A Review Based Analysis of Recent Developments in Acute Pancreatitis: Evaluation and Management

*Maryam Jahangirifar, Hosna Gomari, Mona Moniri, Samira Behboudi-Gandevani, S M Ghazi, Ramin Khameneh Bagheri
Department of Neuroendocrinology, Ethiopia.

*Corresponding Author : Maryam Jahangirifar, Department of Neuroendocrinology. E-mail: fateme.hassani@gmail.com

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Abstract

The incidence of acute pancreatitis (AP) has been increasing worldwide, but the major etiologies remain gallstones and alcohol. Several studies have reported that smoking is an independent risk factor for developing AP. Classification of AP has traditionally used the categories of mild and severe disease. However, a new intermediate category of moderately severe AP has been described with intermediate characteristics including a high incidence of local complications but a low mortality. Assessment criteria that can serve as early predictors of AP severity are often complex and not sufficiently accurate. However, several recently described criteria that rely on criteria such as the body mass index, simple laboratory measurements could prove useful if validated in large prospective studies. Many issues related to the therapy of AP are still unresolved. Although preliminary studies support the importance of early volume expansion for the treatment of acute pancreatitis, optimization of the amount and type of fluids will require further studies. Similarly, preliminary studies suggest that enteral nutrition might benefit patients with AP and could even be useful early in the course of disease. However, the timing and type of fluids as well as the intestinal infusion site require further study. Finally, issues related to the prophylactic use of antibiotics in patients with severe AP have not been resolved.

While the process of clinical investigation moves slowly, progress has been made in clinical studies of AP.

Keywords

acute pancreatitis, severity scoring, diagnostic imaging, management of gallstone pancreatitis

Epidemiology and Etiology

Data from the National Center for Health Statistics have demonstrated a 100% increase in the overall hospitalization for AP in the United States during the last 2 decades.Similarly, there has been a 75% increase in admissions for AP in The Netherlands between 1992 and 2004, and this is predicted to increase by another 9.9% in 2010 Recent studies from the United Kingdom have shown a 3.1% annual increase in the overall incidence of AP, with the highest increase among women younger than 35 years. The age standardized incidence was higher among elderly people (odds ratio [OR], 1.06 per year) and in economically deprived areas (OR, 2.4 between least and most deprived).Additional evidence of an increase in the incidence of AP came from a recent meta-analysis of 18 European studies, which also showed a linear increase in the incidence of gallstone pancreatitis and an increase in mortality with age. The meta-analysis also showed that although the case fatality rate has decreased over the years, the overall mortality rate per 100,000 has been the same.

Alcohol and gallstones are the most common causes of AP. With respect to hypertriglyceridemia as a cause of AP, even though the triglyceride threshold required to cause pancreatitis has been established to be 1000 mg/dL, no correlation between the level of triglycerides and severity of AP has been found.

Drug-induced pancreatitis is difficult to diagnose. The precise role of a drug in causing AP, the duration between the exposure and development of AP, the pathogenic mechanisms, and synergy with cofactors are usually not clear. On the basis of an extensive review of 1214 reports describing drug-induced AP during 50-year duration, Badalov et al. classified 120 drugs that were found to be associated with AP into 4 major classes (Class I, positive re-challenge; Class II, consistent latency; Class III, at least 2 cases in the literature without re-challenge and latency; and Class IV, single case report without re-challenge).

Introduction

A patient complaining of sudden onset of epigastric pain radiating to the back, associated with nausea and vomiting, requires rapid exclusion of a wide range of life-threatening conditions involving the cardiovascular (myocardial infarction, ruptured, and/or dissecting aortic aneurysm) and gastrointestinal (peptic ulcer disease with perforation or bleeding, acute pancreatitis) systems. The clinician’s history and examination findings are augmented by relevant investigations in narrowing the differential diagnoses to eventually guide the management and treatment of a certain condition and its associated complications.

The incidence of acute pancreatitis in the UK is ~56 cases per 100,000 persons per year, while in the US over 220,000 hospital admissions annually are attributed to acute pancreatitis. An epidemiologic study that utilized UK and European data demonstrated an increasing incidence in all-cause acute pancreatitis. The incidence of acute pancreatitis was also noted to increase with age. The male population had an incidence that was 10%−30% higher than females. Despite a reduction in the case fatality being observed over time, the population mortality has remained largely unchanged. Of all hospital admissions with acute pancreatitis, ~20%−30% of patients have a severe course, while severe life-threatening complications will develop in ~25% of these patients. The mortality in severe acute pancreatitis can be as high as 30%, but the overall mortality in acute pancreatitis is estimated to be 5%.
Treatment

Antibiotic Prophylaxis in Acute Pancreatitis

Antibiotic prophylaxis to prevent infection of pancreatic necrosis has been another controversial issue. Despite a number of clinical trials and meta-analyses, a clear consensus still does not exist. Earlier meta-analyses showed beneficial results from antibiotic prophylaxis. However, to date there are only 3 double-blind placebo-controlled trials studying role of antibiotic prophylaxis, and none of them showed any benefit in terms of prevention of infection of necrosis.

Fluid Therapy

AP is associated with a significant amount of third space fluid sequestration. This can lead to hypovolemia and reduced perfusion pressure, which in concert with microvascular alterations can contribute significantly to the development of major local and systemic complications. There are very few high quality human studies that have assessed the role of fluid management in AP, and a recent review by us has addressed these issues. We have recently shown that aggressive fluid therapy (33% or more of the initial 72-hour fluid volume within the first 24 hours of hospitalization) is associated with a significantly lower OF rate compared with nonaggressive therapy (7.1% vs 22.6%; P < .03). The other area, besides volume of fluid that needs further insight is the type of fluid (crystalloid or colloid) for resuscitation.

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>No. of RCTs</th>
<th>Severity of AP</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>McCave et al</td>
<td>27</td>
<td>Severe</td>
<td>↓ Infectious mortality</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↓ Hospital stay</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No effect on organ failure</td>
</tr>
<tr>
<td>2006</td>
<td>Heinrich et al</td>
<td>6</td>
<td>Mixed</td>
<td>Similar in OF and mortality</td>
</tr>
<tr>
<td>2008</td>
<td>Petrov et al</td>
<td>15</td>
<td>Severe</td>
<td>↓ Sepsis and central line infections</td>
</tr>
<tr>
<td>2008</td>
<td>Petrov et al</td>
<td>5</td>
<td>Severe</td>
<td>↓ Infectious complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↓ Mortality, but not significant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↓ Infections</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↓ Mortality</td>
</tr>
</tbody>
</table>

Table 1: Meta-Analysis of Studies Comparing EN With PN in AP

Surgical Intervention in Acute Pancreatitis

All patients with acute gallstone pancreatitis should have imaging of the common bile duct to assess for cholecodolithiasis. Preoperative imaging utilizes noninvasive methods such as transabdominal ultrasound and/or MRCP, while intraoperative cholangiography provides real-time imaging of the common bile duct. Management of cholecodolithiasis is reliant upon availability of local expertise and can be broadly classified into 1) the single-stage approach — laparoscopic or open cholecystectomy with intraoperative cholangiography and common bile duct exploration, or 2) two-stage approach — preoperative ERCP with or without ES followed by laparoscopic or open cholecystectomy. There is no significant difference in the morbidity, mortality, retained stones, and failure rate between the two management approaches for cholecodolithiasis. Local complications of acute pancreatitis include pancreatic necrosis with or without infection, pancreatic pseudocyst formation, pancreatic duct disruption, and peripancreatic vascular complications. These local complications can be managed using a combination of endoscopic, radiologic, and surgical techniques, and have been reviewed previously. Open surgical debridement requires multiple laparotomies and is consequently associated with a high postoperative morbidity. However, surgical techniques have evolved to become minimally invasive, which may be associated with better outcomes.

Conclusion

Acute pancreatitis is frequently encountered on the emergency surgical take. Once the diagnosis is made, clinical efforts should simultaneously concentrate on investigating for the underlying etiology and managing the condition by anticipating its complications, which can be aided by using any of the severity scoring systems described. Management of acute pancreatitis is largely supportive. There is still no consensus on the ideal type and regimen of fluid for resuscitation, but goal-directed fluid therapy is associated with better outcomes. Early enteral nutrition modulates the inflammatory response and improves outcomes by decreasing infective complications of acute pancreatitis.

References