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CASE REPORT

Continuous hypertonic saline for acute liver failure

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Abstract Acute liver failure (ALF) is a clinical condition with high mortality. The most common cause of death in ALF is cerebral edema. We present a 12-year-old boy with hepatitis A-related acute liver failure in grade IV hepatic encephalopathy successfully managed in the ICU using continuous hypertonic saline as the preferred osmotherapy.

Keywords Intracranial pressure · 3% hypertonic saline

Introduction

Increasing cerebral edema with higher grades of encephalopathy is the main cause of mortality in acute liver failure (ALF). Care in the intensive care unit (ICU) should focus towards managing intracranial pressure (ICP). Sedation, optimization of hemodynamics, controlled mechanical ventilation and osmotherapy all play a crucial role in management of cerebral edema. Here we highlight the successful management of a 12-year-old boy in grade IV hepatic encephalopathy (HE) due to hepatitis A virus (HAV) infection-related ALF.

Case report

A 12-year-old boy in grade IV, HE due to HAV related ALF with 48 h jaundice-encephalopathy interval was admitted to our level III ICU. On admission he was hemodynamically unstable (mean arterial pressure <65 mmHg), with oliguric acute kidney injury (AKI), and bilateral dilated fixed pupils. He required noradrenaline (0.05–0.1 μgm/kg/min, 42 h) and dobutamine (2.5 μgm/kg/min, 31 h) infusions, and one hemodialysis session on day 1; mechanical ventilation (day 1 to day 6), and blood product transfusions (10 units fresh frozen plasma, 8 units cryoprecipitate) were administered during his stay in ICU. Metronidazole was used for gut sterilization. Relevant serial investigations are as enumerated in Table 1. All cerebroprotective, ICP reduction measures were strictly implemented and continuous sedation with fentanyl and propofol over the first 4–5 days was utilized to the extent of abolishing response to tracheal and tactile stimulation. $PaCO_2$ was maintained between 30 and 35 mmHg. It was ensured that he did not cough when on mechanical ventilation until his prothrombin time showed a transition towards normalization. His CVP was deliberately kept between 4–5 mmHg and boluses of fluid were avoided as safeguard against sudden escalation in ICP. Continuous hypertonic saline (CHS-3% sodium chloride) for cerebral edema was used inorder to achieve serum sodium between 150–155 mEq/L and the desired serum osmolarity between 300–320 mOsm/L. He received 1,550 mL of 3% sodium chloride as continuous infusion over the first 72 h to raise his serum sodium from 139 mEq/L to 155 mEq/L with the aim to keep sodium correction at <10 mEq/L/day. Mannitol was not used for ICP reduction. Sedation was not interrupted for neurological assessment until a trend towards normalization of prothrombin time was observed, as it was deemed too dangerous in the absence of ICP monitoring. He remained on ventilator for 7 days and was discharged on the 10th day from the ICU with full recovery.

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Table 1 Serial investigations during ICU stay

Variables	Day 1	Day 4	Day 6	Day 8
Liver function test				Not available
Total bilirubin	8.6	7.0	3.8	
Direct bilirubin	4.2	3.2	1.8	
Alanine aminotransferase (IU/dL)	970	435	179	
Aspartate aminotransferase (IU/dL)	370	219	102	
Alkaline phosphatase	330	253	96	
Albumin	3.1	3.42	3.8	
Prothrombin time (control value) (sec)	>120 (12.1)	17.6 (10.3)	15.2 (11.2)	14 (11.7)
Serum creatinine (mg/dL)	2.8	2.5	2.4	1.2
Platelet count	238,000	150,000	136,000	160,000
Prognostication scores[a]				
SOFA	10	6	5	3
PRISM	13	Not calculated	Not calculated	Not calculated
Lactate (mg/dL)	30	18	15	15
Base deficit	−8.4	+1.5	+2	+0.5
Central venous oxygen saturation (CVO_2)	58%	>70%	>70%	>70%

[a] *SOFA* sequential organ failure score, *PRISM* pediatric risk of mortality score

Discussion

Acute liver failure is a devastating syndrome with high mortality rate [1]. Cerebral edema occurs in approximately 80% cases of grade IV hepatic encephalopathy [2]. Major shift in our management focused on the use of continuous hypertonic saline instead of mannitol, and maintaining deep sedation when patient was on mechanical ventilation till PT showed a trend towards normalization. Loss of vascular cerebral autoregulation, inflammatory mediators and increased neural glutamine content caused by elevated arterial ammonia all contribute in development of cerebral edema in ALF [3]. Approximately half of the mortality in ALF is due to raised intracranial pressure which further causes ischemic brain damage or brainstem herniation.

Mannitol does not cross the intact blood-brain barrier and so establishes a concentration gradient between the edematous brain tissue and the intravascular space leading to movement of water outside the brain. It also exerts its beneficial role by reducing blood viscosity and cerebral blood volume, whilst increasing cerebral blood flow, cerebral perfusion pressure, deformability of erythrocytes along with free radical scavenging and inhibition of apoptosis [4]. However, with multiple doses of mannitol there is a possible leakage into damaged brain tissue and so its regular use without documentation of ICP elevations warrants caution [4]. Ideally prior to each dose, serum osmolality should be checked and euvolemia maintained as high serum osmolality increases the risk of renal failure. Normal osmolal gap indicates sufficient clearance of previous doses of mannitol to allow for safe administration of the next dose [4].

Both bolus dose [5] and continuous infusion [6] of varying strengths of hypertonic saline solutions (HTS) offer an attractive alternative to mannitol for the treatment of brain edema in liver dysfunction [7]. HTS plays a beneficial role in cerebral edema by osmotic dehydration of the brain, decreasing blood viscosity, increasing regional brain perfusion from endothelial cell dehydration and possibly pial artery vasodilatation, augmenting cardiac output and mean arterial pressure, along with attenuation of inflammatory responses at the microcirculatory level [4]. More prolonged ICP reduction has been observed with hypertonic saline, than with mannitol but this difference may be restricted to the first bolus and disappears with repeated doses [4]. Hypernatremia is closely linked to continuous hypertonic saline (CHS) infusion and to renal dysfunction when sodium levels rise above 155 mEq/L and 160 mEq/L and therefore these levels should be utilized as cut off in day to day practice. Association between higher incidence of infections or DVT rates has not been found with CHS infusions. CHS however should be used with extreme caution in patients at risk for multiorgan failure or underlying myocardial dysfunction [8]. Carefully designed studies comparing the two agents are needed before superiority of one of them can be firmly established. 3% NaCl is readily available in most settings and continuous infusions of it targeting serum sodium levels between 150–155 mEq/L can be used in critical care settings.

Management of raised ICP in ALF is challenging. Osmotic therapy with continuous hypertonic saline seems to have a beneficial role in cerebral edema by osmotic dehydration of the brain, and may be preferred as first line osmotic therapy.

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