attack, or when a therapeutic period of starvation is indicated for a period of longer than 5–7 days. In these cases EN should be started as soon as possible.	A	
	The indication for PN is simple and uncontroversial. All patients in whom the clinician decides that some form of nutritional support is indicated should have this commenced by the enteral route. Only in those patients who are unable to tolerate targeted requirements is PN indicated. PN, therefore, is required only when the gut has failed or administration of EN is impossible for other reasons (e.g. prolonged ileus, complex pancreatic fistulae, abdominal compartment syndrome).	B	
Route	The central route should be preferred to deliver PN when it is needed in pancreatitis.	B	1.9
Contraindications	In the severe form of AP, if EN is insufficiently tolerated, there is no specific contraindication to starting PN as soon as possible.	C	1.10
	PN should be given after an adequate fluid resuscitation and when the patient has achieved full hemodynamic stabilization (usually 24–48 h from admission).	B	
Pitfalls and complications	The problems are those of PN in general rather than of its use in AP in particular. Particular attention should be given to avoid overfeeding.	B	1.12
Requirements	Patients should receive 25 non-protein kcal/kg per day increasing to no more than a maximal caloric load of 30 kcal/kg per day. This limit should be reduced to 15–20 non-protein kcal/kg per day in cases with SIRS or MODS and when a patient is at risk of refeeding syndrome.	B	1.12
Chronic pancreatitis	Malnutrition is frequent in patients with CP due to pain-induced anorexia and to continuing alcohol abuse. Increased resting energy expenditure is also seen. PN may, on rare occasions, be indicated in patients with gastric outlet obstruction secondary to duodenal stenosis and in those with complex fistulating disease.	C	2.1

worthy of emphasis that no severity and prognosis scoring system is infallible¹³ and the decisions whether to feed or not must be based on the patient's progress irrespective of any classification system.

1.1. Substrate metabolism in acute pancreatitis

Substrate metabolism in severe AP is similar to that in response to severe sepsis or trauma. There is increased protein catabolism, characterized by an inability of exogenous glucose to inhibit gluconeogenesis, increased energy expenditure, increased insulin resistance and increased dependence on fatty acid oxidation to provide energy substrates (A).

Energy needs may differ and change substantially according to severity and stage of the disease, patient's associated diseases, and specific complications occurring during the clinical course of AP (B).

1.2. Is amino acid infusion needed and safe during AP?

Severe AP is characterized by substantial protein catabolism and increased energy requirements (B). Parenteral amino acid infusion does not affect pancreatic secretion or function (A).

Comments: Severe AP is mainly characterized, from a metabolic stand point, by nitrogen waste and protein catabolism with subsequently negative nitrogen balance and secondary malnutrition.¹⁴ Thus, nitrogen supply should be a major objective of nutrition¹⁵ even though a net positive nitrogen balance is difficult to achieve in such severe conditions.¹⁶ In fact patients with AP, similarly to septic subjects, have an impaired capacity for net protein synthesis and are less sensitive to protein sparing effects of glucose infusion.¹⁶ The goal for nitrogen supply during total parenteral nutrition in severe AP should be 0.2–0.24 g/kg per day (equivalent to an amino acid delivery of 1.2–1.5 g/kg per day). This requirement should be reduced to 0.14–0.2 g nitrogen/kg per day in the case of hepatic or renal failure complicating AP. Monitoring urea excretion may be helpful to tailor the actual nitrogen need.

There are sufficient data to state that intravenous infusion of amino acids does not affect the pancreatic secretory response.^{17,18}

1.3. Is the composition of the amino acids given with PN relevant to outcome?

When PN is indicated, parenteral glutamine supplementation (>0.30 g/kg Ala-Gln dipeptide) should be considered (B).

