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The merits of autologous mesenchymal stem cells peripheral vein infusion in patients suffering from end stage liver cirrhosis

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Cirrhosis, the end result of long-term liver damage, places a significant burden on health care worldwide. Liver transplantation is the only definitive therapeutic option for these patients. However, the worldwide shortage of donor livers has prompted the search for alternative cell therapies. The prospective clinical use of autologous multipotent mesenchymal stem cells (MSCs) isolated from bone marrow (BM) holds enormous promise for the treatment of a large number of diseases which among them is end stage liver disease. Sixty patients with post-hepatitis C virus (HCV) end-stage liver disease were included in this study. They were randomized into two groups: Group 1: 35 patients to whom granulocyte colony-stimulating factor (G-CSF) was administered for 5 days to mobilize their hematopoietic stem cells. Following leukapheresis, CD34(+) stem cells were isolated, amplified, and partially differentiated in culture, then re-injected via peripheral-vein infusion. Group 2: 25 patients who received regular liver-supportive treatment only (control group). Hepatic fibrosis was assessed in Group I by detection of procollagen IIIC peptide level (PIIICP) and procollagen III N peptide level (PIIINP). Liver functions were markedly improved in 57.1% of patients in Group I. Significant changes were reported in albumin (P=0.000), bilirubin (P=0.002), increased international normalized ratio (INR) (P=0.017), prothrombin concentration (P=0.029) and alanine transaminase (ALT) levels (P=0.029), with stabilization of clinical and biochemical status in 14.3% of cases. While no significant improvement was detected in any patient in Group II. The pretreatment values of s-PIIICP and s-PIIINP were 8.2±3.7 and 395±175, respectively, with a decrease to 7.3±2.1 and 338±95, respectively, 3 months after MSC therapy, however, the difference was statistically non-significant (P=0.7). A significant correlation coefficient was reported after 3 months between the s-PIIINP and prothrombin concentration (P=-0.5) and between s-PIIICP and ascites (P=0.550). It can be concluded that a combination of G-CSF with MSCs will greatly improve the outcome of stem cell-treated patients with end-stage liver disease. In addition the peripheral intravenous infusion is an easy and convenient way of stem cells delivery, with less-invasive and less traumatic effects compared with intraarterial infusion route. Moreover, IV infusion of MSCs after G-CSF mobilization improves s-albumin within the first 2 weeks and prothrombin concentration and alanine transaminase after 1 month. Furthermore, MSCs may act directly through preventing collagen formation, as evidenced by their ability to reduce the hepatic fibrosis markers. Taken together, our data provides evidence that CD34(+) MSCs followed G CSF mobilization is excellent for liver stem cell therapy to retain liver mass and restore liver functions.

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