Vancomycin Powder Mixed with Autogenous Bone Graft and Bone Substitute May Decrease the Risk of Deep Surgical Site Infection in Degenerative Lumbar Spines Fusion Surgery - An ambispective study

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Introduction

- Deep surgical site infection (DSSI) in instrumented spine surgery:
  - Incidence: up to 0.5 - 7.7%
    

- The most common organism:
  - Staphylococcus species
    

- Intra-wound vancomycin powder:
  - Advantage:
    - High local concentration
    - No systemic side effects
  - Disadvantages:
    - No local carrier to maintain high concentration

Materials and Methods

- Ambispective study

- Inclusion criteria:
  - Degenerative spondylolisthesis
  - All received posterior decompression, instrumentation with PLF ± TLIF

- Exclusion criteria:
  - Spinal infection, tumor, or revision surgery
Materials and Methods

- Vancomycin protocol
  - Pre-op IV cephalosporin 1 dose
  - Post-op IV cephalosporin for 3 days
  - 4 – 6 L normal saline pulsated lavage
  - Vancomycin-impregnated autogenous bone graft for fusion :
    - 1 gm in 2- or 3-level
    - 2 gm in 4-level
    - 1:1 mixed with synthetic bone substitute (β-tricalcium phosphate, [ChronOS®, DePuy, Synthes])
  - Drain removed at post-op day 3 or 4
Materials and Methods

- Vancomycin concentration
  - Serum and drain fluid
    ✓ Measured by ELISA
  - Vancomycin checking points:
    ✓ Post-op day 1 (POD 1)
    ✓ Post-op day 3 (POD 3)

- Fusion Evaluation
  - Plain radiographs
  - Posterolateral fusion
    ✓ Glassman classification
  - Interbody fusion
    ✓ Non-union: disc angulation >5° in flexion-extension views

Glassman Postero-lateral Fusion Assessment

<table>
<thead>
<tr>
<th></th>
<th>1 (Nonfusion)</th>
<th>2 (Partial Unilateral Fusion)</th>
<th>3 (Partial Bilateral Fusion)</th>
<th>4 (Solid Unilateral Fusion)</th>
<th>5 (Solid Bilateral Fusion)</th>
</tr>
</thead>
</table>

Materials and Methods

Definition of DSSI

- Abnormal LBP with high CRP
- MRI:
  - Pedicle screw fluid sign
  - CT guided culture/biopsy for tissue prove
- IV (6 weeks) than oral (6 wees) antibiotic with/without surgical debridement

Results

- Vancomycin concentration
  - Drain tube

<table>
<thead>
<tr>
<th>Post-operative day</th>
<th>1st (POD 1)</th>
<th>3rd (POD 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin concentration</td>
<td>Drain</td>
<td>517.96 ± 161.72 (107.9-932.4)</td>
</tr>
<tr>
<td></td>
<td>Serum</td>
<td>&lt; 0.24</td>
</tr>
</tbody>
</table>

— Serum vancomycin: Undetectable
Results

<table>
<thead>
<tr>
<th></th>
<th>Vancomycin (V)</th>
<th>No Vancomycin (NV)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers of Patients</td>
<td>110</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>Blood Loss (mL)</td>
<td>431 ± 280 (200-1100)</td>
<td>427 ± 295 (250-1000)</td>
<td>0.923</td>
</tr>
<tr>
<td>Operative Times (mins)</td>
<td>281 ± 72 (200-400)</td>
<td>285 ± 63 (220-410)</td>
<td>0.684</td>
</tr>
<tr>
<td>Deep Surgical Site Infection (DSSI)</td>
<td>0 (0%)</td>
<td>3 (3.48%)</td>
<td>0.048*</td>
</tr>
<tr>
<td>Surgical-Related Complications</td>
<td></td>
<td></td>
<td>0.308</td>
</tr>
<tr>
<td>Screws breakage or loosening</td>
<td>2*</td>
<td>4*</td>
<td></td>
</tr>
<tr>
<td>Cage Dislodge or migration</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Incidental Durotomy</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Vancomycin-Related Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red Man syndrome</td>
<td>0</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>0</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Renal toxicity</td>
<td>0</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Ototoxicity or transient hearing loss</td>
<td>0</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Systemic Absorption (Detectable Serum Vancomycin)</td>
<td>0</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Functional Outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual analogue scale over leg</td>
<td>1.3±1.4 (1-4)</td>
<td>1.1±1.5 (0-3)</td>
<td>0.337</td>
</tr>
<tr>
<td>Oswestry Disability Index (ODI)</td>
<td>31.8±5.6 (16-36)</td>
<td>32.9±6.1 (24-44)</td>
<td>0.191</td>
</tr>
</tbody>
</table>

