Evaluation of the efficacy of *E. coli*-derived rhBMP-2 in mini-pig spinal posterolateral fusion

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HA & *E. coli*-derived rhBMP-2

- Posterolateral lumbar fusion with rhBMP-2 /HA-TCP after laminectomy in the nonhuman primate
- Lower dose of rhBMP-2 achieves spine fusion when combined with an osteoconductive bulking agent in non-human primates
- RhBMP-2 produced by mammalian cells: too expensive → major obstacle to its clinical application
- Bacterial expression system (eg, *Escherichia coli*): cost-effective production of rhBMP-2
Purpose of This Study

- To determine whether HA granule could be an adequate carrier for E-BMP-2
- To assess the osteoinductivity of HA granule-E-BMP-2 composite
- To evaluate the bone forming ability depending on the different dosages of E-BMP-2
Materials and Methods

- 31 skeletally mature male Yucatan mini-pigs
- Single control group (n = 8) without E-BMP-2 and two experimental groups (1.0 mg/side, n = 8 and 3.0 mg/side, n = 15)
- To evaluate the bone forming ability depending on the different dosages of E-BMP-2
- *E. coli*-derived rhBMP-2 (3 mg/vial, Daewoong)
- Synthetic HA granules (Bongros®-HA, Bio-Alpha)
Fusion Assessment

- Radiographic analysis
- Manual palpation
- 3D CT (Toshiba, Tokyo, Japan)
- 3D µCT (SKYSCAN, Skyscan-1173, Belgium)
- Histologic examinations
µCT Analysis

Bone Volume Fraction

HA Volume Fraction

Bone volume fraction (\%) = \frac{BV}{TV} \times 100 \quad (\text{lower gray threshold} = 65)

HA volume fraction (\%) = \frac{HA \text{ volume}}{TV} \times 100 \quad (\text{lower gray threshold} = 115)

New bone volume fraction (\%) = BV \text{ fraction} - HV \text{ volume fraction}
### Wound Complication

<table>
<thead>
<tr>
<th>Group</th>
<th>Control (8)</th>
<th>1 mg (7)</th>
<th>3 mg (13)</th>
<th>N (28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developed</td>
<td>1 (12.5%)</td>
<td>2 (28.6%)</td>
<td>4 (30.8%)</td>
<td>7</td>
</tr>
<tr>
<td>Not developed</td>
<td>7 (87.5%)</td>
<td>5 (71.4%)</td>
<td>9 (69.2%)</td>
<td>21</td>
</tr>
</tbody>
</table>

\[ P = 0.623 \]

### Bony Union

<table>
<thead>
<tr>
<th>Group</th>
<th>Control (8)</th>
<th>1 mg (7)</th>
<th>3 mg (13)</th>
<th>N (28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Union</td>
<td>3 (37.5%)</td>
<td>5 (71.4%)</td>
<td>11 (84.6%)</td>
<td>19</td>
</tr>
<tr>
<td>Non-union</td>
<td>5 (62.5%)</td>
<td>2 (28.6%)</td>
<td>2 (15.4%)</td>
<td>9</td>
</tr>
</tbody>
</table>

\[ P = 0.031 \]
Bone Volume

New Bone Volume

$P < 0.001$

$P < 0.001$
Histologic Analysis \( (\times 1) \)

Control

1mg

3mg

\( (\times 1) \) \( (\times 10) \) \( (\times 40) \)
Discussion

- One of major obstacle in fusion surgery using rhBMP-2 is its high cost
- Cost-effective production of rhBMP-2 using an *E. coli* system was introduced and several animal studies demonstrated the osteoinductivity of E-BMP-2 in dose-dependent fashion
- Our porcine posterolateral fusion model showed addition of E-BMP-2 significantly increased the fusion rates
HA carrier-E-BMP-2 Combination

- HA is a major mineral constituent of bone and osteoblasts can deposit bone directly onto this osteoconductive carrier material.

- Considering the mechanical and biologic environment for posterolateral spine fusion, HA is also useful for rhBMP-2 carrier because of its mechanical resistance to compression force and high affinity for rhBMP-2.
Conclusions

- E-BMP-2 adsorbed HA granule could be an alternative to autogenous iliac bone graft

- Dosage of 1 mg/side E-BMP-2 could be effective in posterolateral spine fusion in porcine model when combined with HA carrier

DISCLOSURE STATEMENT
The authors have nothing to disclose