LIVER DISEASE & STEM CELLS: FACT SHEET

INTRODUCTION

There are several types of liver disease that may potentially be treated by cell-based therapies, including metabolic liver diseases, acute liver failure, and chronic liver disease. Metabolic liver diseases include various genetic disorders of liver metabolism that predominantly affect hepatocytes. Acute liver disease, caused by toxins, viral infections, and other factors, results in widespread hepatocyte death and, if severe, can lead to rapid clinical deterioration and even death in patients. Chronic liver disease, stemming from multiple causes such as obesity, alcohol consumption, viral infections, and immune disorders, can result in chronic liver scarring and decreased liver function, ultimately leading to cirrhosis and liver failure.

For severe and end-stage liver disease, the current gold standard of care is whole liver transplantation. However, this approach is limited by the negative side effects of immunosuppression and organ availability. Consequently, the development of cell-based therapies has emerged as an attractive option.

RATIONALE FOR USING CELL-BASED THERAPIES FOR LIVER DISEASE

In the context of genetically-based metabolic liver disease, replacing diseased hepatocytes with corrected ones containing the appropriate gene may offer clinical benefits. Examples of diseases where this approach may work include Tyrosinemia type 1 (caused by fumarylacetoacetate hydrolase deficiency), and Crigler–Najjar syndrome type I (which causes hyperbilirubinaemia). Gene therapy approaches for such genetic diseases are also showing benefits[1]. Although acute liver failure can lead to multi organ failure requiring distinct management, replacing unhealthy hepatocytes may effectively treat the disease.

For chronic liver disease, and its end-stage manifestation, cirrhosis, cell-based therapy can potentially serve as a bridge treatment before transplantation. However, the situation is complex because simply replacing hepatocytes may not be sufficient to correct the disease due to the damage observed in cirrhosis, which causes extensive scarring and inflammation. Therapies targeting scarring and inflammation in addition to replacing or supplementing damaged hepatocytes or biliary cells may be necessary for liver cirrhosis.

CLINICAL STATUS OF CELL-BASED THERAPIES AND CLINICALTRIALS FOR LIVER DISEASE

Several cell-based clinical studies have been conducted for various types of liver disease, including acute and metabolic liver disease, as well as liver cirrhosis. Encouraging clinical results have emerged from hepatocyte transplantation for metabolic liver diseases such as Crigler Najjar, glycogen storage disease type 1, and urea cycle disorders[2]. However, the limited supply of hepatocytes is a challenge and finding new sources of hepatocytes could significantly impact this area.

Currently, there is no clear evidence supporting the efficacy of cell-based therapies for liver cirrhosis. While some small, uncontrolled studies have shown potential benefits, larger randomized controlled trials have yet to demonstrate positive outcomes[3,4]. Therefore, the use of cell-based therapies for liver cirrhosis cannot be recommended outside properly funded clinical trials.

There have been encouraging results from studies that have sought to grow liver cells in the laboratory from various sources including pluripotent stem cells (iPSC) and adult stem cells taken from healthy human livers. Recent research suggests that human hepatocytes and biliary cells can be expanded as organoids, potential allowing them to be used as cell therapies for treating metabolic and acute liver disease[5], as well as serving as a cell source for treating biliary disease[6,7].

ADDITIONAL RESOURCES

About Stem Cells
www.aboutstemcells.org

EuroGCT
https://www.eurogct.org/chronic-liver-disease-how-could-gene-and-cell-therapy-help

Review: Cell transplantation-based regenerative medicine in liver diseases
Stem Cell Reports

Cell-based approaches focused on modulating the liver's innate immunoregulatory microenvironment have also gained attention. A recent first-in-human Phase I trial of autologous macrophage peripheral infusion into cirrhotic patients has been performed and shown to meet its primary outcome of safety and feasibility[8], and a Phase II randomized controlled multi center trial is ongoing[9]. A Phase I safety study, Macrophage Therapy for Acute Liver Injury (MAIL), is currently underway to investigate the use of allogeneic macrophages from frozen stocks for treating acute liver injury.

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