EVALUATING EFFICACY OF AUTOLOGOUS BONE MARROW DERIVED STEM CELLS IN THE TREATMENT OF DRY AGE-RELATED MACULAR DEGENERATION

Dr. Harpreet Kaur Narde
Dr. R.P. Centre for Ophthalmic Sciences
All India Institute of Medical Sciences, New Delhi

Dr. Atul Kumar
Dr. R.P. Centre for Ophthalmic Sciences
All India Institute of Medical Sciences, New Delhi
Financial Disclosures

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- No financial interest.
## Stem cells in AMD

<table>
<thead>
<tr>
<th></th>
<th>Replacement Therapy</th>
<th>Rescue therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cell type used</strong></td>
<td>Embryonic stem cells, Induced Pleuripotent stem cells</td>
<td>Bone marrow derived mononuclear cells</td>
</tr>
<tr>
<td><strong>Route of injection</strong></td>
<td>Subretinal injection</td>
<td>Intravitreal injection</td>
</tr>
<tr>
<td><strong>Main mechanism of action</strong></td>
<td>Replacing dead RPE cells by cellular differentiation.</td>
<td>Paracrine effect on dying RPE cells</td>
</tr>
</tbody>
</table>
Assessment of Central Retinal Function after Autologous Bone Marrow Derived Intravitreal Stem Cells Injection in Patients with Retinitis Pigmentosa using Multifocal ERG: A Pilot Study

Atul Kumar, SN Mohan Raj, Thirumalesh Basavaraj Mochi, Sujata Mohanty, Tulika Seth, Rajvardhan Azad

Evaluating role of bone marrow-derived stem cells in dry age-related macular degeneration using multifocal electroretinogram and fundus autofluorescence imaging

Atul Kumar¹, Neha Midha¹, Sujata Mohanty², Annu Chohan¹, Tulika Seth³, Varun Gogia¹, Shikha Gupta¹
Objective of study

To study the efficacy of injected intravitreal autologous bone marrow derived stem cells in dry age related macular degeneration using

- Vision outcome
- Auto fluorescence imaging
- Multifocal ERG
- Advanced RPE analysis
Methods

▪ **Study Design** - Prospective interventional study.

▪ **Place of study** - Dr. R. P. Centre for Ophthalmic Sciences, AIIMS
  Stem Cell Facility, AIIMS
  Haematology Department, AIIMS

▪ **Funds** - ICMR

▪ **Sample** – 25 cases and 25 controls.

▪ All cases underwent intravitreal injection after written informed consent. Controls underwent conservative management.
Methodology

Bone marrow aspiration
(Iliac crest)

Bone marrow aspirate
(About 25 cc of aspirate taken)
ABSTRACT PRESENTATION

Under laminar flow hood sterility

Ficoll cell layering

Centrifugation 1800 rpm for 30 min

Flow Cytometry (for characterisation of BM-MNCs)
ABSTRACT PRESENTATION

Sterile transport to R P centre OT complex

Stem cell injection
8 million/0.1 ml

Intra vitreal injection
Safety parameters

- High Intraocular pressure was recorded in 2 patients out of 25. (adequately managed with antiglaucoma medications)

- No patient had severe intraocular inflammation or endophthalmitis.

- No patient developed choroidal neovascularisation (CNV) during the course.
Best corrected Visual Acuity

Visual Acuity

<table>
<thead>
<tr>
<th></th>
<th>Pre Procedure</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.27</td>
<td>1.29</td>
<td>1.32</td>
<td>1.32</td>
<td>1.34</td>
</tr>
<tr>
<td>Case</td>
<td>1.31</td>
<td>1.3</td>
<td>1.21</td>
<td>1.19</td>
<td>1.22</td>
</tr>
</tbody>
</table>
## Mf-ERG

**Amplitude** (median values in nanovolts)

<table>
<thead>
<tr>
<th>Ring</th>
<th>Group</th>
<th>Pre Procedure</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2°</td>
<td>Control</td>
<td>447.2</td>
<td>257.2</td>
<td>355.8</td>
<td>452</td>
<td>421.5</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>Case</td>
<td>438.6</td>
<td>238.9</td>
<td>364.3</td>
<td>324</td>
<td>344</td>
<td>0.23</td>
</tr>
<tr>
<td>2-5°</td>
<td>Control</td>
<td>372.4</td>
<td>258</td>
<td>388.4</td>
<td>346.3</td>
<td>312.2</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>Case</td>
<td>317.0</td>
<td>243</td>
<td>364.3</td>
<td>376.8</td>
<td>444</td>
<td>0.05</td>
</tr>
<tr>
<td>5-10°</td>
<td>Control</td>
<td>387.2</td>
<td>322.5</td>
<td>161.9</td>
<td>276.6</td>
<td>311</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>Case</td>
<td>211.5</td>
<td>287</td>
<td>283.5</td>
<td>293</td>
<td>361</td>
<td>0.02</td>
</tr>
<tr>
<td>10-15°</td>
<td>Control</td>
<td>397.8</td>
<td>174.7</td>
<td>223.8</td>
<td>259.6</td>
<td>187</td>
<td>0.134</td>
</tr>
<tr>
<td></td>
<td>Case</td>
<td>360.3</td>
<td>363.2</td>
<td>314</td>
<td>328.5</td>
<td>317</td>
<td>0.38</td>
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<tr>
<td>&gt;15°</td>
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<td>255.7</td>
<td>264.1</td>
<td>169</td>
<td>210.5</td>
<td>161.7</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>Case</td>
<td>232.5</td>
<td>193</td>
<td>218.2</td>
<td>198</td>
<td>176</td>
<td>0.31</td>
</tr>
</tbody>
</table>

