

REVIEW ARTICLE

Nutritional Management in Acute Pancreatitis

Luh Putu Listya Paramita*, Ari Fahrial Syam**

*Faculty of medicine, University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital
Jakarta

**Division of Gastroenterology, Department of Internal Medicine, Faculty of medicine
Universitas Indonesia, Dr. Cipto Mangunkusumo General National Hospital, Jakarta

Corresponding author:

Ari Fahrial Syam. Division of Gastroenterology, Department of Internal Medicine, Dr. Cipto Mangunkusumo General National Hospital. Jl. Diponegoro No. 71 Jakarta Indonesia. Phone: +62-21-3153957; Facsimile: +62-21-3142454. E-mail: ari_syam@hotmail.com.

ABSTRACT

Acute pancreatitis induce a catabolic stress that increase systemic inflammatory response with worsening nutritional status. Current approach in acute pancreatitis therapy was still symptomatic because of no definitive therapy yet to prevent any inflammatory and proteolytic cascade. One of the most important thing to consider in acute pancreatitis therapy was nutritional management. "Pancreatic rest" concept that formerly used have been known to increase cost, sepsis incidence due to catheter use, and also metabolic and electrolyte disorder. Nowadays, "gut rousing" concept was preferable compared to "pancreatic rest" concept, support that nutritional management was needed to stimulate and generate intestinal function. Enteral nutrition administration have to consider patient's hemodynamic status. Necrosis incidence, respiratory failure, intensive care, and mortality was found to be lower in patients given enteral nutrition in first 48 hours compared to after 48 hours. Nutrition administration via nasogastric tube or nasojejunal tube was still in doubt while several studies showed that nasogastric tube administration was safe and tolerated, otherwise could be evaluated in larger population sample study. Nutrition and metabolic monitoring was also an important part to reach nutritional goals and reduce complications.

Keywords: acute pancreatitis, enteral nutrition, gut rousing

ABSTRAK

Pankreatitis akut menyebabkan stress katabolik yang menimbulkan respon inflamasi sistemik dan perburukan status nutrisi. Pendekatan terapi pankreatitis akut saat ini masih bersifat simptomatik karena tidak ada terapi definitif untuk mencegah aktivasi kaskade inflamasi dan proteolitik. Salah satu hal penting yang harus diperhatikan dalam tatalaksana pankreatitis akut yaitu pemberian nutrisi. Konsep "pancreatic rest" yang dahulu diterapkan saat ini diketahui meningkatkan biaya perawatan, meningkatkan kasus sepsis karena pemakaian kateter, gangguan elektrolit dan metabolik. Konsep 'gut rousing' saat ini mulai menggeser konsep "pancreatic rest" yaitu pemberian nutrisi diperlukan untuk menstimulasi atau membangkitkan fungsi saluran cerna. Waktu memulai pemberian nutrisi enteral juga harus memperhatikan hemodinamik pasien. Insidens nekrosis, gagal nafas, perawatan intensif, dan mortalitasnya lebih rendah pada pasien yang diberikan nutrisi enteral dalam 48 jam dibandingkan dengan yang diberikan setelah 48 jam. Pilihan jalur nutrisi melalui selang nasogaster atau selang nasojejunal masih menjadi perdebatan, meskipun pada berbagai studi pemberian nutrisi melalui nasogastric tube (NGT) dapat ditoleransi dan aman namun diperlukan studi dengan jumlah sampel yang lebih besar. Monitor nutrisi dan metabolik juga bagian penting untuk mencapai target nutrisi dan mencegah komplikasi.

Kata kunci : pankreatitis akut, nutrisi enteral, gut rousing

INTRODUCTION

Acute pancreatitis was an inflammatory disorder that can lead to systemic inflammatory response syndrome (SIRS), multiorgan failure, and death. Incidence in several country was various, range for 4,9-73,4 cases per 100.000 population and still increasing every year. United States (US) and Finland was the highest prevalence country with 73 case per 100,000 population in US and 73,4 case per 100,000 population in Finland. Moderate prevalence was found in New Zealand (29.3 case) and Norwegia (34.4 case) per 100,000 population.¹ Most of acute pancreatitis will resolve without therapy or the need of specific therapy. Among 20% of them was progressed into severe acute pancreatitis and need an intensive care with operative management. Severe pancreatitis was marked by sepsis, organ failure in 48 hours, or worsening clinical condition. This condition was caused by infected necrotic tissue. Intestinal bacteria translocation was assumed to be the main cause of infection.²

Some definition and classification changes have been made since Atlanta Classification in 1992. Nowadays, acute pancreatitis was divided into two phases: acute phase and late phase. Acute phase happened less than one week with main characteristic of sign of organ failure (SIRS). Late phase (late onset) occur after one week marked by local complication. Several local complication was peripancreatic fluid, pancreas or peripancreas necrosis (steril or infected), and pseudocyst.³ Scoring system such as APACHE II, Ranson, and Glasgow was an important tools to predict its severity. Mortality among mild pancreatitis was rarely found but can be as high as 40% in severe acute pancreatitis.² In US, a significant increase in acute pancreatitis case was found but its mortality rate was decreasing. This was caused by improvement in diagnosis and management of acute pancreatitis.⁴

Acute pancreatitis cause a catabolic stress that cause systemic inflammatory response with worsening nutritional status.⁵ Until 1990, total parenteral nutrition and resting intestinal function was recommended in acute pancreatitis management due to reduce pancreatic exocrine secretion. Several studies and clinical experience showed that by resting pancreas in too long period will lead to mucosal atrophy and increase bacterial translocation risk so that it could made acute pancreatitis worse.⁶ Acute pancreatitis approach currently symptomatic because of no definitive therapy yet to reduce inflammatory and proteolytic cascade. Nutrition was an important part of acute pancreatitis management where enteral nutrition

was more recommended than total parenteral nutrition.¹ This article will review about nutritional management in acute pancreatitis. Only some studies that investigate mild and moderate acute pancreatitis, so that this review will discuss about acute pancreatitis in general.