Comments: Glutamine is the most abundant free amino acid in the body and has a central role in many metabolic processes (e.g. a vehicle for interorgan transport of nitrogen and carbon skeletons, a precursor for nucleotides and glutathione, and a regulator of acid-base balance).¹⁹ Several studies have documented beneficial effects of Ala-Gln supplemented parenteral nutrition in severely ill ICU patients.^{20,21} In acute pancreatitis, three randomized controlled studies including a total of 82 patients compared PN with ($N = 40$) and PN without glutamine ($N = 42$).^{22–24} The majority of patients in these studies had moderate pancreatitis and there was an overall mortality rate of 4.8%. These studies have slight differences in design and aggregation of the data precluding a meta-analysis. The overall effect on outcome of parenteral glutamine supplementation was however positive.²⁵ The use of PN with glutamine was associated with a trend toward a reduction in overall complications (RR = 0.68; 95% CI, 0.42–1.09; $p = 0.11$) compared with use of PN alone. Two of these studies showed shorter hospital length of stay with PN with glutamine compared with PN alone. A non-significant reduction of length of stay of 3 days was reported in the Xian-Li et al. study²⁶ (25.3 vs. 28.6 days) and a significant reduction of 4 days in the Ockenga et al. study (21 vs. 25 days).²² Another study, by Sahin et al.,²⁷ reported that patients receiving TPN enriched with 0.3 g/kg per day of i.v. glutamine had a significant reduction in complication rate (10 vs. 40% in controls). Clinical and metabolic benefits of early infusion of parenteral glutamine dipeptide have been recently confirmed by Fuertes-Orozno et al.²⁸ and by Xue et al.²⁹ in randomized trials.

No data comparing the optimal dose of glutamine in acute pancreatitis are available. As in other studies in critically ill patients a dose of >0.20 g/kg per day of L-glutamine (>0.30 g/kg per day Ala-Gln dipeptide) should be considered.²⁰

No data are available on parenteral formulas enriched with other types of amino acids (e.g. BCAA, EAA, arginine), in this particular clinical setting.

1.4. Is carbohydrate infusion needed and safe during AP?

Glucose should be the preferred carbohydrate energy source for several reasons: it is cheap, ready available and easy to monitor. Moreover its administration is indicated because it may counteract gluconeogenesis, but meticulous attention is required to avoid hyperglycemia (A). In this case exogenous insulin is recommended to maintain blood glucose as close as possible to the normal range (B).

Parenteral carbohydrate infusion does not affect pancreatic secretion and function (A).

Comments: Glucose should represent the preferred energy supply during AP because it can be easily administered, it may in part counteract the intrinsic gluconeogenesis from protein degradation and provides sufficient calories thus avoiding the use of lipids that may be contraindicated in specific patients. Nevertheless, in patients with severe AP, as in other critically ill patients, glucose oxidation reaches the maximal level of 4–7 mg/kg per min (5–6 g/kg per day). Exceeding this limit may cause lipogenesis, hypercapnia and particularly hyperglycemia. This latter risk is even greater in patients with AP because pancreatic necrosis and inflammation impair insulin release. Hyperglycemia needs to be corrected by exogenous insulin administration, keeping the blood glucose level as close as possible to the normal range³⁰ (B), although there are as yet no specific studies applying this intervention in acute pancreatitis.

Glucose should represent between 50% and 70% of the total calories (C).

Intravenous glucose does not stimulate exocrine pancreatic secretion (A).^{31,32}

1.5. Is there a role for non-glucose carbohydrates?

There are insufficient data at this time.

Comment: Only one small clinical trial has addressed the issue of non-glucose carbohydrates (a mixture of fructose and xylitol) in patients with severe AP. Martinez et al.³³ compared two PN solutions containing either glucose or the above carbohydrate mixture. They reported that the use of this mixture was associated with a significant lower insulin requirement and blood glucose levels. These data are insufficient to give a recommendation.

1.6. Is lipid infusion needed and safe during AP?

Lipids provide an efficient source of calories. The use of intravenous lipids in pancreatitis is safe if hypertriglyceridemia is avoided (C). Triglyceride values below 12 mmol/L are recommended but ideally serum levels should be kept within normal ranges (C).

Current best practice recommendations are to ensure appropriate infusion rates for fat emulsions (from 0.8 to 1.5 g/kg per day) and temporarily to discontinue infusion if persistent (>72 h) hypertriglyceridemia occurs (>12 mmol/L) (C).