The percentage was presented in parentheses, NA meant Non-appreciable, f/u meant follow-up
2 patients had S1 screws loosening in the V group at latest f/u.
2 patients had S1 screws loosening in the NV group at latest f/u. (2: S1 lossening screw, 2: infective non-union)

Culture:
- MRSA*2
- No growth*1

G* power = 0.503
# Results

Table 4. Results of Bone Fusion at Latest Follow-up Between Two Groups

<table>
<thead>
<tr>
<th></th>
<th>Vancomycin (V)</th>
<th>No Vancomycin (NV)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers of Patients</td>
<td>110</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>Glassman Posterolateral Fusion at Latest Follow-up</td>
<td></td>
<td></td>
<td>0.625</td>
</tr>
<tr>
<td>1 (Nonfusion)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2 (Partial Unilateral Fusion)</td>
<td>17</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>3 (Partial Bilateral Fusion)</td>
<td>55</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>4 (Solid Unilateral Fusion)</td>
<td>23</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>5 (Solid Bilateral Fusion)</td>
<td>15</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Bony Fusion Rate at Latest Follow-up *</td>
<td>100%</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

Glassman posterolateral fusion grading was adopted from reference (Spine 2005;30:1694–8)

* Fusion was defined as angulation change less than 5 degrees in the dynamic view (Spine 2001;26(3):320-334.)
Discussion

- Intra-wound vancomycin for preventing SSI remains controversial
- Vancomycin and pseudarthrosis
  - Vancomycin concentration in vitro:
    - > 3000 ug/mL: Osteoblast inhibition
    - > 6000 ug/mL: Cells death

  *Eur Spine J 2015; April 24; CORR 2007;462:200-6.; JOR 2011; 29:1070-4.*

  - In this study:
    - Max concentration: 932 ug/mL (at POD1) (MAY NOT interface bone fusion)
    - Fusion rate: no difference

- Minimal inhibitory concentration (MIC) of vancomycin
  - MRSA: 1.5-2 ug/mL


  - In this study:
    - Minimal vancomycin concentration: 74.3 ug/mL (at POD3)
    - Local vancomycin concentration >> MIC for MRSA
Discussion

- Local delivery system by autogenous bone graft (ABG): **Maintained higher concentration**

<table>
<thead>
<tr>
<th>patients numbers</th>
<th>dosage (gm) applied</th>
<th>vancomycin concentration at post-operative day (ug/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweet FA et al</td>
<td>178</td>
<td>2</td>
</tr>
<tr>
<td>Armaghani SJ et al</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td>Our results</td>
<td>89</td>
<td>1 or 2*</td>
</tr>
</tbody>
</table>

  *1 gm for 2-level or 3-level and 2 gm for 4-level or more

- **Major weakness:**
  - Not prospective randomized
  - Small numbers
  - Low power (G* power = 0.508)
  - Short-term follow-up (Avg. 26 months in Vancomycin group)
  - No CT scan to evaluate fusion status
Conclusion and Thank you! 謝謝！

- Mixed vancomycin powder with autogenous bone graft:
  - High local concentration
  - May not affect bony fusion
  - Decrease incidence of DSSI
  - No systemic side effects

None of the authors has any potential conflict of interest.