ACUTE PANCREATITIS PATHOPHYSIOLOGY

Digestion and absorption was a complex process that need coordination of several secretion function from gastrointestinal organ, motoric function, and also circulatory system. Pancreas plays an important role in this physiology. Acute pancreatitis characterized by severe pain mainly in upper abdomen area with increasing pancreatic enzyme level in serum. Acute pancreatitis started from acinar cell disorder. Several mechanism underlie pancreatic acinar cell disorder⁷:

1. Pancreatic duct obstruction by stone, bile, or Oddi sphincter spasm (e.g. caused by alcoholism).
2. Cholecystokinin hormone stimulation that activate pancreatic enzymes. This hormone was stimulated by high fat and protein diet.
3. Transient ischemia caused by operatif procedure or atherosclerosis. This condition will lead to pancreatic enzyme degradation.

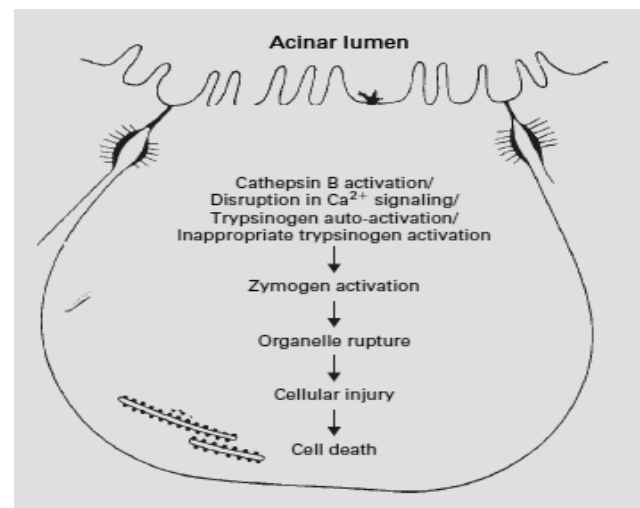


Figure 1. Digestive enzyme activation inside acinar cell

Several mechanism underlie zymogen conversion in pancreas into its active form, such as autoactivation of trypsin from trypsinogen by lysosomal hydrolase cathepsin B (CTSB), zymogen and lysosome leakage to cytoplasm and activation. This acinar cell disorder followed by pancreatic enzyme release to pancreatic tissue. Trypsinogen, chemotrypsin, and elastase in acinar cell will spontaneously activated and furthermore cause autodigestion. Trypsin will also activate complement system, coagulation, and fibrinolysis process. Endothelial

dysfunction would lead to increase vascular permeability that trigger proinflammatory cytokines production (IL-1,6,8, TNF α), free radical, and arachidonate acid metabolite (prostaglandin, platelet activating factor, leukotriene) and proteolytic enzyme which induce thrombosis and tissue hemorrhage.⁷

In mild and moderate acute pancreatitis, the necrotic segment was still sterile. Ischemic and necrotic condition will be worsen by bacterial translocation from intestinal via lamina propria, mesenteric lymphnodes, and then into systemic circulation that cause infected necrosis. Bacterial translocation was caused by increase intestinal permeability that could be measured by increase polyethylene glycol (PEG) excretion in urine and antiendotoxin antibody (Endocab). IL-6 concentration reach its highest concentration in 36 hours after the onset of pain and organ dysfunction was found in the third day, so that 'therapeutic window' was between 48 to 72 hours after the onset of pain.⁷

Immune dysregulation was one of the factors that increase mortality in acute pancreatitis and also played an important role in SIRS and multiorgan failure incidence. Sel Th1 and Th 2 imbalance were the main mechanism of immune dysregulation. Th1 cell release anti-inflammatory factors such as IL-10 and IL-4, while Th2 release proinflammatory factors such as IL-6 and TNF-alpha. A study by Pietruczuk showed that in acute phase, Th1 cell was suppressed so that the more active Th2 will trigger profound inflammatory response.⁸

In acute pancreatitis with sepsis, 80% among patients was in hypermetabolic condition. Nutritional requirement was increase because of increase resting energy expenditure (REE) and protein breakdown. Negative nitrogen balance was also impact patient prognosis. In acute pancreatitis, nitrogen loss was approximately 20-40 gram each day. Several amino acid deficiency will worsen inflammation process. The increasing endogen gluconeogenesis was a severe inflammation manifestation. In patient with sepsis and trauma, endogenous gluconeogenesis could only be suppressed partially by exogenous glucose. Oxygen consumption increase by 20-30% cause the need of more energy supply or reduce perfusion to several vital organs. Both was caused by hypovolemia and reduce cardiac function because of inflammation process.⁸

In acute pancreatitis, capillary permeability will increase and lead to pancreatic enzyme leakage. This will trigger local hydrolysis process of triglyceride that comes from chylomicron. This hydrolysis process was toxic and induce further pancreatic destruction.

