BMP-2 COATING OF TITANIUM IMPLANTS INCREASE BIOMECHANICAL STRENGTH AND ACCELERATE BONE REMODELLING IN FRACTURE TREATMENT

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Introduction:
Bone morphogenetic protein-2 (BMP-2), a member of the TGF-beta superfamily is known to stimulate osteogenic cells. In vivo studies have shown that BMP-2 delivered from collagen sponges enhances fracture healing [1]. This application technique requires the opening of the fracture and may have possible side effects due to the use of bovine collagen. A newly developed coating method for implants based on biodegradable poly(D,L-lactide) allows the incorporation of growth factors and the controlled release of these factors during the healing process without the need of further devices [2]. The effect of BMP-2 (5% w/w) locally released from coated intramedullary implants on fracture healing was investigated with biomechanical and histological analysis in rats.

Methods:
A standardized closed fracture of the right tibia of five months old Sprague Dawley rats (n=80) was performed with a fracture device (impulse p=1.12 Ns). The fractures were intramedullary stabilized with uncoated versus coated titanium K-wires. Following groups were examined:

Group I: implant uncoated, 28 days (n=20)
Group II: implant coated with PDLLA + rh-BMP-2, 28 days (n=20)
Group III: implant uncoated, 42 days (n=20)
Group IV: implant coated with PDLLA + rh-BMP-2, 42 days (n=20)

After fracture of the right tibia, x-ray examinations (p.a. and lat.) were performed throughout the experimental period.

After sacrifice both tibiae were dissected for biomechanical torsional testing using a material testing machine (Zwick 1455, Ulm, Germany). For histological and histomorphometric analyses the tibiae were fixed and embedded in methylmetacrylate. 5µm sections were performed and stained with Safranin O/light green and v. Kossa. The histomorphometry of the calli was performed using an image analyzing system (Zeiss KS 400).

Results:
The results demonstrated a progressed callus consolidation in the BMP-2 treated groups compared to the uncoated groups at both time points (Fig 1). The histomorphometrical analyses demonstrated a progressed callus remodeling with significantly higher mineralization of the cortices and higher mineralization and less cartilage of the periosteal callus (Fig 2 / Table 1).

Discussion:
The results clearly demonstrate that the local application of BMP-2 from PDLLA coated implants significantly accelerates fracture healing. Two time points were investigated to analyze the effect of the BMP-2 coating on the healing process. The biomechanical torsional testing after 28 and 42 days revealed a higher torsional stability compared to the control groups. These data were supported by the histomorphometrical results. The callus treated with BMP-2 demonstrated a progressed callus remodeling with significantly higher mineralization and less cartilage compared to controls.

These results are in accordance with other studies investigating the effect of BMP-2 on fracture healing. However, local administration of growth factors from coated osteosynthetic implants could reduce clinical problems in fracture treatment without opening of the fracture, implantation of further devices, injections with the risk of infection or side effects caused by the carrier.

Table 1: Histomorphometry

<table>
<thead>
<tr>
<th></th>
<th>uncovted 4 wks</th>
<th>BMP-2 4 wks</th>
<th>uncovted 6 wks</th>
<th>BMP-2 6 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibia diameter [mm]</td>
<td>base</td>
<td>base</td>
<td>base</td>
<td>base</td>
</tr>
<tr>
<td>2.5±0.3</td>
<td>2.5±0.3</td>
<td>2.4±0.3</td>
<td>2.4±0.2</td>
<td></td>
</tr>
<tr>
<td>Mineralised Ar/Cortec Ar [%]</td>
<td>92.7±1.1</td>
<td>96.2±1.0</td>
<td>89.4±3.5</td>
<td>96.8±0.9</td>
</tr>
<tr>
<td>Periosteal Callus Ar/ base [mm]</td>
<td>5.5±1.8</td>
<td>5.7±1.5</td>
<td>5.1±1.4</td>
<td>4.9±1.0</td>
</tr>
<tr>
<td>Mineralised Ar/ Ps.Cl.Ar [%]</td>
<td>60.4±1.4</td>
<td>70.5±5.3*</td>
<td>62.6±5.0</td>
<td>86.4±4.3*</td>
</tr>
<tr>
<td>Cartilage Ar/ Ps.Cl.Ar [%]</td>
<td>10.6±1.8</td>
<td>5.8±4.2*</td>
<td>8.6±1.9</td>
<td>1.4±0.9*</td>
</tr>
</tbody>
</table>

* p<0.05 T-Test

References: