Short-term survival in patients with severe alcoholic hepatitis treated with corticosteroid vs. pentoxifylline: a non-inferiority trial

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INTRODUCTION

The treatment of alcoholic hepatitis (AH) remains one of the main challenges to clinicians involved in the management of severe AH (modified discriminant function of 32 or more). Until now, many randomized well designed studies have been reported from all over the world on the use of corticosteroids in the treatment of severe AH.[1, 2] However, the data on the efficacy of corticosteroids in these patients have been conflicting. Corticosteroids are relatively contraindicated amongst patients with severe AH and coexistent sepsis, gastrointestinal bleeding, and acute pancreatitis.[3] Furthermore, specific treatment of AH with corticosteroids far from satisfactory with as many as 40-50% of patients failing to respond to steroids, thus classified as non-responsive to steroids.[4]

Tumor necrosis factor-α (TNF-α) is one of the inflammatory cytokines that contributes to the necro-inflammatory reaction that affects the liver. TNF-α receptor knockout mice are resistant to alcohol-induced liver injury. For patients who have contraindications to steroids, the second option for treatment is oral pentoxifylline, a phosphodiesterase and a possible TNF-α inhibitor.[5]

De et al.[6] suggested that pentoxifylline is superior to prednisolone for treatment of severe AH in that pentoxifylline showed reduced mortality, improved risk-benefit profile and renoprotective effects of pentoxifylline compared with prednisolone. However, few data about the efficacy of pentoxifylline compared with corticosteroid are available and the evidence is not firm; no conclusions can be drawn regarding whether pentoxifylline has a positive, negative, or neutral effect on participants with severe AH.[7] In this study, we evaluated that short-term survival in patients with severe AH treated with corticosteroid *vs.* pentoxifylline.

MATERIALS AND METHODS

Between June 2009 and December 2010, a total of 78 patients with severe AH were prospectively enrolled at 19 University hospitals, all of whom showed modified discriminant function of 32 or more. (Fig. 1) The patients were initially examined clinically, evaluated, and subsequently were admitted for the study. The study protocol was approved by the institutional ethical committee. We conducted a baseline evaluation including family and alcohol history, X-ray, electrocardiography, blood test, electrolyte, liver function test, and viral markers.

Patients were included who had a history of chronic alcohol intake of more than 40 g/d with clinical and biochemical features of severe AH. Patients with any other potential etiology of liver injury (acute or chronic viral hepatitis, autoimmune liver disease, Wilson's disease, or human immunodeficiency virus) were excluded from the study. Patients with infection, sepsis or spontaneous bacterial peritonitis, gastrointestinal bleeding, acute pancreatitis, or malignancy were also excluded.

The included patients were then divided into two groups by randomization: group I, patients receiving prednisolone (40 mg/day for the first 4 weeks), and group II, patients receiving pentoxifylline (400 mg thrice daily). The pharmacotherapy (pentoxifylline or prednisolone) was given during 28 days. Twenty-eight days survival, changes of liver function, and complications were evaluated.

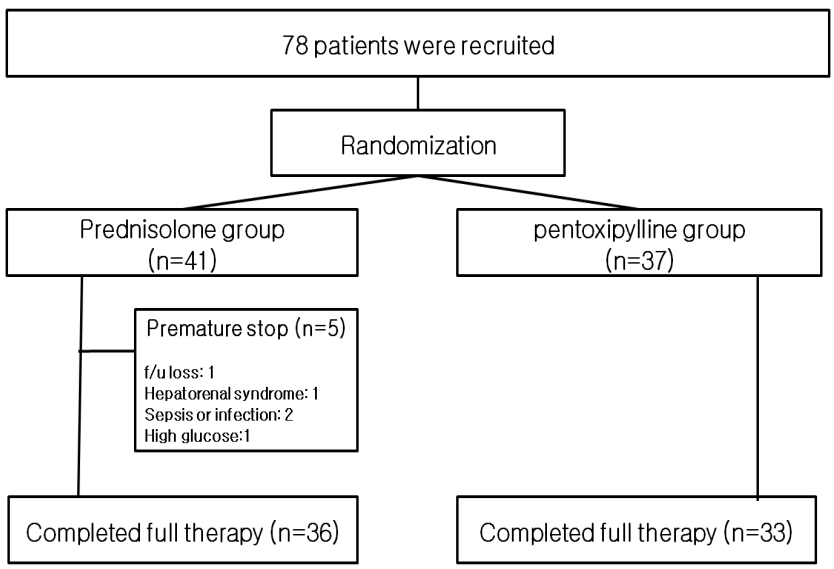

Figure 1. Study flow