

# Liver Cells Proliferation and Apoptosis in Patients with Alcoholic Liver Disease After Autologous Hematopoietic Stem Cell Transplantation

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**Abstract** Alcoholic liver disease is a huge medical and social problem that leads to liver fibrosis, cirrhosis, and hepatocellular carcinoma. Unfortunately, the last stages of the disease do not have efficient treatment, except liver transplantation, and require development of new therapeutical approaches. Transplantation of stem cells might be the most promising approach. In our research, we studied transplantation of autologous hematopoietic stem cells (HSC) into the celiac trunk of patients with alcoholic liver cirrhosis. In this article, we pay particular attention to proliferation and apoptosis—two fundamental processes, which determine the fate of regeneration. Liver biopsy specimens before treatment, 3 and 12 months after transplantation of HSC, were stained immunohistochemically with antibodies against PCNA and Bcl-2. The results showed that treatment was safe and effective, hepatocytes increased proliferation, and inflammatory cells decreased antiapoptotic activity, signifying improvement in liver regeneration. However, effect of treatment after 12 months decreases and requires repeated HSC transplantation.

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## 1 Introduction

Possibility to stimulate liver regeneration with autologous HSC isolated from bone marrow [1, 2] or cord blood [3] was shown in previous studies. Tang XP et al. demonstrated high efficacy of cord blood HSC transplantation in treatment of patients with viral hepatitis [4]. Am Esch II JS et al. showed that transplantation of autologous bone marrow CD133<sup>+</sup> cells into the left branch of the portal vein with embolization of right branch increases regeneration of the liver's left lobe 2.5 times after right lobe's resection [5, 6].

However, most of the studies relied only on biochemistry changes, analysis of clinical symptoms, changes in Child-Pugh or MELD score in assessment of their results. Nevertheless, laboratory and instrumental methods do not give precise information about severity of pathological process in the liver [7]. Morphological study is a “gold standard” for diagnostics of inflammatory changes and fibrosis in the liver, which enables defining activity and stage of chronic hepatitis, predicting the course of disease, finding out the mechanisms of cellular damage, and controlling efficacy of treatment. Lack of studies performing morphological analysis after HSC transplantation in patients with alcoholic liver disease is a reason for a large gap in understanding the cellular mechanisms of liver regeneration. We present a rare example of using morphological study of liver biopsies as a main source of data for analyzing effectiveness of proposed treatment. The aim of this study was to assess the changes in proliferation and apoptosis in liver of patients with alcoholic cirrhosis after transplantation of autologous hematopoietic stem cells.