Chapter

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Interventions in Acute Pancreatitis

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Acute pancreatitis (AP) is a medical emergency presenting usually with acute abdominal pain associated with nausea and vomiting, abdominal distention (ileus), tachycardia and hypotension. About 80% of the patients with AP recover fully within a couple of days. However, the remaining 20% suffer from severe AP (SAP) and they carry a high mortality. It is these 20% of the patients who require intervention and thus need to be identified early. Many clinical and laboratory criteria have been proposed for the purpose (Ranson's criteria >3, Table 1; or APACHE II scores > 8, Table 2; or Balthazar score >, Table 3)[1], and yet it is often difficult to identify them before 48 hrs of the onset of the disease. Furthermore, many patients who start with a mild form of acute pancreatitis initially turn into severe disease[2]. It is therefore wise to treat initially every patient with AP as if he or she was going to suffer from SAP. Within 72 hours the picture becomes clear in the majority and the group of SAP become identified through appearance of an organ failure (Table 4) or a local complication such as peripancreatic fluid collection. The type of intervention does indeed depend on the severity as well as the stage of the disease[3] (Atlanta classification as given below):

Table 1: Ranson's criteria of severity

At admission	
Age > 55 year	
WBC > 16,000/mm^3	
Glucose >200 mg/dl	
LDH > 350 IU/L	
AST > 250 U/L	
During initial 48 h	
Hct decrease of >10	
BUN increase of >5 mg/dl	
CA ++ < 8 mg/dl	
PaO2 < 60 mmHg	
Base deficit > 4 mEq/L	
Fluid sequestration > 6L	

Note: Presence of > 6 signs indicate severe pancreatitis.

Temporal profile of acute pancreatitis:

Day 1:	Acute interstitial pancreatitis
1st week:	Necrosis
2nd week:	Infected necrosis
3rd-4th week:	Abscess.

In this communication I shall review the different types of interventions that may be done and at what stage of the disease and what results are expected from them.

Intravenous fluids: Patients with AP lose a lot of high protein exudates from the pancreas into the retroperitoneal space as well as peritoneal cavity, resulting into intravascular hypovolumia and consequent decrease in pancreatic blood supply which in turn promotes pancreatic necrosis. Pancreatic ischemia also leads to activation of inflammatory mediators.

Vigorous intravenous hydration is thus required in the initial stages to correct the hemoconcentration and that will be indicated by a fall in hematocrit. This is one measure that dictates the final outcome of the patient. Decreased hematocrit during the first 24 hours of care leads to a decrease in morbidity. Indeed, vigorous intravenous hydration has been shown to prevent the development of necrosis[4].

Nasogastric intubation: Although not proven, it is likely to decompress the upper gut and reduce the abdominal distention in the initial stages of the disease. It helps to know if there is any gastrointestinal bleed and

Table 2: APACHE II scoring system

APACHE II score = (acute physiology score) + (age points) + (chronic health points)

Acute Physiology Score

- 1= Rectal temp (C)
- 2 = Mean arterial pressure (mmHg)
- 3 = Heart rate (bpm)
- 4 = Respiratory rate (bpm)
- 5 = Oxygen delivery (ml/min)
- 6 = PO2 (mmHg)
- 7 = arterial pH
- 8 = Serum sodium (mmol/l)
- 9 = Serum potassium (mmol/l)
- 10 = Serum creatinine (mg/dl)
- 11 = Haematocrit (%)
- 12 = White cell count (10^3/ml)

	+4	+3	+2	+1	0	+1	+2	+3	+4
1	> 41	39-40.9		38-38.9	36-38.4	34-35.9	32-33.9	30-31.9	< 29.9
2	> 160	130-159	110-129		70-109		50-69		< 49
3	> 180	140-179	110-139		70-109		55-69	40-54	< 39
4	> 50	35-49		25-34	12-24	10-11	6-9		< 5
5	> 500	350-499	200-349		< 200				
6					> 70	61-70		55-60	< 55
7	> 7.7	7.6-7.69		7.5-7.59	7.3-7.49		7.25-7.3	7.15-7.2	< 7.15
8	> 180	160-179	155-159	150-154	130-149		120-129	111-119	< 110
9	> 7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		< 2.5
10	> 3.5	2-3.4	1.5-1.9		0.6-1.4		< 0.6		
11	> 60		50-59.9	46-49.9	30-45.9		20-29.9		< 20
12	> 40		20-39.9	15-19.9	3-14.9		1-2.9		< 1

