



Overview on the Recent Technical Recommendations on Acute Pancreatitis



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Introduction

A technical review and clinical practice guidelines and recommendations on the initial management of Acute Pancreatitis (AP) are recently published by Vege and coworkers [1]. The recommendation is an outstanding effort that will be helpful for physicians and scientists to improve their understanding and provide potential treatment options for patients suffering from Acute Pancreatitis (AP). The review summarizes almost all aspects of AP diagnostic and treatment strategies including intravenous hydration, prophylactic antibiotics, Endoscopic Retrograde Cholangiopancreatogram (ERCP), early feeding, artificial enteral nutritional support, route of feeding, same-admission versus delayed cholecystectomy, alcohol counseling, and clinical impact of utilizing a risk assessment severity prediction tool. AP is one of the most common reasons for hospitalization with a gastrointestinal condition [2] and it is increasing in prevalence [3,4]. The annual incidence of AP varies from 13-45 per 100,000 people in United States [5]; however, the incidence of acute pancreatitis in the US for gallstone related AP is 15/100,000, for non-gallstone related AP is 25/100,000 and for recurrent AP is 10/10,000.

AP progressively increases in severity with patient age if not diagnosed and properly treated. In the US, both white and black populations are affected by the disease. Overall, most AP patients are middle aged (average age of 58 years) 45% male, and 80% white. The most common etiologies are biliary complications, alcohol, and idiopathic. Patients with alcoholic AP are significantly more likely to be younger, male, and black with a history of tobacco use when compared with AP patients with other etiologies. Development of recurrent AP occurs mainly in patients with non-gallstone related AP, although it can develop in patients with gallstone-related pancreatitis if there is a delay or refused cholecystectomy.

AP is generally more prevalent in more developed countries such as the US, Europe, and Japan; however, several reports

indicate that the AP incidence is increasing in developing countries. There is variability in the change of AP incidence within countries. The incidence of first-attack AP has relatively unchanged in Taiwan, which differs from the increasing trend observed in most western countries [6]. A retrospective study from Netherlands indicates the incidence of acute pancreatitis increased by 28% in recent years [7]. As observed in western countries, alcohol is the major cause of pancreatitis in South Africa, but the worse prognosis raises the question that better supportive care may improve overall survival of AP patients [8]. In Italy, a multicenter study of 1005 reported AP patients (males 53% and females 47%) with mean age 59.6 ± 20 years indicated 5% mortality rate [9]. In Swedish population AP is reported 7.6% per year incidence of acute pancreatitis with gallstone-related pancreatitis however, alcohol-related pancreatitis was decreased by minus (-) 5.1% per year [3]. Acute inflammation and repeated episodes of acute pancreatitis lead to chronic disease, which is characterized by fibrosis and calcification [10,11].

Regarding the question raised for the role of intravenous hydration in initial management, has several reasons to induce pancreatic necrosis and abnormal functioning of pancreas. This fluid therapy appears to be helpful, as reported that aggressive fluid administration during the first 24 hours in severe cases decreases the rate of morbidity and mortality [12]. The International Association of Pancreatology (IAP) and American Pancreatic Association (APA) guidelines provided directions for early and vigorous Ringer's lactate administration for the initial fluid resuscitation in AP. However, the concerns remain regarding fluid therapy for the initial management of acute pancreatitis related to the type of fluid, the rate of fluid delivery and the parameters to gauge effectiveness. We agree with the recent recommendations of Vege and co-workers [1] that intravenous hydration in AP will be considered for the enrolment of only consecutive patients.

The role of prophylactic antibiotics in severe acute pancreatitis (SAP) and necrotizing AP is well discussed in the technical review. Pancreatic and extra-pancreatic necrosis leading to infections of other tissues is very common in SAP. Well-designed meta-analyses [13,14] and double blind trials [15,16] indicated no potential benefits of prophylactic antibiotics in SAP. Moreover, the use of antibiotics in SAP may promote bacterial infection with pancreatic necrosis. The review did not consider the role of inflammatory mediators released from immune cells in promoting cell death and necrosis in AP. Several reports indicate the inflammatory immune cells including mast cells, neutrophils and eosinophils accumulate in AP and thereby contribute to disease pathogenesis and possibly mediate SAP. The technical review has not address the detection or control of these innate immune cells in pancreatic inflammation, which needs attention in future studies. Other recommendations for future studies include a large sample size with a multicenter trial design.

ERCP is a procedure that combines upper gastrointestinal (GI) endoscopy and x-rays to treat problems of the bile and pancreatic ducts. ERCP, invasive procedure with several complications, is also performed on patients having gallstone-associated AP. The complications of ERCP including infection, pancreatitis, hemorrhage, and perforation can occur even with expert. Factors such as patient selection, skill of the operator, and the complexity of procedure, can add to the risks of ERCP [17].

Additionally, ERCP may promote microbial infection [18,19] and about 2% of ERCP cases have reported post sphincterotomy bleeding [20,21], whereas, up to 30% of patients experienced immediate bleeding [22]. Although several reports suggest that ERCP is generally safe, but the role of urgent ERCP in acute biliary pancreatitis is a matter of concern. There is a need to modify our approach by using non invasive tests those avoid the complications ERCP. These non invasive possibilities include Magnetic Resonance Cholangio Pancreatography (MRCP) i.e. a type of Magnetic Resonance Imaging (MRI) and endoscopic ultrasound before conducting ERCP in patients with acute biliary pancreatitis. The technical review [1] strongly recommends following the inclusion and exclusion criteria, as well as definitions for persistent biliary obstruction, cholangitis, and predicted severe biliary AP for future clinical trials. It also recommends observation for 24 hours to allow spontaneous passage of a stone and 48 hours to ensure there is no prolonged biliary obstruction. However, the recommendation has not given any attention to the drawback of an ERCP that may not to provide sufficient tissue for pathological examination. That may be a problem for the patient in the future if immune cell accumulation in the tissue is not detected.

Nutritional interventions in acute pancreatitis maintain the integrity of the gut barrier in the small intestine, which is one of the most important aspects of the initial phase of SAP treatment. In addition, nutrition and nutritional supplements can also

provide important immune modulator and antioxidant effects. Generally, AP patients are maintained on 'Nil Per Os' or nothing by mouth to allow the pancreas to rest until the resolution of pain or normalization of pancreatic serum enzymes [23].

As an alternative, enteral nutrition (EN) or parenteral nutrition (PN) has been recommended. However, both routes have potential risks of infection and other complications. Therefore, optimal nutritional support in AP is under debate for decades because dietary restrictions exacerbate the patient's malnutrition, which leads to catabolism, bacterial translocation and necrosis [24,25]. The recommendations from Vege and co workers [1] regarding feeding related to timing, optimal route (oral vs. NG vs. NJ routes), rate, total calories and composition are very important for patients with severe and necrotizing AP and these recommendations should be considered in future clinical trials.

Conclusion

The current review of AP did not mention the role of food allergens in the AP disease pathogenesis. AP patients should be referred to an allergy clinic to rule out the possibility of food allergen-induced AP. We recently published a review that summarizes the reports available on food-induced acute pancreatitis and that is because of food allergy [26]. Therefore we suggest to include the testing of food allergy during the initial management of patients with acute pancreatitis. We recently published possible mechanisms of AP promotion by food allergies [26]. The initial management of acute pancreatitis patients should include testing for food allergy.

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