

Zinc as a rescue therapy for acute liver failure: report of 3 cases

Abstract

Introduction: Acute liver failure as a rare but potentially life threatening condition occurs most often in individuals without any history of preexisting chronic liver disease. This is report of salvage therapy of 3 cases of acute liver failure by Zinc sulfate as a rescue option.

Cases & method: In a 4 months period we had 3 cases of acute liver failure referred to our center. 2 of them were female and one was male. One of them presented with hepatic encephalopathy (a 16 y old girl) and the others attended by complain of icterus and disturbed liver function tests (a 24 y old man and 28 y old woman). There was no history of any drug usage and serologic profile of viral hepatitis was also negative. The average MELD score was 22 and we deferred liver biopsy due to profound coagulopathy (INR>2.2 on average). Salvage therapy with Zinc sulfate (50mg TDS) in concordance with conservative management began while waiting for results of autoimmune hepatitis serology. Their condition gradually got improve and by preparation of complementary serologic results consistent with AIH, prednisolone added to this drug regimen.

Results: The condition of all 3 cases improved and the function of their livers retrieved. Their coagulopathy got better, jaundice relieved and they regained their consciousness. After average 8 day of admission, they discharged and followed in our outpatient clinic. In one and 6 months follow up, their MELD score declined to 8.3 (6, 8 and 11 respectively) and therapy with prednisolone and Azathioprine continued. Their follow up and close observation have going on up to 1 year thereafter.

Conclusion: Zinc sulfate could be a potential treatment option as rescue therapy in acute liver failure and acts as a bridge to definite therapy (if any at all). We recommend this therapeutic approach to be further verify in future investigations.

Keywords: acute liver failure, zinc sulfate, rescue therapy, autoimmune hepatitis

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Introduction

Acute liver failure as a rare clinical syndrome define as the rapid development of hepatocellular dysfunction, specifically coagulopathy and mental status changes in a patient without known prior liver disease.¹ This syndrome could be the final common pathway of any severe liver injury resulting from numerous infectious, immunologic, metabolic, vascular, and/or infiltrative disorders.² The diagnosis of acute liver failure is made clinically on the basis of physical examination findings such as altered mental status and supportive laboratory results like prolonged prothrombin time.³ The most commonly identified causes of acute liver failure include medications and idiosyncratic drug toxicity, initial presentation of autoimmune hepatitis and viral infections⁴⁻⁷ also we should keep in mind other possibilities for example Eclampsia, Fatty liver of pregnancy, Hepatic ischemia, Malignant infiltration, Toxins and/or Wilson disease.^{4,8-10}

For management of acute liver failure, rapid identification of patients with an unfavorable prognosis is critical and presence of any single adverse characteristic can potentially raise the mortality about 80 to 95% in the absence of liver transplantation.^{4,11,12} On the other hand liver histologic evaluation in acute liver failure is associated with substantial sampling error and potential complications and does not reliably predict outcome so percutaneous or transjugular liver biopsy is not recommended.¹³ A variety of therapies have been proposed and studied in patients with acute liver failure but only liver transplantation, has permitted salvage of patients with irreversible liver failure.¹⁴ The initial management of a patient with acute liver failure should

include rapid identification of any potential treatable condition beside conservative ICU care and preparing patient for liver transplantation.¹⁵⁻¹⁸ The ability of zinc to retard oxidative processes has led to the theory that zinc may be capable of reducing cellular injury that might have a component of site-specific oxidative damage, such as post ischemic tissue damage.¹⁹ Based on these properties of Zinc, It has been evaluated in a varieties of chronic liver disease with inconsistent results.²⁰⁻²² In this article we report the results of treatment with Zinc as a salvage therapy in addition to conservative ICU care and its usage as a bridge until definite diagnosis and management of acute liver failure if any at all.

