Acute pancreatitis (AP) is a common acute medical condition requiring emergent care. Yet, no prevalence data are available from India. Only some idea of incidence can be obtained from patients admitted in tertiary care centers. At the All India Institute of Medical Sciences (AIIMS), New Delhi, 276 patients with AP were hospitalized from January 1997 to June 2002, i.e. about 55 patients per year. This is about the same as in similar centers in England. The incidence of AP has, however, been reported to be much higher in USA, Finland and Scotland (49.3, 46.6 and 41.9 per 100,000 population, respectively). Furthermore, it has been noted that the incidence of AP has been steadily rising during the last decade in European countries and UK.

Gallstones and alcohol are the most common causes of AP, gallstones being about twice as common as alcohol in our population. Other causes include hypertriglyceridemia, hypercalcemia, postendoscopic retrograde cholangiopancreatography (ERCP) and drug-induced pancreatitis, but they are much less common. Microlithiasis is perhaps also fairly common especially in those who present with recurrent AP and should be looked for carefully using endoscopic ultrasound (EUS). Among toxin-induced pancreatitis, smoking is being increasingly incriminated as an important causative factor.

ASSESSMENT OF SEVERITY

Since the morbidity and mortality of AP differ markedly between mild and severe disease (mild < 5% vs severe 20–25%), it is very important to assess severity as early as possible. Multiple clinical criteria, biochemical parameters and imaging criteria have been used for this purpose.

Of them, acute physiology and chronic health evaluation (APACHE)-II is the most widely used method at tertiary care centers. However, it is complicated and requires a long list of parameters to be taken into account. As a result, it is not practical to use it in smaller hospitals with limited staff and expertise.

Contrast-enhanced computerized tomography (CECT) based Balthazar criteria have been used to assess the severity and extent of necrosis and inflammation (Table 1).

The severity of the acute inflammatory process is categorized into stage A through E, corresponding to scores of 0 to 4, respectively. Stage A is when inflammation in minimal (essentially normal pancreas). Stage B represents focal or diffuse gland enlargement, mild heterogeneity of the gland parenchyma and small intrapancreatic fluid collections. Stage C includes, in addition, mild inflammatory changes of the peripancreatic soft tissues. Stage D manifests more prominent peripancreatic inflammatory changes but not more than one ill-defined fluid collection. Stage E represents the most severe stage of inflammation and is manifested by marked intrapancreatic and peripancreatic fluid collections and extravascular fat necrosis, or frank pancreatic abscess formation.

Necrosis is scored as 0 through 6 depending on the extent of pancreas involved as shown in Table 1.

The sum of scores of grade and necrosis give CT severity index (CTSI). In Balthazar’s series, patients with a CTSI of 0–1 had no mortality or morbidity, while those with an index of 2 had 4% morbidity, and those with an index of 7–10 had 17% mortality and 92% morbidity.

It should be noted however, that CTSI in isolation fails to predict the outcome and needs to be combined with one or the other clinical criteria to get a reliable assessment of the severity and expected outcome. A very simple clinical severity assessment tool has appeared recently; it is called BISAP after the following five criteria used:

1. Blood urea nitrogen (BUN) > 25 mg/dL
2. Impaired mental status (Glasgow coma scale score < 15)
3. Systemic inflammatory response syndrome (SIRS) score ≥ 2
4. Age > 60 years and
5. Pleural effusion.

It has been tested prospectively and found to be as accurate as APACHE II in predicting severity and mortality of AP. The great advantage of this scoring system is ease of its application in day to day practice. Another interesting, very simple clinical tool has been used bedside to assess severity of AP. Absence of rebound tenderness and guarding of the abdomen, normal hematocrit and normal creatinine assure the clinician with 98% certainty that the disease is mild. It is known as harmless acute pancreatitis score (HAPS).

Among the single prognostic markers, hemoconcentration stands out to be a simple, readily available and yet reliable indicator of bad outcome. Thus, a hematocrit of 44% or hemoglobin of 14.6 g/dL or more or a BUN of 33 mg/dL or more are associated with increased pancreatic necrosis and complications. It is because of this that early aggressive fluid replacement is recommended.

Many other single prognostic markers have been suggested. They include obesity (BMI > 30), plasma glucose greater than 190 mg/dL, SHS greater than or equal to 2, trypsinogen activated peptide (TAP), serum procalcitonin (> 3.8 ng/ml), C-reactive protein greater than 150 mg/L, coagulation parameters (e.g. d-dimer), interleukin-6 (> 122 pg/ml) and intra-abdominal pressure (> 15 mm Hg).

CLASSIFICATION OF ACUTE PANCREATITIS

The simplistic approach of mild and severe AP has been modified now to recognize many subtypes of each of them. Thus, the revised classification suggested is as shown in Table 2.

