Autologous transplantation of bone marrow mononuclear cells in patients with decompensated cirrhosis

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Liver transplantation is considered as the standard treatment for advanced decompensated liver cirrhosis.

Studies in animal models of liver diseases have demonstrated that BMC transplantation may reduce hepatic fibrosis and improve liver function and survival rate.

Cytokines and growth factors produced by infused hematopoietic cells might support liver function and repair.
Aim

To evaluate the safety and feasibility of BMC transplantation in patients with decompensated cirrhosis
Patients and Methods

Inclusion Criteria

- Age 20-70 years
- HCV related liver cirrhosis Child C
- Ability to give informed consent.

Exclusion Criteria

- Age <20 or >70 years
- Hepatopulmonary syndrome
- Liver tumors/history of other cancer
- Hepatic, portal or splenic vein thrombosis
- Autoimmune diseases
- Patients with active infection
- Recurrent gastrointestinal bleeding
Patients and Methods

• The present study comprised 45 patients with advanced liver cirrhosis.
• 40 male and 5 female patients
• Median age 50 years
• The study protocol was approved by the Ethics Committee of Central University Hospital, Tbilisi, Georgia.
Patients and Methods

**Infusion of 200x10^6 BM Cells into the Hepatic Artery**

- Aspiration of 80 ml BM
- Preparation of MNC (Ficoll-Hypaque)
- Checking the character of MNC
- Intraarterial administration of BMCs

**Endpoint:**
1. Safety & Feasibility
2. 4 weeks and 32 weeks of Liver Function

Checking liver functions by serum blood tests, Ultrasonography
Results

• All patients were discharged 48 h after BMC infusion.
• BMC transplantation was well tolerated by all patients.
• 5 patients complained of mild pain at the bone marrow needle puncture site.
• No other complications or specific side effects related to the infusion procedure were reported.
Results

Serum Albumin level before and after BMC Tx

Serum bilirubin level before and after BMC Tx

![Graph showing changes in Serum Albumin and Serum bilirubin levels over weeks after BMC Tx.](image-url)
Results

INR level before and after BMC Tx

ALT and AST levels before and after BMC Tx
Characteristics of the distribution of serum bilirubin, albumin and INR levels in 45 patients with chronic liver failure at baseline, 1 and 4 month after transplantation of autologous BMCs

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Median</th>
<th>Standard deviation</th>
<th>Relative change from baseline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bilirubin (mg/dl)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.00</td>
<td>6.90</td>
<td>3.21</td>
<td>2.48</td>
<td>2.79</td>
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<tr>
<td>1 month</td>
<td>0.60</td>
<td>7.0</td>
<td>2.53</td>
<td>1.25</td>
<td>3.57</td>
<td>-22%</td>
</tr>
<tr>
<td>4 month</td>
<td>0.50</td>
<td>6.20</td>
<td>2.10</td>
<td>0.85</td>
<td>2.75</td>
<td>-35%</td>
</tr>
<tr>
<td><strong>Albumin (unit)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>2.40</td>
<td>3.90</td>
<td>2.90</td>
<td>2.65</td>
<td>0.68</td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>3.00</td>
<td>4.20</td>
<td>3.58</td>
<td>3.55</td>
<td>0.28</td>
<td>19%</td>
</tr>
<tr>
<td>4 month</td>
<td>3.40</td>
<td>4.90</td>
<td>4.07</td>
<td>4.00</td>
<td>0.69</td>
<td>29%</td>
</tr>
<tr>
<td><strong>INR (unit)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.18</td>
<td>3.63</td>
<td>2.24</td>
<td>2.08</td>
<td>1.03</td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>1.24</td>
<td>2.79</td>
<td>1.91</td>
<td>1.79</td>
<td>0.71</td>
<td>15%</td>
</tr>
<tr>
<td>4 month</td>
<td>1.20</td>
<td>2.20</td>
<td>1.73</td>
<td>1.76</td>
<td>0.51</td>
<td>23%</td>
</tr>
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</table>
Conclusions

• BMC infusion into the hepatic artery of patients with advanced chronic liver disease is safe and feasible
• Transient decrease in mean serum bilirubin and INR levels
• Transient elevation of serum albumin
Next Steps

• Controlled studies are required to evaluate the efficacy of BMC infusion in patients with liver disease
• Determine the number of BMCs required for achievement of therapeutic effect, which may vary with the patient’s age and the etiology of liver disease.
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