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Autologous Bone Marrow Stem Cells in Spinal Cord Injury; Our Experience in Clinical Studies, Animal Studies, Obstacles faced and steps for future

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BACKGROUND

Following traumatic vertebral injuries and resultant spinal cord injury, most patients are doomed to a life either of quadriplegia or paraplegia. Current treatment option is limited to the stabilization of the vertebral fracture along with medications to prevent secondary damage leading to further deterioration and wishful waiting for recovery. In most instances recovery is insignificant. Safety of intrathecal injection of autologous bone marrow stem cells is proven but its efficacy varies between patients (¹). Intraleisional application has been reported to be more efficacious than intrathecal application (², ³, ⁴). We have analyzed our experience in human patients followed up for 3 year period and have found several grey areas in spinal cord injury (⁵) one of them is to explore the differences between Intrathecal and intraleisional application of stem cells with and without scaffolds in the latter technique. Towards achieving this goal we started a pilot study in animals where instead of post-vertebral fixation intrathecal injection, we have performed intraleisional application of autologous BMSC along with scaffolds (⁶). These scaffolds not only help retain the transplanted cells at the site of injury but also allow more neural precursors to grow compared to application without scaffolds (⁷). This study analyses the data retrospectively to plan further prospective studies with a view to improvise the results.

MATERIALS AND METHODS

Study 1: 100 to 120 ml of Bone marrow was tapped from the right posterior iliac crest under local anesthesia from human spinal injury victims (n=108; 76 males, 32 females) about 3 weeks to 18 months after surgical fixation of the vertebrae. The Level of injury was varied- Cervical (13 patients.) Upper Thorax- T1-T7 (35 patients) Lower thorax T8-T12 (46 patients) Lumbar (2 patients.) Age Group Range: 8 yrs to 55 yrs. The bone marrow mononuclear cells were processed under cGMP SOP’s Class 10000 clean room
and class 100 Biosafety hood as reported earlier \(^{(1)}\) and were injected intrathecally into the subarachnoid space of the patients below L2 level after endotoxin tests and confirming CD34 status using flow cytometry.

**Study 2:** 20-30ml of Bone marrow was tapped from the right posterior iliac crest under local anesthesia of canine spinal injury victims immediately after the injury and the bone marrow processed as reported earlier \(^{(6)}\) were injected intralesionally embedded in thermoreversible hydrogel scaffolds at the site of the injury after endotoxin tests and CD34 analysis using flow cytometry. Both the animals had an Olby score of 1 with no CP reflex, Patellar reflex and deep pain reflex.

### RESULTS:

**Study-1**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>4-6 months follow-up(1)</th>
<th>12-36 months follow-up(8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow up attrition rate:</td>
<td>14.02%</td>
<td>69%</td>
</tr>
<tr>
<td>Motor power improvement (atleast 2 grade of power post injection)</td>
<td>14.11%</td>
<td>7.69%</td>
</tr>
<tr>
<td>Motor power improvement resulting in functional recovery</td>
<td>4.70% 3 walk with support, 1 walking without support</td>
<td>5.13%</td>
</tr>
<tr>
<td>Subjective sensory improvement</td>
<td>16.97%</td>
<td>25.64%</td>
</tr>
<tr>
<td>Abnormal sensation</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Autonomic improvement</td>
<td>9.41%</td>
<td>10.26%</td>
</tr>
</tbody>
</table>

**DISCUSSION:**

It was hypothesized that intralesional application at time of surgery may be superior to Intrathecal application of bone marrow stem cells simply because the former technique ensured the delivery of a higher proportion of cells in the damaged area. It is possible that the cells injected intrathecally are carried along with the CSF to parts other than that damaged as well. This has been supported by study 2 when it was applied with scaffold. The injury model used in study 2 is a natural traumatic model and is more akin to real life than any other controlled spinal cord model that one could create in the lab. This study 2 which is still in process allows for the animal to live to its entire course enabling us to follow up the neurological recovery of the patient and on its death perform an autopsy to not only determine the cause of death but to also examine the fate of stem cells injected intralesionally. We hope to determine the percentage of stem cells remaining as stem cells and to determine the nature and magnitude of histopathological changes that might have taken place which facilitated /non facilitated the recovery in the study animals.
CONCLUSION

It is understood from the study 1, that the factors determining outcome are multiple and includes the age of patients, level of injury, time interval between injury and ABMMC injection, dosage of stem cells injected and all these need to be evaluated in future studies. More studies are necessary to ascertain the efficacy. Safety of both intrathecal and intralesional injection with scaffold have been proven in this studies. Inclusion of larger number of cases with a long term follow up is necessary to know the efficacy of intralesional therapy with scaffolds.

References