TREATMENT

Three most important issues initially are pain relief, fluid replacement and nutrition. Thereafter, the issue of preventing or treating infection emerges. However, careful monitoring of cardiorespiratory and renal functions is required all through, particularly in the initial 48 hours to assess if the patient would need treatment in intensive care unit (ICU). Needless to say that prompt intervention for treating any complications is a major determinant of outcome.

Relief in Pain

Pain in AP is usually very severe, often radiating to the back and associated with abdominal distension and nausea/vomiting. Nonsteroidal inflammatory agents are tried initially but if they do not give relief, patients must be provided relief by giving opioids. A combination of pentazocine and Phenergan is very effective.

Fluid Therapy

Adequate fluid replacement to maintain effective circulating volume and perfusion pressure is necessary to maintain pancreatic microcirculation. The fluid requirement may be quite large because of substantial loss of fluid in the retroperitoneal space. Thus, experts and various guidelines started recommending fluid replacement with crystalloids at a rate of 300–350 ml per hour, especially in those with raised hematocrit and BUN. According to the Mayo group, 33% of the first 72 hours of fluid volume requirement should be administered within 24 hours of presentation. It was hoped that such rapid fluid replacement would help prevent necrosis and other local complications. However, it did not happen, and in fact, it was seen that large rapid fluid replacement led to an increase in peripancreatic fluid collections, compartment syndrome and increased occurrence of respiratory failure. In a recent study, it was seen that administration of more than 4 liters of fluid during the initial 24 hours was associated with increased risk of respiratory insufficiency and a longer stay in the ICU. Conversely, those who received less than 4 liters of intravenous fluid within the first 24 hours fared better—less of respiratory failure, less necrosis and lower mortality.

Central venous pressure monitoring may help guide the physician in giving fluid replacement more judiciously and must be done in all patients with severe acute pancreatitis (SAP). In others, maintaining a urine output of 40–50 ml/h may help keep control on adequate and not excessive fluid replacement.

Nutrition

Since AP is a hypercatabolic condition, prompt and adequate provision of nutrition is essential. This was done earlier through intravenous alimentation but over the years it has become clear that enteral nutrition (EN) is far superior to parenteral nutrition (PN) (Table 3).

Enteral nutrition can be instituted within 24 hours of AP in the vast majority of patients. It is advisable to do so in a graduated manner, i.e. start with liquids and then advance to soft diet and then to regular diet. Although no benefit has been shown in giving predigested

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Section 6

Chapter 59  Management of Acute Pancreatitis: Indian Guidelines and Protocols

**TABLE 4 | Meta-analysis of studies on prophylactic antibiotics in acute pancreatitis (AP) with sterile necrosis**

<table>
<thead>
<tr>
<th>Date</th>
<th>Author</th>
<th>No. of trials (patents)</th>
<th>No. of blinded studies</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>Bai et al.</td>
<td>7 (467)</td>
<td>2</td>
<td>No effect on infection of necrosis and mortality</td>
</tr>
<tr>
<td>2009</td>
<td>Hart et al.</td>
<td>7 (429)</td>
<td>2</td>
<td>No effect on infection of necrosis and mortality Decreased in-hospital stay and extrapancreatic infections</td>
</tr>
</tbody>
</table>

nutrition formulae over polymeric formulae, the practice continues in many hospitals particularly in ICUs.

The use of EN in AP has been shown to be associated with significant reduction in infectious complications, need for surgery and mortality. A recent meta-analysis showed a significantly reduced risk of total infectious complications [relative risk (RR), 0.47; 95% confidence interval (CI), 0.28–0.77; p < 0.001]), pancreatic infectious complications (RR, 0.48; 95% CI, 0.26–0.91; p = 0.02), need for surgery (RR, 0.37; 95% CI, 0.21–0.65; p = 0.001), and mortality (RR, 0.32; 95% CI, 0.11–0.98; p = 0.03) with the use of EN in patients with SAP.

If the introduction of EN was delayed to 4 full days in patients with SAP, the expected benefit from EN over PN did not occur. Delays in initiating EN in SAP lead to prolonged ileus and reduced chances for tolerance. In a prospective nonrandomized study of 102 patients with AP, it has been shown that if feeding could be started within 2 days, tolerance to feeding was achieved in 92% of the patients. If, however, the start of enteral feeding got delayed to 5 days or beyond, the tolerance rate was reduced to 50% and if delayed to beyond 6 days, the tolerance to EN was down to 0%. On the other hand, early start of enteral feeding within 48 hours of admission served to maintain gut function and improve tolerance. Fewer problems were encountered with ileus and gastric stasis with this aggressive approach.

