

Fluid Therapy in COVID-19 Disease: Review

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Received: April, 2020

Revised: April, 2020

Accepted: April, 2020

Abstract

COVID-19 pandemic due to the new corona virus 2019 is an important cause global problems. This infection begins with symptoms such as fever, cough, anorexia, malaise, sore throat, and can progress to acute respiratory disease syndrome (ARDS) and necessitating intensive care unit (ICU) admission with an estimated mortality rate of 3%.

There is no confirmed specific antiviral treatment despite different treatment protocols. Supportive care especially fluid therapy plays a very important role in this disease. The aim of this review is to Institute effective strategies for effective fluid therapy in critically ill pediatric patients admitted to ICU.

Keywords: COVID-19; Corona virus disease 2019; SARS-CoV-2; Fluids; Child; Intensive care.

Conflict of interest: The author declares no conflict of interest.

Please cite this article as: Esfandiar N, Kompani F. Fluid Therapy in COVID-19 Disease: Review. J Ped Nephrol 2020;8(2):1-4.
<https://doi.org/10.22037/jpn.v8i2.30254>

Introduction

COVID-19 Presents as a mild disease in 80% of cases but causes rapid and progressive pneumonia in 14% of cases with the involvement of more than 50% of lung tissue. Treatment of critically ill COVID-19 patients is a challenge for ICU personnel. Cause of complications such as ileus, bleeding and myocarditis and hypotension may arise. Reduced renal perfusion results in RAAS activation. On the other hand, stress and pain Cause activation of sympathetic nervous system, RAAS, and secretion of ADH. Inflammation, increased catabolism and vascular permeability and hypoalbuminemia result in hemodynamic instability (1). In a case series from China among 2135 pediatric patients with COVID-19, more than 90% of cases had mild to moderate diseases (2). In a study of 72,314 cases from China, only of cases were under 10 years old (3). Among 1391 cases with COVID-19 who were below 16 years old in Wuhan Children Hospital, 171 cases had confirmed the disease including three cases who were admitted to ICU with comorbidities (4). Water and electrolyte treatment plays a very important role in the

management of these children especially those who are critically ill as a result of COVID-19. In this review we are going to discuss the different aspects of IV fluid therapy.

Septic shock and hemodynamic

By definition, positive Systemic Inflammatory Response Syndrome (SIRS) Refers to the presence of at least two of the four criteria which one of them should be hypo or hyperthermia or leukopenia or leukocytosis and the others should be tachycardia and also tachypnea. Sepsis includes two or more SIRS criteria associated with infection and septic shock occurs when sepsis and hemodynamic instability are both present. Hemodynamic instability includes low blood pressure or vasoactive drugs to maintain blood pressure in the normal range, prolonged capillary filling time, oliguria, metabolic acidosis and high lactate level (5). Rapid and appropriate interventions during septic shock could prevent multi-organ failure especially acute kidney injury (6). According to the SOFA score ≥ 2 by definition of the third

International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) was associated with increased risk of death (7). A Chinese report showed that common complications in addition to acute respiratory disease syndrome (ARDS) were acute kidney injury (AKI, 29%), liver enzyme abnormality (29%) and cardiac involvement (23%) (8).

Fluid resuscitation

According to American College of Critical Care Medicine Clinical Practice (9) when patient is diagnosed with septic shock with hypotension and hemodynamic instability, fluid therapy is the first and the cornerstone of the treatment. The first step is to establish an intravenous line or if not possible, an intraosseous line and then the infusion of 20ml/kg bolus normal saline should be considered. Reevaluation of the patient during treatment is done by reassessing capillary filling, blood pressure, pulse rate, and skin turgor. There are controversies about free fluid therapy especially in COVID-19. According to a systematic review in Cochrane library that was based on three clinical trials in children; there was an increased risk of mortality by 38% associated with free fluid therapy (10). Conservative fluid therapy by definition was, giving no fluid bolus, and fluid therapy was based on urine output, heart rate, capillary filling and the level of consciousness.