An animal study showed that triglyceride cause pancreatitis and increase serum free fatty acid. This will lead to microthrombus formation that cause tissue ischemia.⁹ Negative nitrogen balance was correlate to worse prognosis in severe acute pancreatitis. Pancreas also need amino acid for its protein synthesis program.⁹

Carbohydrate was the main source of energy in acute pancreatitis because of its wide availability, its ability to suppress intrinsic gluconeogenesis, and reduce hyperlipidemia risk. A maximum of 4 mg/kgBW/minute of glucose can be given with always monitor hyperglycemia and hypercapnea risk. Insulin secretion was also impaired in acute pancreatitis so that parenteral nutrition administration will increase hyperglycemia risk. Insulin resistance could only be corrected by exogenous insulin administration.⁹

Table 1. Nutritional requirement in acute pancreatitis

Total calorie	25-35 kcal/kgBW/day
Carbohydrate	Less than 5 mg/kgBW/minute
Fat	Less than 1,5 gram/kgBW/day
Protein	1,5-2 gram/kgBW/day
Vitamin, trace element	Vitamin A,C,E and selenium

KgBW: kilogram of body weight

ENTERAL NUTRITION ROLE IN ACUTE PANCREATITIS

There were no specific therapy yet for acute pancreatitis, but in general an early treatment will improve patient outcome. Fluid resuscitation, analgesic drugs, and antibiotic prophylaxis was the main treatment for acute pancreatitis. However, lower mortality seen in last decade was known to be affected by nutritional management. Enteral nutrition was improved to be the part of acute pancreatitis management.⁴

Table 2. Enteral nutrition guideline for severe acute pancreatitis management⁶

Association	Recommendation
International Consensus Committee	In general, enteral nutrition was chosen rather than parenteral nutrition, or at least being prioritized. Enteral nutrition that used was peptide and medium-chain triglyceride basis.
European Society for Clinical Nutrition and Metabolism (ESPEN)	In necrotic pancreatitis, enteral nutrition was given if possible. Amount was formulated based on safety peptide quantity. Standard nutrition could be given if tolerated.
American Society for Parenteral and Enteral Nutrition (ASPEN)	Patient with severe acute pancreatitis could be given enteral nutrition with gastric or jejunal route. Tolerantion could be increased by changing intact protein into small protein and long-chain fatty acid into medium-chain triglycerides.
American college of gastroenterology	In acute pancreatitis, enteral nutrition was recommended to prevent infection as complication. Parenteral nutrition should be avoided except enteral nutrition was unavailable, intolerated, or nutritional requirement is not fulfilled.

The importance of nutrition role in acute pancreatitis has been known since 70's era. Parenteral nutrition was a standard therapy for the last four decades based on 'pancreatic rest' concept. 'Pancreatic rest' concept told that nutrition administration above mid jejunum will stimulate pancreatic enzyme. According to this, per oral nutrition was started since acute pancreatitis sign reduced so that pancreatic enzyme will turn back to its normal level.⁴

The rationality of this 'pancreatic rest' concept is that by resting inflamed pancreas, it will stimulate proteolytic enzyme release and reduce exocrine stimulation. Otherwise, this pancreatic enzyme secretion was known to be inverse with pancreatitis severity. Patients with severe acute pancreatitis will secrete lower level of trypsin, amylase, and lipase than mild to moderate acute pancreatitis patients because of its insufficiency. Insufficiency severity was based on disease severity. Unfunctional acinar cell could not respond to physiologic secretion stimulus.¹⁰

This 'pancreatic rest' concept was correlate to higher administration cost, increase sepsis risk because

of catheter used, and increase risk of electrolyte and metabolic disorder. Several studies also showed that it also caused gastrointestinal barrier dysfunction and increased permeability. Parenteral nutrition was also induce electrolyte imbalance, hyperglycemia, intestinal barrier dysfunction, and increase intestinal permeability so that 'pancreatic rest' was doubt.⁴

Enteral nutrition was having an immunomodulatory effect for systemic and intestinal mucosa. Intestinal epithelial cell integrity and immune cell along lymphoid tissue together with intestinal barrier played an important role in homeostasis and bacterial translocation. Intestinal epithelial cell was not only functioned as intestina mucosal defence, but also to support lymphocyte cell function and maturation. Intestinal mucosa permeability was the main parameter. Immunoglobulin M was an indirect marker for intestinal permeability. Three RCT shown an IgM reduction in patients received enteral nutrition.^{4,11}

Nowadays, 'gut rousing' concept was slowly replace 'pancreatic rest'. It explained that nutrition administration was needed to stimulate and generate