Comments: Most of the controversies in the field of artificial nutrition in AP are related to the use of lipids and in particular long-chain triglycerides, because it is still unclear whether hyperlipidemia is a cause or a consequence of acute pancreatitis or a combination of both.³⁴ The latter seems more likely, since serum lipids generally normalize spontaneously in a few days during recovery from acute pancreatitis. Hyperlipidemia in the most severe cases of AP might reflect greater disturbances of fat metabolism related to SIRS and sepsis rather than the use of parenteral lipids. Nevertheless, it is of interest that:

- Hypertriglyceridemia (HTG) and chylomicronemia, but not hypercholesterolemia, are found in about 12–38% of patients admitted with acute severe pancreatitis.³⁵
- In some cohort studies, an association between altered lipid metabolism and pancreatic injury^{36–38} was hypothesized, but other clinical reports find no correlation between impaired lipid catabolism/clearance and AP.^{39,40}
- Keeping blood triglyceride levels <4.6 mmol/L, in patients with previous HTG-associated AP can effectively prevent further episodes of pancreatitis.³⁵
- In subjects with hyperlipidemia, the course of acute pancreatitis is more often severe.^{41,42}
- Mutations in the lipoprotein lipase gene have been identified in patients with HTG-associated pancreatitis.^{43,44}
- Very few reports link, from a pathophysiological point of view, infusion of lipid emulsions with the onset of AP. Three cases have been reported in which pancreatitis occurred upon infusion of lipid emulsions, but co-morbidity of these patients and concomitant therapy (e.g. corticosteroids) preclude any firm conclusions.⁴⁵
- Lipid emulsions do not affect pancreatic secretion.^{46–51}

The diagnosis of hypertriglyceridemia-associated pancreatitis is based on lipemic serum, a serum TG level greater than 12 mmol/L and the presence of chylomicronemia.^{52–54} The mechanism(s) by which HTG might lead to pancreatitis is not completely known, but a theory proposed by Havel et al. is generally favored.⁵⁵ Hydrolysis of TG in and around the pancreas by pancreatic lipase secreted by acinar cell leads to accumulation of free fatty acids in high concentrations. Unbound free fatty acids are toxic and could

produce injury to acinar cells and microvessels. Increased concentration of lipids in the pancreatic capillaries then causes vessel plugging and leads to ischemia and acidosis. In the acidotic environment, free fatty acids cause activation of pancreatic proenzymes, proinflammatory cytokines and free radicals, thus initiating acute pancreatitis.

Other authors consider that chylomicrons may play a more relevant role than triglycerides in the association between pancreatitis and HTG.^{53,56} Moreover, circulating lipase and phospholipase released during acute pancreatitis may cleave triglycerides and raise serum free fatty acids (FFA). FFA may lead to intravascular sequestration of calcium by creating FFA-albumin complexes.

In fact, hypocalcemia is a frequent finding in patients with acute pancreatitis and calcium levels below <2 mmol/l are a well-known negative prognostic factor.^{57,58}

The single most important point in respect of hypertriglyceridemia-associated pancreatitis is that treatment of the hypertriglyceridemia may dramatically improve outcomes and can prevent further pancreatic damage.⁵⁹

It is important to recognize that hypertriglyceridemia in pancreatitis generally clears within 48–72 h when there is no continuing exogenous source of lipids.⁵⁴

Only in cases of hypertriglyceridemia-associated pancreatitis should it be necessary to avoid lipid emulsions if PN is needed.⁵² The goal is to maintain TG levels within the normal range.⁵³

If the serum TG level cannot be maintained below 12 mmol/L, drug therapy is indicated to decrease VLDL production and prevent more severe HTG.