Age Points

Age	**Points**
<44	0
45-54	2
55-64	3
65-74	5
> 75	6

Chronic Health Points

History of severe organ insufficiency	**Points**
Non-operative patients	5
Emergency postoperative patients	5
Elective postoperative patients	2

- Organ insufficiency or immunocompromised state must have preceded the current admission
- Immunocompromised if:
  - — Receiving therapy reducing host defences (immunosuppression, chemotherapy, radiation therapy, long-term steroid use, high dose steroid therapy) or
  - — A disease has been interfering with immune function such as malignant lymphoma or leukemia
- Hepatic insufficiency if:
  - — Biopsy proven cirrhosis
  - — Portal hypertension
  - — Episodes of upper GI bleeding due to portal hypertension
  - — Prior episodes of hepatic failure, coma or encephalopathy
- Cardiovascular insufficiency if:
  - — New York Heart Association Class IV
- Respiratory insufficiency if:
  - — Severe exercise restriction due to chronic restrictive, obstructive or vascular disease,
  - — Documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension
  - — Respiratory dependency
- Renal insufficiency if:
  - — On chronic dialysis

Table 3: Balthazar scoring system for severity of acute pancreatitis: Grade and CT severity index (CTSI)

CT grade	*Score*
A = normal	0
B = pancreatic enlargement	1
C = peripancreatic inflammation	2
D = / peripancreatic fluid collection	3
E = > / peripancreatic fluid collection	4
Add to CT score the necrosis score	
Necrosis	Score
None	0
One-third	2
One-half	4
>one-half	6
CTSI= CT grade score + necrosis score (0-10)	
CTSI i.e. CT severity index	
Index	Morbidity / Mortality
0-3	8% / 3%
4-6	35% / 6%
7-10	**92% / 17%**

Modified from: Balthazar EJ, et al. Radiology 1990; 174:331-36

Table 4: Organ failure in acute pancreatitis

Cardiovascular failure	BP < 90 mmHg systolic
Respiratory failure	p O_2 < 60
Renal failure	Serum creatinine > 1.5 mg /dl
	Urine output < 30 ml/hr
Gastrointestinal failure:	Gastrointestinal bleeding > 500 ml in 24 hr

may also be used for feeding in very sick or moribund patients and in patients on ventilatory support. Once the ileus is over, however, it should be removed readily unless it is required on account of the latter 2 indications.

Antisecretory, antiprotease and anticytokine measures: Drug intervention with the intent of reducing pancreatic secretion or protease activity or release of cytokines has so far failed to show any benefit in reducing morbidity or mortality of SAP. Hence, antisecretory drugs like somatostatin or octreotide, or antiproteases like gabexate, or anticytokine like lexipafant (an anti-platelet agglutinating factor) are not recommended[3].

Peritoneal lavage: The collection of enzyme rich fluid in the peripancreatic area and peritoneal cavity tempted many physicians to tap the fluid, examine it and then lavage using normal saline with or without a protease inhibitor such as Gabexate. A couple of double blind controlled trials have been done to test this hypothesis. The short duration lavage did not show any benefit. However, a single study using peritoneal lavage with Gabexate did show a greater chance of recovery and lower chance of developing infection in the pancreatic necrosis [5]. This therapeutic measure has, however, been largely given up because of doubtful benefit and a chance of introducing infection.