**Antibiotic Therapy**

There is no debate on use of aggressive antibiotic therapy for infection either within the necrosed pancreas or in the peripancreatic fluid collections (see below), but use of antibiotics prophylactically remains uncertain. It has been proposed that in SAP patients with pancreatic necrosis greater than 30%, antibiotics with deep penetration in pancreas should be given. However, such an approach did not show benefit in two recent meta-analyses (Table 4). Despite this debate, the treating physician often ends up giving a 7–10 day course of a carbapenem antibiotic to the patient with SAP and organ failure, as such patients carry a high rate of delayed mortality (after 2 weeks).

Fungal infection is not uncommon in patients with necrotizing pancreatitis especially after antibiotic therapy. That is another reason to avoid liberal use of prophylactic antibiotics; fungal infection would naturally increase morbidity and delay recovery. Fluconazole, which has a good pancreatic penetration, is quite effective in controlling the fungal infection. Mortality was shown to be not affected by the occurrence of fungal infection in one of the recent studies.

**Treatment of Infected Necrosis**

Around one-third of necrotic AP may get infected by the second week of SAP. This complication should be suspected if a systemic inflammatory response persists for more than 2 weeks after admission, clinical course worsens or air bubbles appear at CT. After excluding other foci of infection origins, infected necrosis should be confirmed by ultrasound- or CT-guided aspiration followed by Gram smear and culture. If the initial puncture is not diagnostic, it can be repeated after a few days. While waiting for the culture report, intravenous antibiotics should be started. Carbapenem (imipenem or meropenem 1 gram/8 h) or ciprofloxacin plus metronidazole are the preferred choice. If Gram positive bacteria are isolated, vancomycin (1 gram/12 h) should be administered.

Although the standard treatment recommended for infected pancreatic necrosis is open or laparoscopic surgical drainage, there is ample evidence now that many such patients can be treated only with aggressive antibiotic regimen without surgical drainage. So, we recommend antibiotics alone initially and advocate surgery only if patients do not show improvement on antibiotics.

The standard treatment for infected pancreatic necrosis is open or laparoscopic surgical drainage. However, on occasions, percutaneous drainage may work well. As recommended by the International Association of Pancreatology Clinical Guideline, drainage should be effectively established when the patient is septic. A step by step treatment is proposed by which percutaneous or endoscopic drainage should be established first and then necrosectomy with drainage through a minimally invasive retroperitoneal access. When this method was compared with open surgery, it offered several advantages, including the chance to avoid surgery in some patients, less complications and lower cost.

The alternatives to open surgery assume special importance in frail and critically ill patients and those with comorbid conditions, who may not tolerate an aggressive surgery. To recommend these alternative approaches as standard of care, however, they need to be evaluated through controlled trials. Hopefully they will be coming forth soon.

**Endoscopic Sphincterotomy and Common Bile Duct Drainage**

In severe biliary pancreatitis, an urgent endoscopic sphincterotomy (ES) and common bile duct (CBD) clearance has been recommended on the basis of earlier reports of its benefit. However, the latest meta-analysis clearly shows no advantage of this procedure unless there is evidence of cholangitis.

**Cholecystectomy**

It is extremely important that all patients with biliary AP undergo laparoscopic cholecystectomy within 2–4 weeks of resolution of AP. If not done, there is a 30% probability of recurrence of AP within the next 3 months.

**Logical but Unproven Modes of Therapy**

Protease inhibitors such as gabexate and camostat, anticytokines such as lexapitant and antisecretory agents like somatostatin or octreotide have been shown to decrease the severity of AP in occasional uncontrolled studies. Similarly, some Chinese medicines have been touted as being very effective in treating AP. However, none of them can be recommended as an accepted mode of therapy.

**CONCLUSION**

The incidence of AP has been increasing globally over years. The predominant cause is gallstone disease (60%) but the next common cause is alcoholism (30%). Smoking has been recognized as yet another important cause of AP. Up to 30% patients suffer from severe AP and they carry high mortality (up to 20%).
**Gastroenterology**

Aggressive fluid resuscitation is the single most important therapeutic intervention initially but caution should be exercised in ensuring that the patient does not become overloaded, resulting into respiratory failure or compartment syndrome. Enteral nutrition is the next most important therapeutic intervention and should be started at the earliest possible, preferably within 24–72 hours of disease onset. The role of prophylactic antibiotics remains controversial but that of potent antibiotics like carbapenems in infected necrosis is well established. Indeed, many patients with infected necrosis can be treated successfully with antibiotics and may not need any surgical intervention.

Although surgical debridement of infected necrosis has been the standard of care, many alternative methods have appeared, the predominant among them being ultrasound- or CT-guided percutaneous drainage and endoscopic debridement. Prophylactic randomized clinical trials are needed to prove their value. Endoscopic sphincterotomy should be reserved for patients with biliary AP with cholangitis. Currently, there is no evidence that supports the use of probiotics, immunomodulatory diets and agents like gabexate, aprotinin, lexipafant and octreotide.

**REFERENCES**