Plasma exchange has been used to lower lipid and pancreatic enzymes levels, and to improve the signs and symptoms of AP.⁶⁰ Lipoprotein apheresis seems even more effective because it removes only large molecular weight complexes from plasma (such as lipoproteins) and retains immunoglobulins, albumin, and clotting factors, thus reducing the possibility of infection and bleeding.^{61,62}

If lipids are administered, serum triglycerides must be monitored regularly, but the use of intravenous lipids as part of parenteral nutrition in severe acute pancreatitis is certainly feasible on condition that hypertriglyceridemia is avoided.^{45,63}

At present there are no strong data to suggest that infusion of alternative parenteral lipids such as omega-3 fatty acids, olive oil, medium chain triglycerides, or structured lipids, have major clinical advantages compared to soybean oil emulsion. Only one randomized double-blind trial by Wang et al. ($N = 40$) showed that subjects receiving fish oil emulsion compared to soybean oil, had a reduced inflammatory response, need of renal replacement therapy and improved respiratory function.⁶⁴ Larger studies are required to confirm these preliminary data.

1.7. Is micronutrient infusion needed in AP?

As in all critically ill patients, a daily dose of multivitamins and trace elements is recommended (C). Although patients with severe AP have demonstrable deficits of plasma and tissue levels of several micronutrients, at present there are insufficient data to support supranormal doses (C).

Comments: Du et al., randomized 84 patients with AP into two groups, receiving either 1 or 10 g/day of vitamin C. They demonstrated that subjects treated with the higher dose of vitamin C had a higher cure rate, fewer complications and shorter hospitalization than the low dose group.⁶⁵ These results were not confirmed by a case-control study carried out in 46 consecutive patients with severe AP. The authors reported no clinical benefit from using

a high dose of a multivitamin mixture and selenium.⁶⁶ Negative results on relevant outcome parameters were also reported from a randomized double-blind controlled trial by Siriwardena et al.,⁶⁷ who tested a similar treatment protocol in patients with severe AP.

1.8. When is PN indicated in acute pancreatitis?

In cases of mild disease, patients can be fed orally after a short period of starvation if pain has ceased (A). Spontaneous recovery with resumption of oral intake generally occurs within 3–7 days, and therefore, there is no need for special nutritional treatment (neither PN nor EN) unless such patients are malnourished prior to the initial attack, or when a therapeutic period of starvation is indicated for a period of longer than 5–7 days (A). In this case EN should be started as soon as possible.

The indication for PN is simple and uncontroversial. All patients in whom the clinician decides that some form of nutritional support is indicated should have this commenced by the enteral route. Only in those patients who are unable to tolerate targeted requirements is PN indicated. PN, therefore, is required only when the gut has failed or administration of EN is impossible for other reasons (e.g. prolonged ileus, complex pancreatic fistulae, abdominal compartment syndrome) (B).

As EN tolerance increases, the volume of PN should be decreased. When tolerated EN is associated with improved outcomes compared to PN (A).

PN does not significantly stimulate pancreatic secretion in humans and there is no adverse effect of PN on pancreatic function (A).^{68–70}

Comments: There is only one randomized controlled trial, conducted by Sax et al. in 54 patients with mild AP,⁷¹ that has compared the effects of early PN (within 24 h of admission) with no feeding. PN did not affect the number of days to oral intake, total hospital stay or number of complications of pancreatitis. Moreover, the authors found that patients with AP had a significantly higher rate of catheter related sepsis compared to other groups treated with PN in the same hospital (10.5 vs. 1.5%). Thus, in mild pancreatitis artificial nutrition within 5–7 days appears to have no positive impact on the course of disease and is therefore not recommended unless such patients are malnourished prior to the initial attack or starvation is indicated for period longer than 5–7 days. Fluid and electrolytes can be administered parenterally by standard peripheral routes as required by balance.

If early oral refeeding is not feasible due to persistent pain or changes in severity during the clinical course of the disease, enteral tube feeding should be delivered.^{1,72} Normally, most of the patients with predicted severe AP can be fed enterally and reach the target energy requirement within 3–4 days from admission.⁷³ If it is predictable that enteral infusion cannot be started early or not fully tolerated, PN should be started as soon as possible and a combination of PN and EN is advisable (B).

The advantages of the enteral route over the parenteral one in severe AP have been extensively discussed in the ESPEN guidelines on enteral nutrition.¹ Since the publication of these guidelines, other systematic reviews have been published.^{74–76} They too confirm the superiority of EN on relevant outcome parameters, particularly in patients who tolerate enteral infusion.