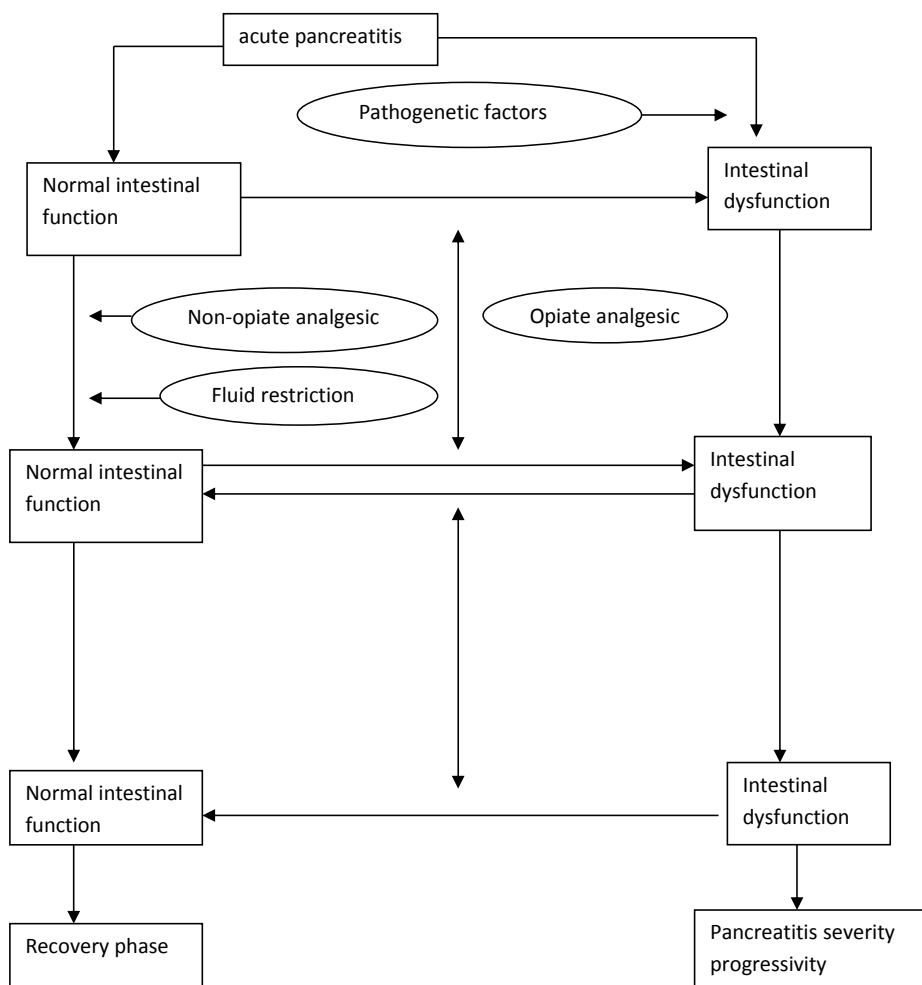


Figure 2. 'Gut rousing' concept, four phases of nutritional management in acute pancreatitis¹

intestinal function, contrastly differ to 'pancreatic rest' concept. In 'gut rousing' concept, there were four important phase: (1) Phase I: from onset of acute pancreatitis until hospital administration; (2) Phase II: from hospital administration until 24 hours after fluid resuscitation; (3) Phase III: final phase of resuscitation to fulfilled calorie needs (48-72 hours after resuscitation end); (4) Phase IV: after phase III until recovery stage.

There were several factors that affect intestinal function and patients outcome in each phase. Acute pancreatitis was started from local pancreas inflammation so that in Phase I intestinal function is normal. But, not all patients was having normal intestinal function so that therapy in the next phase will have an impact on the later phases. In phase II, fluid resuscitation and pain management was done. Resuscitation in acute pancreatitis should be done aggressively with positive balance, but this increased risk of intestinal submucosal edema and ileus. Opiate as analgesic have a side effect to delay gastric emptying, inhibit gastric motility, reduce pancreatic enzyme secretion and intestinal hormone so that intestinal dysfunction was mainly caused by iatrogenic etiology. Strategies to reduce this effect was giving per oral nutrition in normal intestinal patients and nasogastric tube for patients with intestinal dysfunction. If there were no enteral nutrition administration during phase III, it will worsen intestinal dysfunction and cause a progressive acute pancreatitis. In this phase, per oral nutrition should be consider, or using tube. This nutritional optimization in this phase III will affect patient prognosis.¹⁰

Meta-analysis done by McClave, Marik, and Zalogan showed that enteral nutrition will reduce infection complication, length of stay, and organ-failure risk. However, enteral nutrition in this studies did not reduce mortality. Meta-analysis by Petrov et al involving 202 severe acute pancreatitis patients showed significant mortality difference of 4% compared to 15,9%. A study by Cao et al showed a reduced mortality and organ failure incidence among enteral nutrition intervention group while a

metaanalysis by Yi et al showed a reduced mortality, infection complication, and surgical intervention, but no significant difference in length of stay. In clinical stings, there were no specific contraindication for enteral nutrition administration. This could still be administered although a fistula, ascites, or pseudocyst present, except in severe ileus.¹²

ENTERAL NUTRITION ADMINISTRATION TIME

During pancreatitis, intestinal dysfunction will increase inflammatory response and organ failure risk. In multicenter study, Besselink et al showed that bacteremia was happened in the first seven days. Bacterial translocation will trigger SIRS and could lead to sepsis. Early enteral nutrition administration could improve intestinal barrier and prevent bacterial translocation.¹²

Unstable hemodynamic level cause intestinal ischemia so that enteral nutrition in this phase will worsen ischemia and could lead to necrosis and bacterial overgrowth. Fluid resuscitation was needed to fill depleted intravascular fluid and reduce splanchnic vasoconstriction reflex before enteral nutrition administration. Therefore, enteral nutrition was recommended no to be given too early until phase III, exactly after fluid resuscitation. Enteral nutrition could be administered 24-48 hours after stable hemodynamic and intestinal function, and expected to fulfill nutritional target in 48-72 hours.

Absolute enteral nutrition contraindication was multiple trauma with peritonitis and retroperitoneal hematoma, intestinal obstruction, active intestinal bleeding, and unstable hemodynamic level. Relative contraindication where parenteral nutrition was still needed is diverticle abscess, malabsorption, fistula, bad tolerance, and malnutrition.¹¹

A metaanalysis by Petrov et al that reviewed 11 RCT showed a reduction in organ failure risk, infection complication, and mortality in patients given enteral nutrition in the first 48 hours. If enteral nutrition administered after 48 hours, there were no significant differences. An RCT study by Sun et al investigate

