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"If a fake friend stays in your vodkabulary as a stem friend": Granulocyte colony-stimulating factor promoted stem cell therapy in severe alcoholic hepatitis

Singh V, Sharma AK, Narasimhan RL, Bhalla A, Sharma N, Sharma R. Granulocyte colony-stimulating factor in severe alcoholic hepatitis: A randomized pilot study. Am J Gastroenterol 2014; 109: 1417-23.

The burden of alcoholic hepatitis is increasing throughout the world. Unfortunately, there is no magic gun for therapy of severe alcoholic hepatitis and the short-term mortality rates are approximately 25 to 35 percent high at one month (1,2). Several studies showed the efficacy of granulocyte colony-stimulating factor (GCSF) in mobilizing bone-marrow derived stem cells, which can spontaneously populate the liver and differentiate into liver cells and promote hepatic regeneration (3,4).

Singh et al. (5) performed a randomized, non-blinded trial with 46 cases of severe alcoholic hepatitis patients who satisfied the study criteria between July 2010 to June 2012. The study inclusion criteria were age 18-75 years, severe alcoholic hepatitis with Maddrey's discriminant function (mDF) ≥32 and an average alcohol intake of more than 100 g/day during the 3 months before the enrolment. The exclusion criteria were the presence of any hepatocellular carcinoma, portal vein thrombosis, prior steroid treatment, hepatorenal syndrome, grade 3 or 4 hepatic encephalopathy, upper gastrointestinal bleeding within the preceding 10 days, uncontrolled bacterial infection, HIV, hepatitis B or C virus infection, autoimmune hepatitis, hemochromatosis, Wilson's disease, alpha-1-antitrypsin deficiency, pregnancy or previous hypersensitivity to GCSF. The primary end point of the study was survival at 90 days.

The patients were randomly separated in two therapy groups as standard medical care group and standard medical care plus GCSF group. The mDF/MELD scores were 79/30 vs 85/27 in the groups respectively (p>0.05). The standard medical care was pentoxifylline with other supportive measures in both groups whereas, the second group patients also received 5 mcg/kg subcutaneous GCSF every 12 hours for five days. Ninety day survival was higher in the GCSF treated group than the standard medical care alone group (78% vs 30%).

Granulocyte colony-stimulating factor therapy was well tolerated with minor complaints of bone pain in 3 patients and headache in 2 patients. The authors' medical center did not use corticosteroids as standard medical therapy for severe alcoholic hepatitis. The survival rate in the standard care alone group was lower than previous studies of pentoxifylline most likely secondary to higher mDF/MELD scores in the study of Singh et al. (5).

Granulocyte colony-stimulating factor therapy increased mobilization of CD34+ hematopoietic stem cells shown by the increase in CD34+ count in peripheral blood of GCSF therapy group (p=0.019). MELD and mDF scores' reductions at 1, 2 and 3 months in GCSF group were significantly better than the standard medical care group.

Hydration, vitamins, appropriate nutritional support, prevention and treatment of alcohol withdrawal, pharmacologic therapy with prednisolone or pentoxifylline are indicated for severe alcoholic hepatitis cases. In this study, Singh et al showed that GCSF therapy may give one more chance to some patients with severe alcoholic hepatitis by mobilization of hematopoietic stem cells and liver regeneration. Alcoholic hepatitis patients need psychosocial assessment. All alcoholic hepatitis patients need to follow an alcohol abuse rehabilitation program. Alcohol should be just an evil friend in their vocabulary, "not vodkabulary". Simple rules are better than complicated algorithms. Since, staying away is the landmark in the therapy of any substance abuse. All patients with alcoholic hepatitis should follow programs to achieve a strict abstinence of alcohol to stop the slow suicide.

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