The systemic inflammatory response associated with severe acute pancreatitis increases metabolic demands and may progress to multiple organ dysfunction syndromes. The disease and its complications are associated with the release of proinflammatory cytokines, activation of the complement cascade, release of oxygen derived free radicals and nitric oxide, and generation of prostaglandin E₂, thromboxane A₂ and leukotriene-4 from the

metabolism of arachidonic acid. These changes, if prolonged and combined with starvation lead to a rapid loss of lean body mass with associated morbidity and mortality. Impaired gut barrier function may lead to translocation of bacteria and their products from the lumen into the circulation.^{77,78} The effects of catabolism are compounded by an inability or reluctance to maintain an adequate oral intake, and patients become malnourished during the course of their illness. Micronutrient and vitamin deficiencies may also be present on admission or develop during hospitalization. In addition to hypocalcemia, which is seen in up to 25% of patients with severe AP, deficiencies of magnesium, zinc, folate and thiamine have been described.⁷⁹ With this background, intuitively, artificial nutrition should improve outcome in patients with severe acute pancreatitis when compared with those receiving no nutritional support. Yet, there is only one small randomized controlled study that compared the effects of enteral nutrition on 13 patients with severe acute pancreatitis with results from 14 patients who did not receive nutritional support. This study did not show a benefit of nutritional support on patient outcome, but interpretation is limited by the fact that it was insufficiently powered.⁸⁰

At present there is no definitive evidence that artificial nutritional support alters outcome in most patients with AP unless malnutrition is also a problem. A diagnosis of AP is not therefore in itself an indication for instituting artificial nutrition. Nevertheless, in severe cases that are catabolic and/or have and anticipated period of inadequate oral intake (<1000 kcal/day) longer than 5–7 days, it is prudent to begin artificial nutrition either via the jejunum or stomach^{81–84} as soon as possible in order to prevent the clinical consequences of malnutrition. Sometimes, the establishment and maintenance of jejunal access in patients with severe AP may be problematic, and it may be difficult to achieve the targeted intrajejunal nutrient delivery within the first few days, not least because of impaired upper gastrointestinal motility. A combination of EN and PN is, therefore, a reasonable way to meet metabolic demands in these patients and the amount of nutrients delivered parenterally can be progressively reduced as larger volumes are tolerated enterally.⁸⁵ There are no randomized studies available comparing the effects of EN alone with EN supplemented with PN. One study⁸⁶ randomized 100 patients with severe acute pancreatitis to receive PN alone or individually staged nutritional support (ISNS) which consisted of PN + albumin in stage 1 (9 ± 6 days), PN + EN in stage 2 (6 ± 3 days) and EN alone in stage 3 (3 ± 2 days). When compared with the PN regimen, the ISNS regimen significantly reduced the incidence of sepsis or infection from 30 to 8%, intra-abdominal infections from 12 to 4%, hepatic dysfunction from 12 to 4%, days to resuming oral diet from 25 to 18 days, and length of hospital stay from 30 to 24 days. However, on the whole, the data are insufficient to determine whether supplemental EN enhances the efficacy of PN in this group of patients. Nevertheless supplementing PN with 10–30 ml/h of an enteral diet perfused into the jejunum or stomach may help to maintain gastrointestinal integrity and by providing luminal nutrition (C).⁸⁷

Complications of acute pancreatitis such as persisting ileus, large pseudocysts, intestinal and pancreatic fistulae, intestinal edema, retroperitoneal edema, pancreatic ascites, pancreatic or peripancreatic collections and infected necrosis may sometimes make enteral feeding difficult to conduct and tolerate, and PN should be instituted along with appropriate treatment for these conditions (C).

Several of the above conditions may also predispose to intra-abdominal hypertension or the abdominal compartment syndrome.^{88,89} Both air and fluid within the hollow viscera can be responsible. Gastrointestinal ileus is common both among patients at risk of developing the syndrome and in those who have already developed it.⁸⁹ A statistical relationship has been observed

between maximal intra-abdominal pressure and overall prognosis in acute pancreatitis.⁹⁰ Nasogastric and/or rectal drainage, or endoscopic decompression offer simple and relatively non-invasive methods for reducing intra-abdominal pressure and treating mild to moderate intra-abdominal hypertension, and in these patients enteral feeding may be feasible.⁹¹ Continued enteral feeding in the presence of increasing bowel edema and ileus may however worsen the situation. Non-occlusive bowel necrosis can occur in critically ill patients receiving enteral nutrition⁹² and this too may be related to worsening of the intra-abdominal compartment syndrome. PN will often be necessary in patients with acute pancreatitis and intra-abdominal hypertension who are not tolerating enteral feeding or who are clinically deteriorating (C).

