

Fluid Replacement Strategy in Severe Acute Pancreatitis

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Abstract

Adequate fluid resuscitation, pain control and organ support represent the cornerstones of treatment for acute pancreatitis. In this review, following questions will be answered on the basis of recent literature data: 1. What is the adequate volume of fluid to be administered and when should it be administered? 2. What type of fluid should be utilized? 3. What are the contraindications of an excessive amount of fluid?

The suggestion to the practicing physician is that the amount of fluid administered patients with acute pancreatitis should be in the range of 3.1-4.1 l during the initial 24 hours after admission. The fluids used should be the lactated Ringer's solution because the pH is more balanced than simple saline solution. Caution should be recommended regarding early fluid administration; the fluid should be administered under continuous monitoring.

Keywords: Acute pancreatitis; Clinical; Prognosis; Medical treatment; Fluid resuscitation

Questions

At the moment, adequate fluid resuscitation, pain control and organ support represent the cornerstones of treatment for acute pancreatitis, especially for the severe forms of the disease [1]. Regarding fluid resuscitation in severe acute pancreatitis, the following questions should be answered: 1. What is the adequate volume of fluid to be administered and when should it be administered? 2. What type of fluid should be utilized? 3. What are the contraindications of an excessive amount of fluid? Future developments of this topic will be also discussed.

Microcirculatory Derangement

From a pathological point of view, alteration of the pancreatic microcirculation plays a central role in the pathogenesis of acute pancreatitis because a disruption of pancreatic microcirculation may be involved in the transformation from interstitial edematous pancreatitis to severe, necrotizing pancreatitis [2-5]. Alteration in the pancreatic microcirculation may be due to hypovolemia, increasing capillary permeability, and hypercoagulability causing microthrombi, among other things, and the generation of oxidative free radicals with subsequent capillary endothelial damage has also been implicated. This alteration in microcirculation significantly increases the degree of pancreatic ischemia, irrespective of etiology, thus exacerbating the systemic inflammatory response syndrome [6,7] and leading to multisystem organ failure. Inflammatory mediators cause an increase in vascular permeability [8-13], and a decrease in endothelial tone causes significant extravasation of both interstitial fluid, leading to acute edematous changes around the acinus, and inflammatory cells [14]. In addition, hypercoagulability leading to microthrombi formation also contributes to pancreatic ischemia and subsequent pancreatic tissue necrosis [15].

Clinical Evidence

From a clinical point of view, more than 10% of patients are admitted to the hospital with hypovolemia, defined as systolic blood pressure of less than 100 mmHg [16]; in addition, hypovolemia correlates with increased hospital mortality [16]. In fact, at the time of admission, patients with severe acute pancreatitis are usually volume-depleted due to poor oral intake, third space loss and increased vascular permeability due to a generalized inflammatory response

[17]. Finally, an Italian survey on the treatment of acute pancreatitis [18] assessed the compliance of 56 medical and surgical centers equally distributed throughout Italy with the Italian guidelines on acute pancreatitis [19]. The severity of the disease was clinically assessed according to the Atlanta criteria [20]; the majority of patients was observed and treated early after the onset of acute pancreatitis with an interval between the onset of pain and hospital admission of 15 hours for patients with mild acute pancreatitis and 18 hours for those having severe pancreatitis. In these patients the amount of fluids administered during the first 72 hours was significantly higher in patients with severe acute pancreatitis than in those with the mild form. Adequate fluid replacement may be one of the reasons for the low mortality (3.1%) observed in the patients with acute pancreatitis enrolled in this study [18]. However, the following questions should be answered: 1. What is the adequate volume of fluid to be administered and when should it be administered? 2. What type of fluid should be utilized? and finally, 3. What are the contraindications of an excessive amount of fluid?

Experimental Evidence

The adequate amount of fluids that should be administered

Regarding the question as to what the adequate volume of fluid needed by patients is and when it should be administered, Kuwabara et al. [20] revised the data of 9,489 acute pancreatitis patients 18 years of age or older who were categorized into four study groups: ventilation, hemodialysis, a combination of ventilation and hemodialysis, and neither ventilation nor hemodialysis. They analyzed the Fluid Volume (FV) administered during the initial 48 hours (FV48) and during hospitalization (FVH), and calculated the FV ratio (FVR) as FV48/FVH. The authors found that the FV48 and the FVR were higher in

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patients requiring ventilation as compared to those not requiring ventilation. An elevated FV48 increased mortality and an elevated FVR decreased mortality in patients with severe acute pancreatitis. An elevated FV48 required ventilation in patients with severe acute pancreatitis which was independently associated with mortality; the obvious conclusion was that adequate fluid administration is required in acute pancreatitis.

Gardner et al. [21] evaluated the impact of the initial intravenous fluid resuscitation rate within the first 24 h of presentation to the emergency room on outcomes in severe acute pancreatitis and divided 45 patients into two groups: 17 who received more than 33% of their cumulative 72-hour intravenous fluid volume within the first 24 h of presentation (early resuscitation group) and 28 who received less than 33% of their cumulative 72-hour intravenous fluid volume within the first 24 h of presentation (late resuscitation group). The amount of fluid was 4.895 L during the first 48 hours in the early resuscitation group and 1.714 L in the late resuscitation group ($P < 0.001$) whereas the amount of fluid administered within the first 72 hours after admission was 12.190 L in the early resuscitation group and 7.664 L in the late resuscitation group ($P = 0.074$). They found that patients in the late resuscitation group experienced a greater significant mortality rate than those in the early resuscitation group (18 vs. 0%) and demonstrated a trend toward greater rates of persistent organ failure [22].