Prophylactic antibiotics: Initial febrile reaction is due to pancreatic imflammation. Antibiotics will not help in its control in any way, but may instead promote the growth of antibiotic resistant bacteria and fungi in case infection occurs later. So, routine use of antibiotics in AP must be discouraged. In case of SAP which is very often associated with pancreatic necrosis, however, prophylactic antibiotics are strongly recommended and the choice of antibiotics should be such that are capable of penetrating into the pancreas. Indeed, six randomized controlled trials have shown benefit from prophylactic use of antibiotics active against Gram negative bacteria in SAP[6-11]. The commonly recommended antibiotic is imipenem-cilastin 500 mg three times a day for two weeks. A cheaper alternative for our patients in India may be cefotaxime, ofloxacin and metronidazole based on the profile of bacterial infection commonly seen in them[12].

It is prudent, however, to mention that a recent study[13] which included Medline search as well as a study of the Cochrane controlled trials has shown that antibiotic use was not associated with a reduction in infected necrosis (RR 0.77), mortality (RR 0.78), non-pancreatic infections (RR 0.71) or surgical intervention (RR 0.78), but it was associated with a reduction in the length of hospital stay.

Endoscopic treatment of gallstone pancreatitis: Gallstones are the leading cause of acute pancreatitis all over the world. The most pronounced feature of acute biliary pancreatitis is transient biliary obstruction in the form of raised serum bilirubin, serum alanine aminotransferase and serum alkaline phosphatase and hence it is logical to expect benefit from an endoscopic sphincterotomy and common bile duct clearance. Four randomized trials have addressed this issue[14-17]. Two of them, one from UK[14] and the other from Hong Kong[15], are most well known and well performed; they support early endoscopic intervention in patients with acute biliary pancreatitis. Their results suggest that patients with severe disease are likely to have decreased morbidity and mortality. The applicability of their results has been questioned by the randomized-controlled trial from Germany that suggested that patients without

obstructive jaundice would not benefit from early endoscopy[16]. However, the German study ain my opinion compliments further the earlier studies because it specifically included patients that were unlikely to be included in the UK and Hong Kong trials. Preliminary findings from Poland suggest that all patients, irrespective of the severity of their disease, would benefit from early endoscopic intervention[17].

It is recommended therefore that an emergent ERCP should be performed in patients with acute pancreatitis of suspected or proven gallstone etiology when criteria for severity are met and/or there is coexistent cholangitis, jaundice, dilated CBD, or when there is clinical deterioration in patients with initial mild prognostic signs. As endoscopic sphincterotomy almost certainly protects against recurrence of gallstone pancreatitis, we consider performing sphincterotomy in a patient with significant local and/or systemic complications, a dilated bile duct without demonstrable stones, and a gallbladder containing stones, if cholecystectomy is neither possible nor contemplated.

Nutritional Support: TPN vs Enteral Nutrition

Traditionally, any form of enteral feeding during acute phase of illness was considered contraindicated as that might result in an exacerbation of acute pancreatitis. Hence, total parenteral nutrition was the standard practice in all sick patients who did not recover promptly and could not be initiated into regular oral feeding in 3-4 days. However, recent studies on intensive care patients with trauma and sepsis showed that enteral feeding was associated with a restriction in the acute phase response and the severity of septic complications compared to TPN[18]. Taking a cue from this, leading groups in UK and continental Europe employed early enteral nutrition in preference to intravenous feeding in patients with severe acute pancreatitis and found that they were well tolerated and produced less complications, specially infectious complications[19-22]. Thus, the present practice is to insert a naso-enteral tube on day 3 or 4 under endoscopic or fluoroscopic guidance and a semielemental diet is begun. This should have a concentration of 1 calorie/ml. If tolerated, the feeding is advanced to a polymeric formula. Most groups have used nasojejunal feeding which carries difficulties in maintaining the tube position and patency. Thus, in a pilot study on 26 patients with prognostically severe acute pancreatitis were all fed by fine bone nasogastric tube soon after admission. This was shown to be both practical and safe in 22 of 26 patients. Feeding began within 48 hrs of hospital admission and starting with 30 ml/hr it was possible to increase the feed to 100 ml/hr in most of these patients within a further 36-48 hours of treatment. Subsequently, a randomized study of nasogastric versus nasojejunal feeding in severe acute pancreatitis has shown little difference in terms of CRP response, pain, analgesic input or clinical outcome from these two approaches to early naso-enteric feeding[29]. All of these studies are still rather small but the indication is that clinical practice, particularly in continental Europe and the UK, is swinging towards the early use of naso-enteric feeding with a lowering of the risk to the patient associated with TPN. If enteral nutrition is not tolerated, parenteral nutrition is required. The preferred solution contains carbohydrate, protein and lipid. The exception to this is hypertriglyceridemia, in which case lipid should be excluded. A patient's individual caloric requirement is calculated using the Harris-Benedict equation with appropriate modifications for stress factors[23] or using indirect calorimetry. In general, patients with severe acute pancreatitis require 2000-2500 calories/day: 50-60% from glucose, 15-20% from proteins and 20-30% from lipids.