Table 3. Studies that compared enteral and parenteral nutrition¹²

Reference	Year	Country/Institution	Sample Size	Control	Benefit of enteral compared to parenteral nutrition
Paraskeva et al	2001	Yunani/Pireus General Hospital	23	Parenteral nutrition	Lower surgical intervention
Olah et al	2002	Hungaria/Petz A. Teaching Hospital,	89	Parenteral nutrition	Lower sepsis complication
Abou-assi et al	2002	Amerika Serikat/Virginia Univ. Hosp.	53	Parenteral nutrition	Lower sepsis complication, lower cost
Gupta et al	2003	Inggris/Southampton General Hospital	17	Parenteral nutrition	Shorter length of stay, lower cost
Louie et al	2005	Kanada/University of Alberta	28	Parenteral nutrition	Lower complication and better glycemic control
Eckerwall et al	2006	Swedia/Lund University Hospital	69	Parenteral nutrition	Lower mortality and organ failure
Petrov et al	2006	Russia/Nizhny Novgorod Hosp	22	Parenteral nutrition	No significance in mortality

Table 4. Studies investigate the benefit of enteral nutrition at first 48 hours vs after 48 hours¹²

Study	Year	Country/institution	Sample size	Control	Benefit of early 48 hours enteral nutrition
Sun et al	2013	Cina/ Nanjing Medical University	60	Enteral nutrition in day-8	Lower SIRS, organ failure, and complication
Wereszczynska-Siemiakowska et al	2013	Polandia/ Medical University Bialystok	197	Enteral nutrition after > 48 hours	Lower mortality and complication
Sun et al	2013	China/Nanjing Medical University	60	Enteral nutrition in day-8	Lower intraabdominal hypertension

enteral nutrition administration in 48 hours and its relation to immune function and outcomes in 60 severe acute pancreatitis patients. Patients received enteral nutrition in first 48 hours showed a lower multiple organ failure syndrome, SIRS, and pancreatic infection compared to patients received enteral nutrition after day-8. Otherwise, mortality among both group was not significantly difference.¹²

Wereszczynska-Siemiakowska et al investigate 197 patients with severe acute pancreatitis, result in lower necrosis incidence, respiratory failure, intensive care, and mortality among patients received enteral nutrition in first 48 hours compared to after 48 hours. Surgical intervention and multi organ failure was also found to be lower. Enteral nutrition in this study was using nasojejunal route. All death subject (9 patients) was from group that received enteral nutrition after 48 hours. There were no difference in local complication among both groups. Infection complication predictor was SIRS > 48 hours, enteral nutrition > 48 hours, and APACHE score in day-3.¹²

In mild acute pancreatitis, enteral nutrition could be administered early without any specific intervention. Study by Eckerwall et al that randomized 50 acute pancreatitis patients to compare the efficacy and safety of enteral nutrition in 24 hours to total parenteral nutrition. Enteral nutrition was given via nasogastric route. There were no difference in amilase level and SIRS between both group, but hyperglycemia was found to be lower in enteral nutrition group. Nutrition should not always be started from liquid diet, but it is more safe to give low fat soft diet. Early nutritional intervention will reduce length of stay.⁸

OPTIMAL ROUTE FOR ENTERAL NUTRITION

There were still in debate which location is the best for enteral nutrition administration. There are two options: postpyloric, especially jejunum, and prepyloric in stomach. Postpyloric tube insertion needs endoscopy specialist or radiologist, and this could lead to late enteral nutrition administration.⁴

Tube insertion in jejunum was correlate to 'pancreatic rest' concept. Based on that concept,

nutritional administration in upper GI tract (above jejunum) will stimulate pancreatic enzyme secretion that worsen patients condition, so that gastric tube insertion was avoided. Nasogastric tube considered to increase aspiration and pancreas stimulation risk. This opinion have been investigated in several studies.⁴

Several RCT and meta analysis showed that nutritional administration via nasogastric route and nasojejunal route have a better safety and toleration in critical patients. Acute pancreatitis patients tend to have ileus caused by inflamed pancreas. This also support the evidence that jejunal nutritional administration was better.⁴

Meta analysis that compare nasogastric and nasojejunal route was reviewing three RCT. In that study, there were insignificant difference in mortality (RR = 0.69; 95% CI: 0.37-1.29; p = 0.25), aspiration (RR = 0.46; 95% CI: 0.14-1.53, p = 0.20), diarrhea (RR = 1.43; 95% CI: 0.59-3.45; p = 0.43), exacerbation of pain (RR = 0.94; 95% CI: 0.32-2.70; p = 0.90) and nutritional sufficiency (RR = 1.00; 95% CI: 0.92-1.09; p = 0.97) among both groups. In general, patients toleration from both group was not significantly differ and no aspiration incidence in both group. RCT that included were consistently found no difference in safety and toleration of both group.¹³ A study by Kumar et al showed a higher mortality rate in both group because of late nutritional administration in conservative acute pancreatitis treatment will increase mortality rate.¹¹

Eatock et al investigate the use of gastric tube for severe acute pancreatitis patients, followed by two another RCT, concluded that enteral nutrition administration via nasogastric tube (NGT) was well-tolerated and no significant difference in mortality and the need of surgical correction. Two meta analysis with 131 severe acute pancreatitis concluded that there were no difference in mortality, length of stay, infection complication, and multi organ failure in patients having nutrition via nasogastric tube and conventional method. However, there were still need a larger sample size study for the effectivity of NGT nutritional route toleration and safety.¹²

Table 5. Studies of nasogastric tubes for acute pancreatitis patients^{12,13}

Study	Country	Method	Control group	Average APACHE score (NGT/NJ)	Time of administration	Nutrition formula	Duration
Eatok et al (2005)	UK	RCT	Nasojejunal	10/12	24-72 hours	Semielemental	5 days
Kumar et al (2006)	India	RCT	Nasojejunal	10,5 ± 3,8/ 9,6	48-72 hours	Semielemental	7 days
Eckerwall et al (2006)	Sweden	RCT	Parenteral	10	< 24 hours	Polymeric	5-9 days
Singh et al (2012)	India	RCT	Nasojejunal	8,5/8	4-23 hours	Semielemental	7 days