1.9. Which is the preferred route for PN?

The central route should be preferred to deliver PN when it is needed in pancreatitis (B).

Comments: The American Society of Parenteral and Enteral Nutrition (ASPEN) Guidelines of 2002³⁰ recommend a percutaneously inserted catheter advanced into the superior vena cava as the route of choice for the delivery of PN, with appropriate confirmation of correct location of the catheter tip.⁹³ Peripheral PN can however be offered if the anticipated period of nutritional support is less than 14 days, with the advantages of needing less special expertise and lower morbidity than central venous cannulation. Although this would seem attractive when PN is needed in AP peripheral PN is prone to provoke thrombophlebitis.^{94,95} This complication is normally reduced by the use of lipid-orientated regimens which are less suitable in AP (see above). The need for more prolonged PN, and the presence of peripheral edema or poor quality peripheral veins may also make this route unsuitable. As most patients with severe AP will warrant central venous access for other reasons it will usually be appropriate for PN to be administered via a dedicated lumen of a central catheter.

1.10. When is PN contraindicated in AP?

In the severe form of AP, if EN is partially or not tolerated, there is no specific contraindication to start PN as soon as possible (C). PN should be given after an adequate fluid resuscitation and when the patient has reached a full hemodynamic stabilization (usually 24–48 h from admission) (B).

Lipid administration in PN should be stopped temporarily if the plasma triglyceride level rises over 12 mmol/L, and should be avoided completely in cases of HTG-associated AP (C).

Comments: Xian-Li et al.²⁶ randomized 64 patients with severe acute pancreatitis (no definition of criteria for severity) to receive PN, PN with glutamine or no nutritional support within 24–48 h after “fluid resuscitation”. Patients given PN plus glutamine, and patients given PN alone had a significantly better outcome than those in the control group when overall complications, length of hospital stay and mortality were considered. It is not known exactly when nutritional support was commenced in this study, but the probable delay of at least 1 day, may have led to PN being started after the peak of SIRS. Therefore, it may be wise to delay the initiation of PN in patients with severe acute pancreatitis after adequate fluid resuscitation, achievement of complete hemodynamic stabilization, and the period of the peak inflammatory response has passed (usually 24–48 h from admission)^{73,96} (B). Such a period is necessary anyway to re-evaluate prognostic and severity scoring systems and consequently to reassess the metabolic needs of the patient.

There are no specific contraindications to continuing PN in patients with severe acute pancreatitis once it has commenced except for the lipid infusion component in patients with persistent hypertriglyceridemia (>12 mmol/L) (B).

1.11. How should weaning from PN be conducted?

Follow general guidelines for PN weaning.

Comments: There are no specific instructions for weaning patients with acute pancreatitis from PN and the general guidelines for weaning any patient from PN should be followed. Improvement in the patient's condition should prompt the institution of tube feeding or oral nutritional supplements and there should be a period of overlap. PN should be progressively weaned and stopped when the patient is able to tolerate the required amount of nutrients by the enteral or the oral route. Sudden cessation of PN may result in rebound hypoglycemia which can be prevented by gradual withdrawal.

Oral refeeding with a diet rich in carbohydrates and proteins and low in fats is recommended (C), but no clinical trials on this are available. If the diet is well tolerated, oral nutrition can be increased progressively.⁷² Specific oral supplements are not recommended.

1.12. Which are the potential pitfalls and complications of PN?

The problems are those of PN in general rather than to its use in AP in particular. Particular attention should be given to avoid overfeeding (B). Patients should receive 25 non-protein kcal/kg per day increasing to no more than a maximal caloric load of 30 kcal/kg per day. This limit should be reduced to 15–20 non-protein kcal/kg per day in case with SIRS or MODS and when a patient is at risk of refeeding syndrome (B).

