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ORIGINAL ARTICLE

Ribavirin as a Therapeutic Modality in Patients with Severe Acute Hepatitis E

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ABSTRACT

Background: With the postulation that ribavirin, an antiviral agent, can modulate the clinical course of severe acute hepatitis due to hepatitis E virus (HEV), a clinical trial was conducted in patients with acute hepatitis E.

Materials and methods: A total of 24 patients with severe acute hepatitis E were enrolled in this study. Ribavirin was given at a dose of 400 mg, twice a day for 28 days. The clinical course of the disease was assessed on a regular basis.

Results: Out of 24 patients in this cohort, three patients were lost during follow-up and their prognosis remains unknown. A total of six patients died during follow-up. The rest 15 patients showed improvement of their pathological conditions during observation period.

Conclusion: Although preliminary, this study indicates that more information is required about beneficial and detrimental effects of ribavirin in patients with severe acute hepatitis E. This study inspired optimism that a randomized-controlled trial of ribavirin should be adopted in severe acute hepatitis E to develop proper in sights in this regard.

Keywords: Acute hepatitis E severe, Ribavirin, Therapy of HEV.

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INTRODUCTION

Hepatitis E virus (HEV) infection is highly endemic in developing countries and is an emerging autochthonous (locally acquired) disease in advanced and developed countries.[1] Although acute hepatitis E is regarded as a self-limiting pathological process, recent studies have shown that this disease may cause high mortality rate in certain groups of people, such as older persons, pregnant women, and patients with underlying chronic liver diseases.[2-5] Also, HEV is the major cause of acute insult in patients with chronic liver diseases that lead to development of acute on chronic liver failure.[6] The role of HEV infection is also alarming in immunosuppressed patients when acute HEV infection can progress to chronicity.[7] Contrary to infection with other hepatitis viruses, acute HEV infection, is associated with a significant morbidity and mortality in some series.[1-8]

These facts indicate that acute hepatitis E should not always be considered as a self-limiting infection and proper treatment should be initiated in susceptible persons. However, no drug is recommended for treatment of patients with acute HEV infection. Recently, some investigators have used ribavirin in patients with severe acute hepatitis E[9] and chronic hepatitis E.[10] Their studies have shown that ribavirin can positively modulate the pathological process of these patients.

Bangladesh is a developing country with about 160 million people. HEV is endemic in Bangladesh and epidemic outbreaks of HEV infection are reported in each year. HEV is the main etiological agent of acute hepatitis and also the principal trigger of acute on chronic liver failure.[11,12] However, there is paucity of information about course of disease and mortality from acute HEV in Bangladesh due to poorly developed health reporting system over here.

We have encountered several deaths due to severe acute hepatitis E in our clinical practice. In this perspective, we postulated that the efficacy of ribavirin may be checked in patients with severe acute hepatitis E at Bangladesh. The clinical trial presented here provides the first use of ribavirin in patients with severe acute hepatitis E at Bangladesh.

PATIENTS AND METHODS

A total of 24 patients with acute severe hepatitis E were enrolled in this study. The age of the patients ranged from 18 to 72 years. Twenty patients were male and the rest four were female. There was no specific relation between occupation and acquisition of severe acute hepatitis E in these patients (student: 21.7%, service holder: 21/7%, businessmen: 17.4%, housewife: 13% and farmer: 13%). We could not find any specific factors underlying their HEV infection, i.e. use of same water sources or taking food from same reservoirs. They have taken drinking water from various sources. In fact, the patients attended Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, the only tertiary Post Graduate Medical University of Bangladesh. They came to hospital for treatment and management of their illness. A departmental review board provided the permission for the study. All patients gave consent to take medication after explaining the nature and purpose of the study.

Out of total 24 patients, 15 patients complained of abdominal pain, seven had itching, nausea was presented by 18 patients and eight patients had ascites. Three patients were pregnant and postpartum hemorrhage was seen in one patient. History of abortion was given by one patient. Hepatorenal syndrome was developed on one patient during admission. Features of coagulopathy were detected in 11 patients and superimposed infection was observed in four patients. Duration of illness varied from 5 to 365 days.

The levels of serum bilirubin ranged from 9.80 to 52.20 gm/dl on the day of admission. The levels of alanine aminotransferase (ALT) were elevated in all but one patient (15-2,628 IU/l). Prolongation of prothrombin time above normal limits was detected in 13 of 24 patients during their admission. Elevated level of serum creatinine was detected in one patient.

All patients were expressing IgM type antibody to HEV, but were negative for IgM type antibody to hepatitis A virus, hepatitis B virus (HBV) and hepatitis C virus (HCV). Six patients were expressing hepatitis B surface antigen (HBsAg) in the sera indicating that they were infected with HBV but the acute hepatitis was not due to HBV-related. All patients were also negative for antibody to HCV. Ribavirin was given at a dose of 400 mg, 12 hourly, for 28 days. Patients were followed up for variable duration after termination of ribavirin intake.

RESULTS AND DISCUSSION

Out of 24 patients, where about three patients could not be ascertained and we could not record their prognosis. Six patients died during observation period. The cause of death was renal failure in three patients. One pregnant patient died after giving birth of a healthy child by cesarean section. The rest 15 patients were improved after taking ribavirin. The patients who were improved revealed progressive fall of serum bilirubin and decreased ALT. Also, they showed improvement of prothrombin time along with therapy.

The study conducted here was initiated to assess the effects of ribavirin in patients with severe acute hepatitis E. Most of the patients had elevated levels of bilirubin and increased levels of ALT. Prothrombin time was also in increasing trend in these patients. Most of the patients also complained of abdominal pain, ascites, coagulopathy and superimposed infection.

The proper assessment of effects of ribavirin was difficult in this study because one of the major limitations of the present study is an absent of a control group of patients. Thus, it remains elusive how many patients would die if no ribavirin was prescribed in these patients. At the same time, six patients died and renal failure was mainly recorded in most patients. We are not sure if ribavirin induced renal failure of other factors that may induce their death. The roles of ribavirin on renal failure in these patients remain to be properly assessed in a future clinical trial.

Two previous case reports have shown that ribavirin seems to be beneficial in patients with serious acute hepatitis E. However, we assume that randomized controlled trial should be accomplished to assess the beneficial and detrimental effects of ribavirin in these patients because we could retrieve inconclusive role of ribavirin in this clinical trial. The case reports that focused on beneficial effects of ribavirin in acute and chronic hepatitis E were published from developed countries. However, Goyal et al from India has reported that ribavirin can induce acute on chronic liver failure in patients with HEV infection.[13] Thus, it remains to evaluate the real impact of ribavirin in HEV infection in different countries. Also, the genotype and molecular characterization of HEV have not been accomplished in this study or in published case reports. More elaborative studies may unmask factors related to beneficial or detrimental effects of ribavirin in severe acute hepatitis E.

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