EFFICIENCY OF INTRAMYOCARDIAL INJECTION OF AUTOLOGOUS BONE MARROW MONONUCLEAR CELLS IN PATIENTS WITH ISCHEMIC HEART FAILURE

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Nothing to disclosure
Background

- At present, bone marrow cell transplantation is regarded as a promising potential therapy for the treatment of patients with chronic ischemic heart disease.

- Known clinical studies confirmed the safety and efficacy of intramyocardial injections of BMMCs to reduce anginal symptoms, enhance myocardial perfusion, and improve cardiac function.

BMMMC transplantation versus MED

- The aim of this study was to assess long-term follow-up results of modern medical therapy and intramyocardial bone marrow cell injections in patients with chronic ischemic heart failure.

BMMC transplantation versus MED

- The primary end-point of the study was the efficacy of the intramyocardial injection of autologous BMMC, measured by change in myocardial perfusion defects at rest and under pharmacological stress between baseline and 6, 12-months follow-up SPECT.

- The secondary end-points were the safety of the intramyocardial BMMC therapy, quality of life, CCS angina class, NYHA functional class, LV function, life-threatening arrhythmias, mortality between two groups and NOGA change in voltage as assessed by NOGA follow-up endocardial mapping (unipolar voltage).
Inclusion and Exclusion Criteria

Inclusion criteria:

- A history of myocardial infarction >12 months before the enrollment and a fixed perfusion defect on Tc-99m tetrofosmin SPECT
- The class of clinical symptoms of heart failure
- Non revascularisable patient who is symptomatic on optimal medical therapy
- LVEF <35%

Exclusion criteria:

- Eligibility for PCI, CABG
Study Design

Ischemic heart failure patients
(n=109)

BMMC+MED
(n=55)

MED alone
(n=54)
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>BMMC group (n=55)</th>
<th>Control group (n=54)</th>
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<tbody>
<tr>
<td>Age (yrs.)</td>
<td>61 ± 9</td>
<td>62 ± 5</td>
</tr>
<tr>
<td>Male, %</td>
<td>48 (87%)</td>
<td>46 (85%)</td>
</tr>
<tr>
<td>Time since MI (yrs.)</td>
<td>9 ± 8</td>
<td>8 ± 5</td>
</tr>
<tr>
<td>No. of major coronary arteries narrowed ≥50%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2 (3%)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>2</td>
<td>1 (2%)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>3</td>
<td>52 (95%)</td>
<td>48 (90%)</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>20 (36%)</td>
<td>16 (29%)</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>39 (71%)</td>
<td>41 (76%)</td>
</tr>
<tr>
<td>Previous ICD</td>
<td>4 (7%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>28 (51%)</td>
<td>32 (59%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5 (9%)</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>Hyperlipidemia (total cholesterol &gt;5 mmol/L)</td>
<td>53 (96%)</td>
<td>52 (96%)</td>
</tr>
<tr>
<td>6-mWT, m</td>
<td>185±39</td>
<td>197±34</td>
</tr>
<tr>
<td>NYHA, FC</td>
<td>3.3±0.2</td>
<td>3.5±0.1</td>
</tr>
<tr>
<td>CCS, FC</td>
<td>3.1±0.4</td>
<td>3.5±0.5</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>27.8±3.4</td>
<td>26.8±3.8</td>
</tr>
<tr>
<td>EDV LV, ml</td>
<td>243±32</td>
<td>239±38</td>
</tr>
<tr>
<td>ESV LV, ml</td>
<td>146±39</td>
<td>149±43</td>
</tr>
<tr>
<td>Number of MI</td>
<td>2.8±0.6</td>
<td>2.9±0.7</td>
</tr>
<tr>
<td>MLwHF, points</td>
<td>65.3±21</td>
<td>63.2±23</td>
</tr>
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BMMC injections

- LV electromechanical mapping with the NOGA system was performed to guide the injections of bone marrow cells to the area of ischemic myocardium as assessed on gated SPECT
BMMC injections
Procedural data

- No periprocedural complications developed
- The mean number of BMMC injected to each patient was $41 \pm 16 \times 10^6$
- The fraction of CD34/CD45-positive cells amounted to $2.5\pm1.6\%$
- The total duration of the procedure was $59 \pm 19$ minutes
- The fluoroscopy time was $11 \pm 6$ minutes.
- The electromechanical map had $90 \pm 22$ points
Results. Perfusion

- In the BMMC group, after 6 months, 39 (72.9%) of the 55 patients showed improved myocardial perfusion.

- No change of myocardial perfusion was apparent in 12 (21.8%) patients.
Results. Perfusion

- The summed rest score improved within 6 months and underwent no further change after 12 months.
- The improvement of the summed stress score was more pronounced than that of the rest score.
Results. Clinical data

- The NYHA class in BMMC group decreased from $3.3 \pm 0.2$ at baseline to $2.7 \pm 0.2$ at 3 months; $2.5 \pm 0.2$ at 6 months and $2.5 \pm 0.1$ at 12 months ($p=0.006$)

- CCS angina class in BMMC group improved from $3.1 \pm 0.4$ at baseline to $2.4 \pm 0.6$ after 3 months, $1.6 \pm 0.6$ after 6 months and $1.6 \pm 0.4$ after 12 months ($p=0.001$)

- Conversely, in the control group, the CCS angina class, NYHA did not change during follow up, $3.4 \pm 0.6$ and ($p=0.82$ and $p=0.64$, respectively)
Results. LV function and Noga data

- The LVEF improved from $27.8 \pm 3.4\%$ to $32.3 \pm 4.1\%$ in BMMC group ($p=0.04$)

- In the control group, LVEF tended to decrease from $26.8 \pm 3.8\%$ to $25.2 \pm 4.1\%$; $p=0.61$

- Total UV increased significantly from $9.1 \pm 2.4$ mV to $12.4 \pm 2.1$ mV after 6 month and also improve to $14.2 \pm 3.2$ after 12 month ($p=0.026$)
Results. Mortality

- In the BMMC group 6 (10.9%) patients died at 12 month follow up compared with 21 (38.9%) in control group (Log-Rank test, p=0.0007)
Conclusion

- Intramyocardial bone marrow cell transplantation in patients with chronic ischemic heart disease and marked left ventricular dysfunction is safe and improves clinical outcome.

- Cell injections into ischemic segments promotes perfusion without inducing additional scarly areas.

- Unfortunately, there is currently no other alternative to the adequate treatment of patients with manifest ischemic heart failure producing the minimal number of negative effects and giving patients a real chance to benefit from this therapy.

- Our findings can be expected to stimulate new clinical studies aimed at elucidating the role of intramyocardial bone marrow cell transplantation in patients with chronic ischemic heart disease.
Thank you for your attention