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

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 infections [4-7] 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 intoxication 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 therapeutic option while waiting for laboratory results to make a clear the definite etiology and commencing specific therapy if any at all. 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.

References

1. Hoofnagle JH, Carithers RL Jr, Shapiro C, Ascher N (1995) Fulminant hepatic failure: summary of a workshop. Hepatology 21(1):240-252.
2. Riondan SM, Williams R (2003) Mechanisms of hepatocyte injury, multiorgan failure, and prognostic criteria in acute liver failure. Semin Liver Dis 23(3):203-215.
3. O'Grady JG, Schalm SW, Williams R (1993) Acute liver failure: redefining the syndromes. Lancet 342(8866): 273-275.
4. Ostapowicz G, Fontana RJ, Schiodt FV, Larsen A, Davern TJ, et al. (2002) Results of a prospective study of acute liver failure at 17 tertiary care centers in the United States. Ann Intern Med 137(12): 947-954.
5. Bernau J, Ruff B, Benhamou JP (1986) Fulminant and subfulminant liver failure: definitions and causes. Semin Liver Dis 6(2): 97-106.
6. Acharya SK, Panda SK, Saxena A, Gupta SD (2000) Acute hepatic failure in India: a perspective from the East. J Gastroenterol Hepatol 15(5): 473-479.
7. Kessler WR, Cummings OW, Eckert G, Chalasani N, Lumeng L, et al. (2004) Fulminant hepatic failure as the initial presentation of acute autoimmune hepatitis. Clin Gastroenterol Hepatol 2(7): 625-631.
8. Hamid SS, Jafri SM, Khan H, Shah H, Abbas Z, et al. (1996) Fulminant hepatic failure in pregnant women: acute fatty liver or acute viral hepatitis? J Hepatol 25(1): 20-27.
9. Rowbotham D, Wenden J, Williams R (1998) Acute liver failure secondary to hepatic infiltration: a single centre experience of 18 cases. Gut 42(4): 576-580.
10. Korman JD, Volenberg I, Balflo J, Webster J, Schiodt FV, et al. (2008) Screening for Wilson disease in acute liver failure: a comparison of currently available diagnostic tests. Hepatology 48(4): 1167-1174.
11. O’Grady JG, Alexander G, Hayllar KM, Williams R (1989) Early indicators of prognosis in fulminant hepatic failure. Gastroenterology 97(2): 439-445.

12. Anand AC, Nightingale P, Neuberger JM (1997) Early indicators of prognosis in fulminant hepatic failure: an assessment of the King’s criteria. J Hepatol 26(1): 62-68.

13. Hanau C, Munoz SJ, Rubin R (1995) Histopathological heterogeneity in fulminant hepatic failure. Hepatology 21(2): 345-351.

14. Liou IW, Larson AM (2008) Role of liver transplantation in acute liver failure. Semin Liver Dis 28(2): 201-209.

15. Harrison PM, Keays R, Bray GR, Alexander GJ, Williams R (1990) Improved outcome of paracetamol-induced fulminant hepatic failure by late administration of acetylcysteine. Lancet 335(8705): 1572-1573.

16. Polson J, Lee WM (2005) AASLD position paper: the management of acute liver failure. Hepatology 41(5): 1179-1197.

17. Stockmann HB, IJzermans JN (2002) Prospects for the temporary treatment of acute liver failure. Eur J Gastroenterol Hepatol 14(2): 195-203.

18. Wagner M, Kaufmann P, Fickert P, Trauner M, Lackner C, et al. (2003) Successful conservative management of acute hepatic failure following exertional heatstroke. Eur J Gastroenterol Hepatol 15(10): 1135-1139.

19. Powell SR (2008) The antioxidant properties of zinc. The Journal of nutrition 130(5): 1447S-1454S.

20. Marchesini G, Fabbri A, Bianchi G, Brizi M, Zoli M (1996) Zinc supplementation and amino acid-nitrogen metabolism in patients with advanced cirrhosis. Hepatology 23(5): 1084-1092.

21. Stremmel W, Meyerrose KW, Niederau C, Heffer H, Kreuzpaintner G, et al. (1991) Wilson disease: clinical presentation, treatment, and survival. Annals of internal medicine 115(9): 720-726.

22. Zhou Z, Sun X, Lambert JC, Saari JT, Kang YJ (2002) Metallothionein-independent zinc protection from alcoholic liver injury. Am J Pathol 160(6): 2267-2274.

23. Lee WM (1993) Acute liver failure. New England Journal of Medicine 329(25): 1862-1872.

24. Essani NA, Fisher MA, Farhood A, Manning AM, Smith CW, et al. (1995) Cytokine-induced upregulation of hepatic intercellular adhesion molecule-1 messenger RNA expression and its role in the pathophysiology of murine endotoxin shock and acute liver failure. Hepatology 21(6): 1632-1639.