Comments: Parenteral nutrition is only required in the management of patients with AP when they are critically ill and have acute intestinal failure precluding EN, or when they have multiple metabolic problems. Parenteral nutrition in this setting is best provided by a dedicated nutrition support team and this approach has been shown to reduce the prescription of inappropriate PN and also to reduce complications.⁹⁷ If the central route is being used particular attention should be paid to catheter insertion in order to prevent procedure-related complications. Catheter care should be meticulous in order to minimize the risk of catheter related sepsis.⁹⁸ If the peripheral route is being used cannulae should be changed at regular intervals and prophylaxis against thrombophlebitis must be given.

Patients with acute pancreatitis often have large fluid deficits and may require aggressive fluid resuscitation. Salt and water overload is common in these patients and can be aggravated by PN. Meticulous attention to fluid and electrolyte balance is mandatory. In AP fluid overload may also predispose to abdominal compartment syndrome.⁸⁹

Patients with severe acute pancreatitis, especially those with a history of chronic alcoholism and who are malnourished may be at risk of developing the refeeding syndrome.^{99,100} Particular attention should be paid to potassium, magnesium, phosphate, thiamine and sodium balance in these patients. Appropriate supplements should be given to prevent the development of the syndrome. If the syndrome does develop, it should be recognized early and treatment measures instituted immediately.

Hyperglycemia is common in patients fed parenterally during AP. This may be the consequence of several factors: insulin resistance, destruction of islet cells, and excessive carbohydrate support.

Tight control of glucose (between 4.4 and 6.1 mmol/L) with insulin therapy in critically ill patients has been shown to have a benefit on outcome in selected patient groups (although not specifically in patients with AP) and would therefore appear to represent good practice.^{101,102} Yet, aggressive use of exogenous insulin does put the patient at risk of severe hypoglycemic episodes.^{103,104}

PN carries the risk of overfeeding the patient, which may adversely affect outcomes.¹⁰⁵ Overfeeding is detrimental for cardiopulmonary and hepatic function and for carbohydrate and lipid metabolism. To avoid overfeeding, PN should be initiated with a low calorie regimen and built up step by step with progressive increase with a tight evaluation of patient's metabolism. Hyperglycemia, hyperlipidemia and hepatic dysfunction and steatosis may necessitate temporary discontinuation of PN. Administration of carbohydrates in this situation might be not appropriate because this aggravates hepatic steatosis, since these patients have some degree of insulin resistance.⁷⁹

2. Chronic pancreatitis (CP)

2.1. When is PN indicated in CP?

Malnutrition is frequent in patients with CP due to pain-induced anorexia and to continuing alcohol abuse. Moreover, increased resting energy expenditure is not rare in these subjects.

PN may, on rare occasions, be indicated in patients with gastric outlet obstruction secondary to duodenal stenosis and in those with complex fistulating disease (C).

Comments: More than 80% of patients suffering CP can be treated adequately with normal food supplemented by pancreatic enzymes (B) and only about 10–15% of all patients will require oral nutritional supplements. Tube feeding is indicated in approximately 5% of patients with chronic pancreatitis (C).

Therefore, PN is seldom used in patients with CP and its use will generally be restricted to those with gastric outlet obstruction in whom gastric decompression is necessary and a tube cannot be introduced into the jejunum. PN may also be indicated in patients with chronic pancreatitis and complex pancreatic fistula (C). There are no reported series of patients with chronic pancreatic insufficiency who have been treated with intravenous nutrition for a long period. PN is mainly performed over the short term, e.g. in apparent severe malnutrition prior to pancreatic surgery if enteral feeding is not possible.¹

2.2. When is PN contraindicated in CP?

No specific contraindications.

There are no specific contraindications to PN in CP, but less than 1% of patients with chronic pancreatitis will ever need PN (C).¹

Refeeding syndrome may occur in these malnourished patients if excessive amounts of calories and nitrogen are delivered in the first days of PN.

Conflict of interest

Conflict of interest on file at ESPEN (espenjournals@espen.org).

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