Pancreatic Duct Stenting

SAP is often associated with pancreatic duct disruption and leakage of pancreatic juice causing pancreatic ascites. The leakage occurs because of the pancreatic necrosis damaging the duct. Thus, it makes sense to stent the duct at an early stage and stop the leakage of the pancreatic juice. That would likely prevent the tissue damage from the leaked enzyme rich pancreatic juice and the resultant systematic inflammatory response syndrome.

Lau and colleagues evaluated 144 patients with SAP and found that the presence of a pancreatic leak was significantly associated with the development of necrosis. Patients with a pancreatic duct leak had a longer length of stay compared with the patients with acute pancreatitis and the absence of a pancreatic duct leak. In this retrospective study, patients who underwent early ERCP and had a pancreatic duct stent placed were less likely to have other more invasive interventions performed, such as placement of external drains[24]. This apparent advantage must, however, be balanced against the possibility of seeding sterile necrosis with microbes leading to infected necrosis. Kozarek did indeed find recently that pancreatic duct stent placement was associated with polymicrobial contamination of the pancreatic duct[25]. Clearly, further studies are needed before this therapeutic intervention can be accepted as a standard therapeutic measure.

Surgical Intervention in Acute Pancreatitis

The most difficult decision for the treating unit is to intervene surgically for necrosectomy in patients with severe necrotizing pancreatitis not improving with conservative treatment. Timing for intervention has changed from 7–10 days (earlier studies) to 21–25 days (recent studies) on the realisation that results of early intervention might have included many patients with sterile necrosis who are better off treated medically. There is increasing non-randomized evidence from sequential audit that sterile pancreatic necrosis can be successfully managed by continued conservative therapy. In a large retrospective analysis of a prospective audit, it is reported that in a speciality center few, if any, patients die in the first two weeks of illness provided antibiotic therapy is routinely available[26]. While the general guideline of conservative management for sterile necrosis versus active intervention for infective necrosis is agreed, there is certainly a considerable need for further studies. Some have argued that a lack of stabilization or improvement with full supportive intensive care therapy over 72 hours should constitute an indication for surgical intervention to establish intra-abdominal peritoneal lavage, but no randomized study has validated this approach. When a patient has clinical evidence of sepsis (usually >7 days of onset) unexplained by normal microbiology studies a contrast enhanced CT scan should be performed followed by a fine needle aspiration (FNA) with immediate Gram stain and subsequent culture of the fluid. The odour of the fluid itself may indicate sepsis. In such situations active intervention to remove the pus and adjacent peri-pancreatic or pancreatic necrosis is mandatory. In very ill patients a percutaneous drain may be placed at the time of FNA using CT guidance. Such drainage of pus may allow further stabilization of the patient before removal of the infected necrotic tissue.

Finally, there are complications of acute necrotising pancreatitis which pose difficulties in deciding the best treatment approach. Prominent amongst them are endoscopic versus percutaneous drainage (or only aspiration) of acute pseudocyst of the pancreas and percutaneous versus surgical drainage of pancreatic abscess. Acute upper gastrointestinal bleeding from direct erosion of a pancreatic or peri-pancreatic artery or vein is a serious complication. Its preferred treatment will be selective visceral angiography and occlusion of the bleeding vessel or pseudo-aneurysm[27]. However, if the expertise is not available the treating team will have little choice but to intervene surgically.

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