Autologous Bone Marrow Transplantation for Muscle Strength Improvement in Traumatic Brachial Plexus Injuries. Preliminary Results of a Phase-1 Clinical Study

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Introduction: Traumatic brachial plexus injuries (BPI) can cause severe loss of elbow flexion [1]. After neurosurgery, partial muscle reinnervation can be obtained, but active elbow flexion often remains insufficient. For these patients, muscle strength amelioration via cell therapy could represent a tremendous improvement and make extensive muscle transfer surgery unnecessary. Long-term denervation causes muscle atrophy, interstitial fibrosis and fatty degeneration. The number of myogenic precursor cells (satellite cells) declines [2]. Transplantation of satellite cells was shown to increase muscle force in rabbits [3]. In man, transplantation of the mononuclear cell (MNC) fraction of adult bone marrow (BM) has increased muscle function in peripheral artery disease [4]. The goal of the study was to improve muscle strength of partially reinnervated biceps muscles through autologous MNC transplantation.

Materials and Methods: Fifteen adult BPI patients with insufficient force recovery of elbow flexion (MRC 1-3) were included. Three escalating doses of MNCs were injected in the biceps muscle (group A, B and C). The quantity of aspirated BM and the MNC dose per patient group are shown in Table 1. Prior to and 3 and 6 months after transplantation quantitative needle EMG of the affected and contralateral biceps muscle was performed, resulting in mean amplitude, duration and number of phases (NP) of motor unit potentials (MUPs). Prior to and 3 months after transplantation, a biopsy of the biceps muscle was taken. Muscle morphology was assessed (e.g. fibrosis, fatty degeneration. The diameters of at least 200 myofibers were measured.

Results: Results of nine patients were obtained. Postoperatively, the mean decrease in hemoglobin (Hb) concentration was 0.3 g/dl (group A), 1.6 g/dl (group B) and 2.9 g/dl (group C). Six months after transplantation the Hb concentration of all patients had normalized. Quantitative EMG demonstrated a significant increase in amplitude, duration and the NP between the affected and contralateral biceps muscle was performed, resulting in mean amplitude, duration and number of phases (NP) of motor unit potentials (MUPs). Prior to and 3 months after transplantation, a biopsy of the biceps muscle was taken. Muscle morphology was assessed (e.g. fibrosis, fatty degeneration. The diameters of at least 200 myofibers were measured.

Discussion: This is the first study to use autologous MNC transplantation for improvement of muscle strength in BPI. No negative side effects were observed. A decrease in Hb concentration was anticipated, but had no negative side effects. Quantitative EMG demonstrated an increase in MUP amplitude and polyphasia, suggestive of increased reinnervation. Another sign of reinnervation is an increase in the duration of the MUPs. In our study, this increase could not be detected, possibly because of the limited sample size. The MNC dose applied in group B could represent the optimal cell dose to ameliorate muscle atrophy. Whether the transplantation increased the number of satellite cells, or paracrine effects of the injected cells are responsible for the increase in myofiber diameter is currently under investigation. These preliminary data suggest that autologous MNC transplantation may help treat muscle atrophy and could assist in reinnervation in traumatic BPI with insufficient force recovery of the biceps muscle.


Table 1: The quantity of aspirated BM and the MNC dose per patient group.

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<thead>
<tr>
<th>Group</th>
<th>BM (cc)</th>
<th>MNC (x 10⁶)</th>
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<tbody>
<tr>
<td>A</td>
<td>60</td>
<td>0.01 ± 0.01</td>
</tr>
<tr>
<td>B</td>
<td>350</td>
<td>4</td>
</tr>
<tr>
<td>C</td>
<td>625</td>
<td>8</td>
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Figure 1: Distribution of myofiber diameters of the biceps muscle. The preoperative biopsy of patient 2 had an insufficient number of myofibers and was excluded.

Figure 2: Hematoxylin-and-eosin staining of a pre- (A) and postoperative (B) muscle biopsy of a patient in group B (magnification 20x).