## Implicit time (median values in milliseconds)

<table>
<thead>
<tr>
<th>Ring</th>
<th>Group</th>
<th>Pre Procedure</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2°</td>
<td>Control</td>
<td>42.6</td>
<td>41.4</td>
<td>41</td>
<td>38.4</td>
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<td>0.012</td>
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<td>Case</td>
<td>46.0</td>
<td>46.9</td>
<td>38.4</td>
<td>38.75</td>
<td>36.5</td>
<td>0.03</td>
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<td>2-5°</td>
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<td>50.5</td>
<td>42.8</td>
<td>43.6</td>
<td>45.9</td>
<td>44.8</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Case</td>
<td>43.0</td>
<td>44.2</td>
<td>43.9</td>
<td>42.8</td>
<td>41.4</td>
<td>0.049</td>
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<td>52.1</td>
<td>49.4</td>
<td>0.14</td>
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<td>Case</td>
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<td>49.2</td>
<td>52.77</td>
<td>50.4</td>
<td>52.1</td>
<td>0.55</td>
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<td>10-15°</td>
<td>Control</td>
<td>47.9</td>
<td>53.6</td>
<td>55.8</td>
<td>48.2</td>
<td>45.9</td>
<td>0.62</td>
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<tr>
<td></td>
<td>Case</td>
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<td>56.8</td>
<td>43.7</td>
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<td>46.4</td>
<td>0.509</td>
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<tr>
<td>&gt;15°</td>
<td>Control</td>
<td>45.8</td>
<td>45.5</td>
<td>42.7</td>
<td>45.5</td>
<td>43.1</td>
<td>0.652</td>
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<tr>
<td></td>
<td>Case</td>
<td>48.5</td>
<td>47.1</td>
<td>44.5</td>
<td>45.8</td>
<td>48.1</td>
<td>0.446</td>
</tr>
</tbody>
</table>
Fundus autofluorescence

Change in Greatest Linear Dimension (GLD)

<table>
<thead>
<tr>
<th>Duration</th>
<th>pre procedure</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>4.76</td>
<td>4.74</td>
<td>4.73</td>
<td>4.72</td>
<td>4.87</td>
</tr>
<tr>
<td>case</td>
<td>4.6</td>
<td>4.46</td>
<td>4.41</td>
<td>4.22</td>
<td>4.2</td>
</tr>
</tbody>
</table>
Advanced RPE analysis

Sub RPE slab

<table>
<thead>
<tr>
<th>Duration</th>
<th>control</th>
<th>case</th>
</tr>
</thead>
<tbody>
<tr>
<td>pre procedure</td>
<td>0.2</td>
<td>0.12</td>
</tr>
<tr>
<td>1 month</td>
<td>0.17</td>
<td>0.15</td>
</tr>
<tr>
<td>3 months</td>
<td>0.19</td>
<td>0.18</td>
</tr>
<tr>
<td>6 months</td>
<td>0.22</td>
<td>0.183</td>
</tr>
<tr>
<td>9 months</td>
<td>0.22</td>
<td>0.178</td>
</tr>
</tbody>
</table>

Sub RPE slab

<table>
<thead>
<tr>
<th>Area of sub rpe illumination</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>pre procedure</td>
<td>8.4</td>
</tr>
<tr>
<td>1 month</td>
<td>7.8</td>
</tr>
<tr>
<td>3 months</td>
<td>7.4</td>
</tr>
<tr>
<td>6 months</td>
<td>7.9</td>
</tr>
<tr>
<td>9 months</td>
<td>7.7</td>
</tr>
</tbody>
</table>

p-value=0.012
Case 1 - Fundus Autofluorescence

Baseline

Post-injection 9 months
ABSTRACT PRESENTATION

Advanced RPE Analysis: Macular Cube 512x128

Current Visit

Prior Visit

Sub-RPE Slab

RPE Profile™

*The calculated difference does not consider test-retest variability.

<table>
<thead>
<tr>
<th>RPE Elevations</th>
<th>Current</th>
<th>Prior</th>
<th>Difference*</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area in 3 mm Circle (mm²)</td>
<td>0.8</td>
<td>1.1</td>
<td>0.3</td>
<td>37.5%</td>
</tr>
<tr>
<td>Area in 5 mm Circle (mm²)</td>
<td>1.7</td>
<td>2.0</td>
<td>0.3</td>
<td>15.6%</td>
</tr>
<tr>
<td>Volume in 3 mm Circle (mm³)</td>
<td>0.02</td>
<td>0.04</td>
<td>0.02</td>
<td>100%</td>
</tr>
<tr>
<td>Volume in 5 mm Circle (mm³)</td>
<td>0.05</td>
<td>0.07</td>
<td>0.02</td>
<td>40.0%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sub-RPE Illumination</th>
<th>Current</th>
<th>Prior</th>
<th>Difference*</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area in 5 mm Circle (mm²)</td>
<td>10.6</td>
<td>14.2</td>
<td>3.6</td>
<td>34.0%</td>
</tr>
<tr>
<td>Closest distance to Fovea (mm)</td>
<td>0.0</td>
<td>0.2</td>
<td>0.2</td>
<td>infinity</td>
</tr>
</tbody>
</table>
Multifocal Electroretinogram

Baseline

Post-injection 9 months
Limitation

• Long term effect needs to be studied.

• Study conducted for advanced disease.

• Survival and homing of subretinal stem cells not evaluated.
• Intravitreal autologous bone marrow derived stem cells injection may have a promising outcome in Dry AMD.

• Further studies are required to determine the stage of disease at which the maximal benefit can be achieved and to standardize the dose and frequency of stem cell injection.
Thank you