Vincent and Backer established a model for fluid treatment that consisted of four clinical phases (11). In the rescue or Salvage phase, if life-threatening shock is present, bolus fluid is recommended. In optimization phase in patients with compensatory shock, additional fluid bolus is given cautiously only if needed. Stabilization phase refers to administration of fluid for maintenance and ongoing loss and finally de-escalation phase points to removal of fluid in volume overload conditions. Balanced fluid therapy in order to avoid hypo or hypervolemia is of great importance because both conditions are hazardous (12). Fluid can adversely affect pulmonary and renal function and consequently the outcome of critically ill children (13). In critically ill patients, especially those with COVID-19, fluid overload should be avoided because of increasing risk of ARDS (6). The amount of fluid overload in percent can be calculated by subtracting daily output from the input, divided by ICU admission weight (13). In Bouchard's study, more than 10% fluid overload was associated with

a higher mortality (14). In a recent study by Gorga (15) among 357 children who received CRRT while being on extracorporeal membrane oxygenation (ECMO), patients with a higher percent of fluid overload had a higher mortality. In another prospective study on 320 patients aged one month to sixteen years, early fluid overload was associated with an increased risk of AKI and mortality rate (16). Finally, Silversides (17) in a meta-analysis of 11 randomized trials (2051 patients) concluded that in patients with ARDS and SIRS, conservative or de-escalation fluid therapy had a better outcome comparing to liberal strategy.

Fluid responsiveness

Fluid responsiveness is defined as having at least a 10% increase in cardiac stroke volume (SV) following fluid challenge. With failure to notice these parameters, recurrent and additional infusions of bolus fluid would result in fluid overload.

To evaluate effective intravascular volume and decide about the adequacy of fluid therapy, clinical, paraclinical static and dynamic parameters should be taken into account (18). They will be reviewed in the following paragraphs.

Clinical parameters include: daily body weight changes, balance between fluid intake and output, orthostatic hypotension, heart rate, urine volume, capillary filling time, skin turgor, presence of hepatomegaly, pulmonary edema, and passive leg raising. Passive leg raising (PLR) is a simple, practical method to evaluate fluid responsiveness in critically ill patients especially when associated with more than 10% increase in SV and predicts whether our patient can benefit from more fluid challenge. It is a postural maneuver that is considered positive when changing patient posture from semi-recumbent to an angle of 45 degrees of leg raising would result in an increase of more than 10% in SV (19). PLR has a sensitivity of 86% and a specificity of 90% to determine fluid responsiveness (20).

Laboratory parameters of fluid responsiveness include: urine sodium concentration, fractional excretion of sodium, fractional excretion of urea nitrogen, urinary specific gravity, hematologic changes, and serum lactate level (18).

Static variables that determine preload include central venous pressure (CVP), end-diastolic volume, and inferior vena cava (IVC) diameter (20). Finally, dynamic parameters which are only

measurable in patients using mechanical ventilation include variation in the following factors: SV, pulse pressure, and systolic pressure (21). A systematic review in children showed that similar to adults, static variables were not good predictors of fluid responsiveness and among dynamic variables, only aortic blood flow peak velocity changes with respiration could predict fluid responsiveness (22).

Choice of fluid

Several studies are done about selecting the best type of fluid. Choosing between crystalloid, colloid, a combination of them, or different types of them (e.g. starches, dextrans, gelatins, albumin, fresh frozen plasma (FFP) vs. saline, lactated, Ringer's solution or Plasma-Lyte) is a challenge. Due to a higher molecular weight, colloids remain in the intravascular space for a long time, whereas crystalloids may move to interstitial space rapidly. High doses of crystalloids leads to abdominal compartment syndrome and bolus infusion of 0.9% saline may result in metabolic acidosis. Among balanced crystalloid solutions, Lactated Ringer's is too hypotonic to use in neurologic patients and the other one which is Plasma-Lyte, has the risk of increasing acetate level which can be troublesome (12).

A meta-analysis based on 59 RCTs in critically ill patients showed that colloid infusions increased the risk of acute kidney injury (AKI) and the need for renal replacement therapy (RRT) (23). The reason was probably related to high oncotic load of these solutions (24). Another systematic review by Rochwerg, concluded that the rate of mortality was lower in patients who received balanced crystalloid or albumin compared to other solutions (25). According to another study albumin infusions in sepsis due to its antioxidant effects had relatively good results (26). Antequera Martín published a review in Cochrane Database based on 21 RCTs. There was no difference between buffered crystalloids and 0.9% saline in terms of AKI or mortality rate (27). Finally, Lewis studied 65 RCTs comparing crystalloids with different types of colloids (e.g. starch, gelatin, dextran, albumine or FFP) which showed no meaningful difference (28).

Conclusion

In critically ill patients with COVID-19 that led to shock, conservative approach and balanced

crystalloid solutions (not colloids) are recommended.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Support

Not declared.

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