These data were further confirmed by a retrospective study of Warndorf et al. [23] on a larger number of patients. These authors evaluated the data of 434 acute pancreatitis patients stratified into two groups on the basis of early or late resuscitation fluid infusion. In a similar approach described by Gardner et al. [21], they defined early resuscitation as those patients receiving more than one-third of the total 72-hour fluid volume within 24 hours of presentation and late resuscitation as subjects with acute pancreatitis receiving less than one-third of the total 72-hour fluid volume within 24 hours of presentation. The fluids administered in the two groups were significantly different in the early resuscitation group (mean $\pm$ SD: 3.493 L $\pm$ 1.700 of fluids given in the first 24 hours from admission, 2.571 $\pm$ 1.325 between 24 and 48 hours from admission, 1.841 L $\pm$ 1.391 between 48 and 72 hours from admission; total fluids administered within the first 72 hours from admission 7.600 L $\pm$ 3.574) as compared to the late resuscitation group (mean $\pm$ SD: 2.403 L $\pm$ 1.216 of fluids given in the first 24 hours from admission, 3.578 L $\pm$ 2.490 between 24 and 48 hours from admission, 3.353 L $\pm$ 1.615 between 48 and 72 hours from admission; total fluids infusion within the first 72 hours from admission was 9.514 L $\pm$ 4.469). Early resuscitation was associated with decreased Systemic Inflammatory Response Syndrome (SIRS), reduced organ failure, reduced rate of admission to the intensive care unit and a reduced length of hospital stay. Thus, early fluid administration should be considered a valuable therapeutic measure for the early management of acute pancreatitis. The fact that, in a subgroup analysis, the beneficial effects of early fluid resuscitation were most pronounced in patients admitted with interstitial rather than severe disease further supports the fact that the need for adequate fluid administration should be the first line therapeutic approach to acute pancreatitis.

The amount of fluids needed by patients with acute pancreatitis comes from the study of de-Madaria et al. [24]. These authors prospectively included consecutive adult patients with acute pancreatitis. The 247 patients enrolled in this study were divided into three groups according to the amount of fluid administered during the initial 24 h: Group A (less than 3.1 L), Group B (fluid amount

ranging from 3.1 to 4.1 L), and Group C (more than 4.1 L). They found that the administration of more than 4.1 L of fluids administered during the initial 24 hours was significantly and independently associated with persistent organ failure, acute collection, respiratory insufficiency and renal insufficiency. The administration of less than 3.1 L during the initial 24 hours was not associated with organ failure, local complications or mortality and, finally, patients who received an amount of fluids between 3.1 and 4.1 L during the initial 24 hours had an excellent outcome. The optimal amount of fluid administered in this study is similar to that administered by Warndorf et al. [23], and is lower than that of Gardner et al. [21].

The type of fluid which should be administered

The answer to the question regarding which kind of fluids should be administered comes from the study of Wu et al. [25]. The authors carried out a randomized controlled trial involving 40 patients with acute pancreatitis; the patients received goal-directed fluid resuscitation with lactated Ringer's solution, goal-directed fluid resuscitation with normal saline, standard fluid resuscitation with lactated Ringer's solution or standard fluid resuscitation with normal saline. Systemic inflammation was measured on the basis of the levels of SIRS and C - reactive protein (CRP) after 24 hours. The authors found that the volumes of fluid administered during a 24-hour period were similar among patients given goal-directed or standard fluid resuscitation. Goal-directed resuscitation did not significantly reduce the incidence of SIRS as compared to standard resuscitation or levels of CRP after 24 hours. By contrast, there was a significant reduction in SIRS after 24 hours among the subjects resuscitated with lactated Ringer's solution as compared to normal saline; the administration of lactated Ringer's solution also reduced the levels of CRP as compared to normal saline.

Contraindications of fluid administration

Regarding the last question, i.e. the contraindications of excessive amounts of fluid, we should point out that, in the absence of important cardiac dysfunction, adequate amount of fluids should be administered. Fluids should be given by an arterial catheter, with at least two peripheral lines, and, in cases of simultaneous renal dysfunction or hemodynamic instability, a central venous line should be placed; in addition to electrocardiograms, appropriate continuous oxygen saturation and fluid balance should be monitored [17].

Future developments

In order to improve pancreatic microcirculation and tissue oxygenation and, subsequently, to prevent the progression from edematous acute pancreatitis to the necrotizing form it has been evaluated the influence of improved isovolemic hemodilution associated with enhanced oxygen supply. Experimental studies have shown that isovolemic hemodilution with hydroxyethyl starch or without plasmatic hemoglobin reduce mortality and preserves pancreatic microcirculation [8,26,27]. Studies in humans are not conclusive because based on a small number of patients [28].

Conclusion

The suggestion to the practicing physician is that patients with acute pancreatitis be resuscitated with lactated Ringer's solution because the pH is more balanced than simple saline solution, and the amount of fluid administered should be in the range of 3.1-4.1 L during the initial 24 hours after admission. Caution should also be recommended regarding early fluid administration; the fluid should be administered under continuous monitoring and should also be

managed according to the chronic cardiovascular comorbidities of patients with acute pancreatitis.

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