Method

During a 4 months period, 3 cases of acute liver failure referred to our hospital. Of them 2 were female and one was male. One of them who was a 16 y old girl, presented with overt hepatic encephalopathy and immediately admitted in ICU. The other 2 cases referred with minimal hepatic encephalopathy, overt icterus and disturbed liver function tests (a 24 y old man and 28 y old woman). They also admitted in GI ward under close supervision. None of them had any history of drug consumption or toxication and their serologic profile for viral hepatitis including HBS Ag, HBC Ab, HCV Ab and HAV IgM were negative.

Average MELD score of these patients was 22 and we deferred liver biopsy due to profound coagulopathy (INR>2.2 on average). Salvage therapy with Zinc sulfate (50mg TDS) in concordance with

conservative management and coordination with liver transplant center began while waiting for results of autoimmune hepatitis serology. Their condition gradually got improve and by preparation of complementary serologic results consistent with AIH in the next few days, prednisolone added to this drug regimen.

Results

In the following days, the condition of all 3 cases gradually improved and the function of their livers retrieved. Their coagulopathy got better, degree of serum bilirubin decreased and jaundice relieved and they regained their consciousness. The level of improvement was dramatic and after average 8 day of admission, we were able to discharge them.

They followed in our outpatient clinic. In one and 6 months follow ups, their MELD score declined to 8.3 (6, 8 and 11 respectively) and therapy with prednisolone and Azathioprine continued. Their follow up and close observation have going on up to 2 year thereafter.

Discussion

Acute liver failure occurs when the rate and extent of liver cell death are not adequately balanced by regenerative activity.² Pathophysiology of acute liver failure include extensive loss of hepatocytes or massive necrosis as a result of inflammatory mediators and cytokines such as TNF- α and IL-1 infiltration and up regulation of ICAM-1 mRNA in the liver during endotoxemia.^{23,24} There are no differences in the histopathology corresponding to different etiologies and histologic classification and prognosis based on biopsy specimens alone may be misleading.¹³

Although, the most successful treatment of acute liver failure is orthotopic liver transplantation, mortality rates for liver failure remain high because of the shortage of available donor organs. Therefore, there has been interest in finding temporary treatment methods for patients with acute liver failure to either allow liver regeneration or await liver transplantation.¹⁷ In this regard one of the possible targets could be breaking the vicious cycle of necrosis and inflammation by using antioxidants and supportive management which is specially truth in the cases of acetaminophen toxicity induced liver failure.¹⁵

The ability of zinc to retard oxidative processes has been recognized for many years and its mechanism of antioxidation can be divided into acute and chronic effects.¹⁹ Chronic effects involve exposure of an organism to zinc on a long-term basis, resulting in induction of some other substance that is the ultimate antioxidant, such as the metallothioneins. The acute effects involve two mechanisms: protection of protein sulfhydryls or reduction of -OH formation from H₂O₂ through the antagonism of redox-active transition metals, such as iron and copper.¹⁹ These properties has led to the theory that zinc may be capable of reducing cellular injury that might have a component of site-specific oxidative damage such as post ischemic tissue damage¹⁹ and also there are some hopeful experiences in management of advances liver cirrhosis and hepatic encephalopathy.²⁰

In our experience, we used Zinc sulfate as a temporary therapeutic option while waiting for laboratory results to make a clear the definite etiology and commencing specific therapy if any at all of liver transplantation become available. Although it's better that validity of any therapeutic effect be verify in a randomized clinical trial, but it should be keep in mind that due to high mortality rate and poor prognosis, designing a randomized clinical trial for management of acute liver failure is so difficult and encounter many ethical issues. So

if these dramatic response repeat in other cases and in other centers, it worth to consider zinc as a salvage therapy for management of acute liver failure.

Conclusion

Based on antioxidant properties, Zinc sulfate could be a potential therapeutic option as rescue therapy in acute liver failure with undetermined etiology and acts as a bridge to definite therapy (if any at all). We recommend this therapeutic approach to be further verify in future investigations.

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Conflicts of interest

The authors declare there is no conflict of interests.

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