NGT: nasogastric tube; NJ: nasojejunal

Table 6. Safety and tolerance of nasogastric tube^{12,13}

Study	Sample size	Diarhea (%) NGT/NJ	Pain after nutritional administration (%) NGT/NJ	Aspiration (%) NGT/NJ	Nutritional sufficiency NGT/NJ
Eatok et al (2005)	27	11,1/4,5	7,4/0		78% /77,2% After 60 hours
Kumar et al (2006)	16	25/21	6,3/7,1	0/7,1	100%/100% after 7 days
Eckerwall et al (2006)	23	0	-		66% after 7 days
Singh et al (2012)	39	10,4/7,6	7,7/12,8	7,6/15,3	100%/100% After 7 days
Total	131	10,7	4,5		N/A

NGT: nasogastric tube; NJ: nasojejunal

Table 7. Outcome pancreatitis patients with nasogastric tubes^{12,13}

Study	Ventilator (%)	MODS (%)	Infected necrosis (%)	Operation (%)	Mortality (%)	Length of stay (day)
Eatok et al (2005)	25,9%	-	-	-	18,5/31,8	16
Kumar et al (2006)	93,8%	18,8%	31,3%	6,3%	31,3/28,5	24
Eckerwall et al (2006)	8,7%	4,3%	4,3%	4,3%	4,3%	9
Singh et al (2012)	66,7%	28,2%	10,2%	10,2%	10,2/17,9	17
Total	46,5%	16%	11,5%	12,2%	14,5%	N/A

MODS: multiple organ dysfunction syndrome

From several study above, nasogastric tube location was not stimulating pancreas but less known about its effect on pancreatic secretion stimulation. A developed hypothesis told that nasogastric tube will stimulate pancreatic enzyme but clinically insignificant.¹⁴ This was investigated by O'keefe et al. Per oral liquid polymeric diet compared to placebo showed an increase amilase, trypsin, and lipase significantly. Polymeric enteral formula administration into duodenum also stimulate amilase, trypsin, and lipase, otherwise elemental formula only slightly increase lipase. Studies also compared secretory response in nutritional administration at duodenum, mid-jejunal (40-60 cm distal ligamentum treitz) and distal jejunum (100-120 cm distal ligamentum treitz). There were no significant difference among those three different locations. Low trypsin and lipase secretion were found in elemental formula administration in mid jejunum. This response was similar to control group (fasting).⁴

The benefit of nasogastric tube was not only in severe acute pancreatitis, but also in mild and moderate acute pancreatitis.⁵ Per oral nutritional administration via nasogastric route still stimulate pancreas but its effect was subclinical and did not affect outcomes.¹ Mild to moderate acute pancreatitis early nasogastric tube feeding compared with pancreatic rest (MIMOSA) was a study that firstly investigate the safety,

tolerant, and efficacy of nutritional administration via nasogastric tube in non-severe acute pancreatitis patients. Approximately in 30%, SIRS was found in the early hospital admission with median APACHE score of 6 in both group. This study compared enteral nutrition via nasogastric tube in first 24 hours after hospital admission to non enteral feeding patients. The result showed that patients given enteral nutrition was not having progressive pancreatitis. This study was also showed that enteral nutrition reduce intensity and duration of abdominal pain, reduce opiate-analgesic needs, and reduce intolerance risk.¹⁴ From several studies, 'pancreatic rest' have not been proven to improve acute pancreatitis patients and now 'gut rousing' concept was used as an important part of acute pancreatitis management.¹⁵

ENTERAL NUTRITION FORMULA

In acute pancreatitis nutrition management, besides tube location, nutritional formula was also an important thing. Several composition could increase pancreatic secretion response so that in 'pancreatic rest' concept, nutritional formula was very important. There were more than 100 variety of formula, mainly classified into three types: (1) Elemental, composed of amino acid or oligopeptide, maltodextrin, and medium-chain or long-

chain triglyceride; (2) Polymeric, composed of non-hydrolyzed protein, maltodextrin, oligofructosaccharide, and long-chain triglyceride; (3) Immune enhancing, composed of substrate that enhance immune activity such as glutamine, arginine, and omega-3 fatty acid, probiotic, and fiber-rich formula.

In acute pancreatitis patients, elemental nutrition showed several benefit compared to polymeric in absorption, less stimulating pancreas, and higher toleration. Otherwise, this elemental nutrition was high cost. Elemental nutrition and immune enhancing formula have a higher osmolarity than polymeric formula, so that it could cause diarrhea.¹⁰ Nutritional composition could increase toleration and patients compliance. Patients with severe acute pancreatitis were recommended to receive peptide and medium-chain triglyceride formula. Medium-chain triglyceride was known to have anti-inflammatory effect, but its evidence was limited to animal studies.⁶

High-fiber formula with prebiotic vs high-fiber formula

Microbiota inside intestinal lumen have an important role in infection at acute pancreatitis. In peripancreatic fluid analysis, bacteria that cause infection was known to come from intestinal. Therefore, improving intestinal bacteria balance was one of the management target that now being studied. In previous study, probiotic has a lowering effect of CRP level and also APACHE II score.⁶ But, a study by Besselink et al doubt the effects of prebiotic. Besselink randomized 298 patients predicted as severe acute pancreatitis into two groups. Intervention group received probiotic, compared to placebo group. Infection complication in both group was not significantly different. Mortality was found to be higher in intervention group.⁹

Meta analysis from 13 RCT comparing high-fiber diet with no-fiber diet showed a reduce diarrhea incidence. This study explained that fiber could be considered clinically to reduce diarrhea.¹¹ This enteral formula was significantly reduce sepsis complication, but not in mortality of both group.¹⁰ Several studies showed that there were no significant different in toleration, infection complication risk, and mortality between polymeric and enteric formula nutrition. High-fiber diet was also safe, but adding immunonutrient or probiotic did not improve patients outcome.

