Case Study

N-ACETYL CYSTEINE IN ACUTE LIVER FAILURE SECONDARY TO HEPATITIS B

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ABSTRACT

Acute liver failure (ALF) is a clinical syndrome resulting from massive necrosis of hepatocytes or from severe functional impairment of hepatocytes. Leading cause in developing countries is viral hepatitis, autoimmune diseases, whereas in developed countries, drugs mainly acetaminophen is the most common cause of acute liver failure. N-Acetyl Cysteine (NAC) is a glutathione, having antioxidant properties that scavenges reactive oxygen and nitrogen species and improves hepatic blood flow via oxygen extraction through its vasodilator properties. Administration of NAC to children with ALF has appeared to be safe and associated with a better outcome. The duration of hospital stay was shorter for children receiving NAC and they also appeared to have a higher incidence of native liver recovery and a better survival after liver transplantation [2].

CASE REPORT

A 15 years old female patient, presented in HIHT emergency with complaints of pain in abdomen and yellowish discoloration of eyes for 15days, fever for 10days followed by vomiting and altered sensorium for last 1day. On enquiring, patient had history of multiple injectable medications from village for previous illness, mostly fever. Birth, Development and Menstrual history was normal for age. Immunization was incomplete. On examination, the general condition was sick with GCS score of E3V3M4, associated with tachycardia, tachypnea. However, blood
pressure and saturation was normal. Icterus was present on sclera along with staining of skin. Blood sugar levels were raised (RBS – 234mg/dl). Flapping tremors (Asterexis) were present. No signs of vitamin deficiency or other signs of liver failure were noted.

On CNS examination, patient was disoriented, with pupils of size 3mm bilaterally, normally reacting. Tone was markedly increased in all 4 limbs with power of 3/5 in all muscle group. DTR’s were exaggerated with planters bilaterally extensors. Signs of meningeal irritation were present (neck rigidity & Kernig’s sign). Ophthalmology examination was done which showed no evidence disc oedema.

On Per Abdomen examination, abdomen was soft, non-tender, with hepatomegaly of 4cm BCM and span of 12cm. Liver was firm in consistency with round margins. Outside Investigations were suggestive of HBsAg positive status with hyperbilirubinemia with elevated liver enzymes. Diagnosis of Hepatic encephalopathy stage II was made. Relevant investigations were sent which revealed HBsAg positive status with conjugate hyperbilirubinemia, elevated liver enzymes and deranged coagulation profile. Treatment was started in the form of iv fluids, iv antibiotics, high bowel wash and supportive care along with FFP transfusion.

Condition of the patient gradually deteriorated and patient landed into hepatic encephalopathy stage IV. Need for ICU care was explained but attendants refused for the same. In view of Acute liver failure, N-Acetyl cysteine (NAC) infusion was started as a continuous infusion in divided doses for a total of in total 72hours. Following NAC infusion, patient initially showed improvement in first 10hours as patient became conscious with improved GCS score and had landed into hepatic encephalopathy stage II from stage IV.

However, after 24 hours of initiation of NAC, patient had and two episodes of GTCS, following which the condition of the patient deteriorated. Patient was intubated and shifted to PICU and put on SIMV mode of ventilation. Secondary to the disease process, patient further developed alterations in the vital parameters (HR – 160/min, BP – 70mm hg systolic, no spontaneous respiration), with dyselectrolytemia (hyperkalemia), which was managed accordingly. Despite all best efforts, patient succumbed to her illness on 23/1/17.
Acute liver failure is a fatal condition, which is often fatal without liver transplantation. It includes biochemical evidence of acute liver injury (duration < 8 weeks) with no evidence of chronic liver disease with PT > 15 sec or INR > 1.5 not corrected by Vitamin K in the presence of clinical hepatic encephalopathy or a PT > 20sec or INR > 2 regardless of the presence of clinical hepatic encephalopathy. The leading cause of ALF in children is viral hepatitis, followed by autoimmune hepatitis and others such as metabolic diseases (eg. Wilson’s disease, Tyrosinemia, Galactosemia, etc.) and drugs (eg. Amanita Phalloids, Acetaminophen, Isoniazid, Sodium valproate, etc.) 1.

The pathogenesis involves the depletion of intracellular substrates involved in detoxification, particularly glutathione. Other factors contributing to the illness are impaired hepatocyte regeneration, altered parenchymal perfusion, endotoxemia, and decreased hepatic reticuloendothelial function 1. Treatment is challenging because of rapid progression of coma and death. Supportive measures aim at improving hemodynamic instability, reversing coagulopathy, preventing or controlling infections, and early consideration of liver transplant 3.

N-acetyl cysteine (NAC), the acetylated variant of the amino acid L-cysteine and a precursor of reduced glutathione (GSH), is an excellent source of sulfhydryl (SH) groups, and is converted in the body into metabolites capable of stimulating glutathione (GSH) synthesis, promoting detoxification, and acting directly as free radical scavengers. Extensive first pass metabolism by the cells of the small intestine and the liver results in the incorporation of NAC into protein peptide chains and the formation of a variety of metabolites of NAC. It is the drug of choice of acetaminophen poisoning 4. However, various studies have shown its efficacy and usage in non-acetaminophen induced ALF (NAI-ALF). Dosage of NAC in NAI-ALF is 150mg/kg body-weight in 250ml of 5% dextrose over 1hour, followed by 50mg/kg in 500ml of 5% dextrose over 4hours and 125mg/kg in 1000ml of 5% dextrose over 19hours, then 150mg/kg in 1000ml of 5% dextrose per 24 hours for additional 48hours 5.

A retrospective study by Kortasalioudaki et al, was conducted in children diagnosed with NAI-ALF 2. It was found that patients who received acetyl cysteine, had a greater survival rate as compared to patients who did not received NAC therapy. Also the survival rate post liver transplantation was also increased in patients receiving NAC therapy with shortened hospital stay.

Eisen et al, reported the successful use of NAC therapy in a 3 month old girl developing ALF 6. It was concluded that current guidelines do not include the use of NAC in treatment of NAI-ALF. Currently, the data are limited to provide further insight into the use of NAC in treatment of NAI-ALF. Also any improvement in the rate of mortality may be due to the offset by the failure of multi-organ systems in the critically ill patients. Further studies are required to determine the optimal dose, route and duration of the therapy, to establish the guidelines in Non-acetaminophen induced Acute Liver Failure.

REFERENCES