The infusion of haematopoietic stem cells in patients with liver insufficiency

Cirrhosis, the end result of long-term liver damage, and its related morbidity represnt a significant burden on health care worldwide. Liver transplantation is the only definitive therapeutic option for those patients. However, the paucity of donors, the incidence of rejection and the high costs are hindering factors. Cell-based regenerative therapies, particularly the adult haematopoietic stem cell (HSC)-based therapies, are evolving as valuable clinical alternatives.

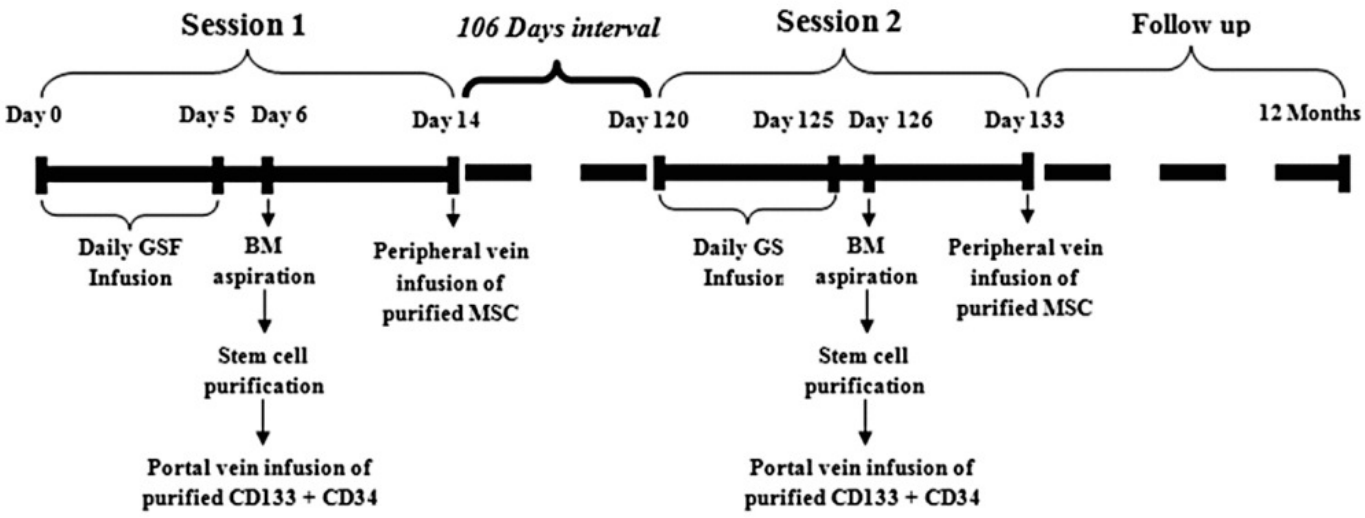

Fig. 1. Stem cell treatment schedule of patients who received two sessions. BM bone marrow, G-CSF, MSC mesenchymal stem cell

Stem cells (SCs) are clonogenic, self-renewing cells, capable of differentiating into multiple cell lineages. During tissue injury, the bone marrow stem cells (BMSCs) are mobilized and migrate to the injured organ. This has formed the basis for regenerative therapy whereby treatment with appropriate stem cells might ameliorate specific diseases.

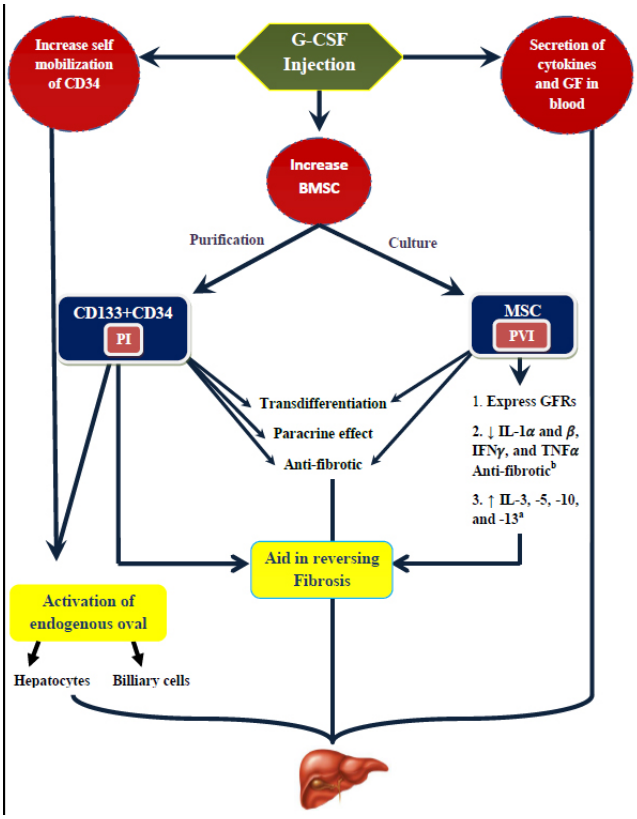

Fig. 2. The proposed mode of action of both growth factors (GFs) and different stem cell types on liver regeneration: a: Up-regulate anti-inflammatory Th2 cytokines. b: Down-reg. pro-inflammatory
Th1 cytokines. G-CSF: Granulocyte colony stimulating factor; MSC: Mesenchymal Stem Cells; PI: portal
infusion; PVI: peripheral vein infusion.

Previous data in our lab as well as other labs have proved the supportive role of stem cell therapy (SCT) in the end stage liver disease. However, the exact SC type, treatment protocol and the number of treatment sessions are still under investigation. In our study, which is one of the pioneer studies that clearly showed that concomitant treatment of GCSF as immunomodulator followed by infusion of different stem cell types (CD133+CD34 followed by MSC) through different routes (portal and peripheral vein infusions) is significantly superior to the single type of cell infusion (Fig. 1 and 2). Thus, it opens the gate for the delivery of better protocols for SCT in liver disease.

Repeated HSC infusions gives more sustained clinical efficacy and improvement in liver functions and the quality of life during 12-month follow-up compared to single HSC infusion. Accordingly, stem cell therapy could be a promising therapeutic modality in patients with end stage liver disease, which may replace or decrease the need for whole organ transplantation in the future,

especially if gene manipulation of the stem cells makes them able to resist viral infection or in concomitant with the new direct anti-virus drugs.

Publication

The impact of repeated autologous infusion of haematopoietic stem cells in patients with liver insufficiency.
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