Local bone antibiotic delivery using porous alumina ceramic: clinical and pharmacological experience

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Conflict of interest

- Employed by I.Ceram
Context

- Replacing infected bone
- High risk of implant's infection
- => No foreign body during infection

Proposition:
- Implantation of a "protected" device (antibiotic loaded)
- Prophylaxis
Main characteristics

- **Pure alumina $\text{Al}_2\text{O}_3$**
- **Proven biocompatibility, inert**
- **Mechanical strength more than 20 MPa**
  - 3 times cancellous bone strength in compression
- **Non absorbable**
- **A certain level of resistance to bacterial infection**
- **Interconnected porosity**
- **Unique capacity of osseointegration**
  - Porosity range from 100 to 900 μm
A very similar structure
Antibiotics

- Antibiotic loaded:
  - Gentamicin
  - Vancomycin
  - Both of them

- Start of release: immediately

- Release duration: 48 – 72 h \textit{(in vitro)}

- Release: 100 %
Four patients received this loaded sternum
More than 3 years of follow-up for the 1st one without relapse
Chronic osteomyelitis (MRSA)

Follow-up

All samples grew with MRSA

Loaded with gentamicin

M+11

M+17

M+17
Infected ankle Prosthesis

Skin fistula – Infection lasting for 10 years

Ceramic loaded with vancomycin
Chronic osteomyelitis: femoral tile

Man 64 year-old
Chronic osteomyelitis – MSSA
Evolution: 30 years
Gentamicin cement beads

Gentamicin loaded

X-Ray follow-up M3
Chronic osteomyelitis: tibial tile

Man 48 year-old
Chronic osteomyelitis after fracture
> 5 surgeries
Pseudoarthrosis MSSA
Fistula
Already had a muscle flap
## In vivo – local concentrations

### Local dosages

<table>
<thead>
<tr>
<th>Device</th>
<th>Loaded dose</th>
<th>H+1</th>
<th>H+24</th>
<th>H+48</th>
<th>H+60</th>
<th>Pharmacological parameter needed</th>
<th>Pharmacological parameter obtained</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gentamicin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sternum</td>
<td>320 mg</td>
<td>1,500 mg/L</td>
<td>395 mg/L</td>
<td></td>
<td></td>
<td></td>
<td>&gt; 1,500</td>
</tr>
<tr>
<td>Sternum</td>
<td>160 mg</td>
<td>2,100 mg/L</td>
<td>36.9 mg/L</td>
<td></td>
<td></td>
<td></td>
<td>&gt; 2,100</td>
</tr>
<tr>
<td>Bone flap</td>
<td>160 mg</td>
<td>184 mg/L</td>
<td>13 mg/L</td>
<td></td>
<td></td>
<td>(\frac{C_{max}}{MIC}) &gt; 10</td>
<td>&gt; 370</td>
</tr>
<tr>
<td>Sternum</td>
<td>320 mg</td>
<td>6,650 mg/L</td>
<td>4.7 mg/L</td>
<td></td>
<td></td>
<td></td>
<td>6,650 (K. pneumoniae) 17 (MRSE)</td>
</tr>
<tr>
<td><strong>Vancomycin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankle spacer</td>
<td>250 mg</td>
<td>548 mg/L</td>
<td>172 mg/L</td>
<td>26 mg/L</td>
<td></td>
<td>(\frac{AUC}{MIC}) &gt; 400</td>
<td>2,400</td>
</tr>
<tr>
<td>Sternum</td>
<td>250 mg</td>
<td>390 mg/L</td>
<td>28 mg/L</td>
<td></td>
<td></td>
<td></td>
<td>16,000 (MRSE)</td>
</tr>
</tbody>
</table>
Surpassing resistance

Mediastinitis

Bacteriological sampling and sensitivity interpretation
EUCAST

*K. pneumoniae*
- gentamicin **S** (MIC = 1 µg/mL)

MRSE
- gentamicin **R** (MIC = 384 µg/mL)
  - EUCAST Breakpoint: 1 µg/ml
- vancomycin **R** (MIC = 8 µg/mL)
  - EUCAST Breakpoint: 4 µg/ml

Administration route

**Intravenous**
⇒ Expected to fail (MRSE)

**Locally (MRSE)**
- Gentamicin
  - $C_{\text{max}}$/MIC = 17
- Vancomycin
  - AUC/MIC = 16,000
⇒ Expected to be efficient
- M+2 : no relapse
**In vivo** – Blood concentrations

- Very low and undetectable blood passage
- Decreasing side effects and toxicity

<table>
<thead>
<tr>
<th>Device</th>
<th>H1</th>
<th>H3</th>
<th>H6</th>
<th>H12</th>
<th>H24</th>
<th>H48</th>
</tr>
</thead>
<tbody>
<tr>
<td># 1 Sternum (gentamicin)</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
</tr>
<tr>
<td># 2 Sternum (gentamicin)</td>
<td>&lt; 0.5</td>
<td>0.6</td>
<td>0.6</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td></td>
</tr>
<tr>
<td># 3 Femur flap (gentamicin)</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td></td>
</tr>
<tr>
<td># 4 Sternum (gentamicin)</td>
<td>&lt; 0.5</td>
<td></td>
<td></td>
<td>&lt; 0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td># 5 Femur tile (gentamicin)</td>
<td></td>
<td>1.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td># 6 Sternum (gentamicin)</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td></td>
</tr>
<tr>
<td># 6 Sternum (vancomycin)</td>
<td>&lt; 1.1</td>
<td>&lt; 1.1</td>
<td>&lt; 1.1</td>
<td>&lt; 1.1</td>
<td>&lt; 1.1</td>
<td></td>
</tr>
</tbody>
</table>
Comparison to other local delivery means
Conclusion

CERAMIC IMPLANT
(Mechanical properties)

ANTIBIOTIC LOADED
CERAMIC IMPLANT

Infected area
Thank you for your attention

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