Prospective trial showed that probiotic administration in severe acute pancreatitis patient will increase intestinal ischemia risk, organ failure, and mortality, significantly. But, it should be noted that probiotic

given in this study was widely varied so that high-fiber diet combined with probiotic will increase mortality.¹⁵

Immunonutrient in acute pancreatitis

Meta analysis by Asrani et al involving 505 patients from 12 studies showed that glutamine supplementation significantly reduce mortality (RR = 0.30; 95% CI: 0.15-0.60; $p < 0.001$) and infection complication (RR = 0.58; 95% CI: 0.39-0.87; $p = 0.009$), but did not reduce length of stay. The benefit of glutamine supplementation was clearly found in enteral nutrition. Enteral nutrition supplemented by intravenous glutamine will reduce pancreatic necrosis, infection complication, and length of stay.¹²

PARENTERAL NUTRITION IN ACUTE PANCREATITIS

Based on ESPEN recommendation, parenteral nutrition indication in acute pancreatitis was inadequacy of enteral nutrition after 5-7 days. This period could be shorter in formerly malnourished patients. Complication such as ileus, pseudocyst, pancreatic fistula, intestinal edema, pancreatic ascites, and infected necrosis impair enteral nutrition administration so that those patients was recommended to receive parenteral nutrition. There were no absolute contraindication for parenteral nutrition. Parenteral nutrition could be started in 24-48 hours after resuscitation and stable hemodynamics.¹⁴ In mild acute pancreatitis study, parenteral nutrition for 5-7 days have no positive effect so that it is not recommended, except in malnourished patients. Substrate metabolism in severe acute pancreatitis was similar to severe sepsis patients. Daily nitrogen target was 0,2-0,24 gram/kgBW. This target was similar to amino acid administration of 1,2-1,5 gram/kgBW/day. A reduction of 0,14-0,2 gram nitrogen/kgBW/day should be done in patients with chronic kidney disease or liver disease.¹⁶

Glutamine was an amino acid that have a central role in metabolism process such as nitrogen transport between organs, anabolize carbons, nucleotide and glutation precursor, and acid base regulator. An RCT study in moderate acute pancreatitis explained that parenteral nutrition with glutamine reduce overall complication and also reduce length of stay. There were no data for other amino acid administration in acute pancreatitis patients, such as BCAA, EAA, and arginine.¹⁴

Glucose should fulfill 50-70% of total calorie needs. Glucose was also prevent gluconeogenesis,

but hyperglycemia as side effect should be prevented. In acute pancreatitis and other critical condition, glucose oxidation reach its maximum level, about 4-7 mg/kgBW/minute, similar to 5-6 gram/kgBW/day. if glucose consumption higher than this limit, lipogenesis, hypercapneu, and hyperglycemia will happen. This risk was increasing in severe acute pancreatitis because of pancreatic necrosis and inflammation reduce insulin secretion. Data of non-carbohydrate glucose in acute pancreatitis patients was very limited.¹

OR TOLERANTION AND NUTRITIONAL ADEQUACY

Nutritional and metabolic monitor was aimed to control macronutrien (glucose, protein, fat) and micronutrient level, evaluate energy, and control glycemia. Macronutrien was evaluated intensively in 48 hours. In acute phase, blood glucose level was evaluated several time in a day, and reduce to once a day after acute phase. Electrolyte, ureum, creatinine, phosphate, magnesium, and liver function

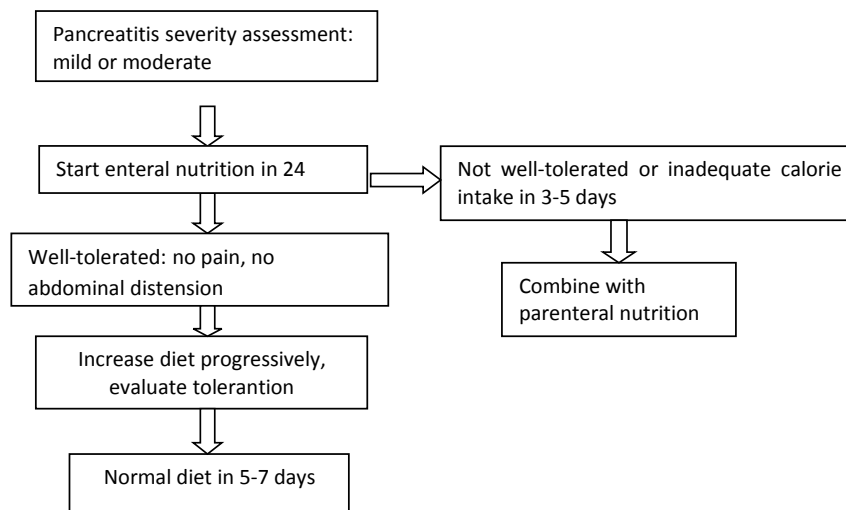


Figure 3. Nutritional management of mild to moderate acute pancreatitis

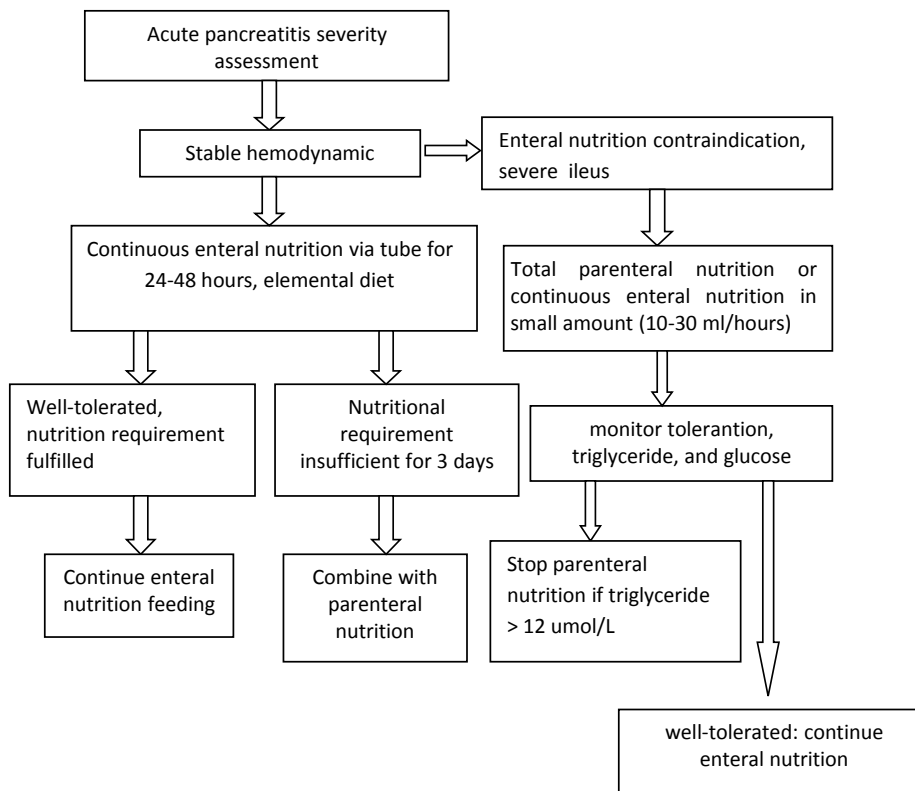


Figure 4. Nutritional management in severe acute pancreatitis

Table 8. Monitoring parenteral and enteral nutrition in severe acute pancreatitis¹⁷

Criteria	Aim	Method	Period
Energy target	Prevent energy deficit	Calculation of energy expenditure with indirect calorimeter	In 48 hours at past acute and rehabilitation phase
Protein and fat target	Prevent protein and fat deficit	Prediction	In 48 hours at post acute and rehabilitation phase
Micronutrien	Prevent micronutrient deficiencu and optimize macronutrien metabolism	Monitoring sheet	Daily
Glycemia	Prevent overfeeding and hypoglycemia	Laboratory examination	In acute phase: several times In post acute phase: daily
Insulin dosage	Prevent overfeeding and hypoglycemia	Dynamic algoritmn of therapy	In acute phase: several times In post acute phase: daily
Electrolyte, ureum, creatinine, liver function	Prevent refeeding syndrome	Laboratory examination	At the beginning. If abnormal, evaluate daily. If normal, evaluate 2-3 times/ week
Albumin	Know nutritional status while inflammation not present	Laboratory examination	Post acute: weekly Not recommended in cute phase because of inflammation present
Body weight, BMI	Nutritional status evaluation	Body weight instrument	In post acute and rehabilitation phase. Not in acute phase because of hidration variety
Free fat mass, intra and extra- cellular fluid	Nutritional status	Bioimpedance analysis	Postacute and rehabilitation phase when no fluid retention
Muscle strenght	Evaluate muscle strenght	Dynamometer	Rehabilitation phase (post ICU)

BMI: body mass index; ICU: intensive care unit

were monitor before nutritional administration. If abnormalities found, daily evaluation was done until normal, then continued to several times in a week. Albumin was not evaluated in acute phase but every week in post acute and rehabilitation phase. Body weight and muscle mass were evaluated in post acute and rehabilitation phase.¹⁶

CONCLUSION

Acute pancreatitis management was aimed to support hemodynamic and prevent infection complication. Patients with acute pancreatitis was susceptible to be malnourished because of lower intake and higher catabolism processs so that nutritional management was very important especially to fulfill nutritional requirement and modulate immunity. 'Pancreatic rest' concept' was now slowly replaced by 'gut rousing' concept. Enteral nutrition was chosen rather than parenteral nutrition or fasting because it lower length of stay, infection complication risk, and have a lower budget. Parenteral nutrition was still be used if nutritional intake was inadequate during 3-5 days or therapy, or in the condition of enteral nutrition contraindicated. Otherwise, otatl parenteral nutrition will increase infection risk, metabolic complication, electrolyte disturbance, higher cost, and higher mortality risk in general. Fulfill nutritional requirement and prevent pancreas exocrine stimulation should not alter the main goal of therapu to increase intestinal function.

In mild acute pancreatitis, enteral nutrition could be administered as soon as possible since there were

no contraindication. Nutritional administration via nasogastric tube was better than nasojejunal, and proven not to worsen pancreatitis condition. Parenteral nutrition should be acouded except enteral nutrition could not fulfill daily calorie requirement. Nutritional and metabolic nutrition should be done regularly to control macronutrien (glucose, protein, fat) and micronutrient, evaluate total energy, control glycemia and hypertriglyceride.

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