Comparison of Short and Long Courses of Antibiotics in Patients with Prosthetic Joint Infection: A Systemic Review and Meta-analysis

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Background
- Current treatment for prosthetic joint infections (PJI) requires prompt surgical intervention and months to years of lifelong course of oral and/or intravenous (IV) antibiotics. However, previous studies on the optimal course of antibiotics for PJI showed inconsistent results1-3.

Objectives
- To conduct a systematic review and meta-analysis on the antibiotics treatment of PJI with a hypothesis that a short course and long course of antibiotics are similarly effective.

Methods
- Literature search
  - Database: PubMed and Embase
  - Pre-defined search term: three separate queries composed of MeSH or EMTREE and title/abstract key words for three focuses: antibiotics, treatment duration, and PJI (Supplement table 1).
  - We also screened references cited in included studies not retrieved from the initial search. We did not limit our search based on study type.
  - Excluded studies: PJI caused by atypical bacteria and non-bacterial pathogens (e.g. Mycobacterium, Brucella, fungus, virus).
  - Two authors independently screened the retrieved studies for three rounds (title/abstract, full text, extraction). Discrepancies were resolved by the involvement of the senior author. Data of the final included studies were extracted.

Results

Study analysis
- Primary endpoints: cure rate, recurrence rate, mortality rate, complication rate and rate of secondary treatments
- Definition of treatment failure: PJI-related death, re-infection and persistent infection
- Quality assessment of studies:
  - Randomized controlled trials (RCTs): Modified Jadad scale
  - Observational studies: Newcastle-Ottawa Quality Assessment
- Statistical analysis: DeSimonian and Laird method for random effect models. Heterogeneity was quantified with I² statistics.

Publication bias was assessed by Begg’s and Egger’s tests.

Study inclusion
- A total of 10 studies and 856 patients were included in our study.
  - 1 RCT, 9 observational studies
  - 9 studies focused on THA and TKA, while 1 study also included ankle, shoulder, and elbow arthroplasties.
  - In 5 studies (including one RCT), patients were treated with debridement and implant retention (DAIR); in 3 studies, patients were treated with staged exchange arthroplasty (SER); in 2 studies, patients received mixed procedures.

- 5 studies investigated the duration of IV antibiotics, while the other 5 studies focused on the total duration of IV and oral antibiotics.

- 1972 citations identified from literature search, 1163 from PubMed and 609 from Embase database

- 228 overlapped studies excluded

- 1731 studies excluded after first round (screening of titles and abstracts)

- 13 studies included for full-text review

- 0 studies identified from the reference lists of included studies

- 13 studies included for full-text review

- 3 studies excluded because of lack of comparison of the outcomes of a long and short course of antibiotics

- 10 articles included in our study

- Main meta-analysis
  - 9 out of 10 studies showed a short course and a long course of antibiotics were similarly effective.
  - Our meta-analysis also showed similar outcomes between a short course and a long course of antibiotics (RR 0.87 [0.62, 1.22]), with moderate heterogeneity (I² 46.6%).

- Table 1: Subgroup analysis

<table>
<thead>
<tr>
<th>Subgroup analysis (study number)</th>
<th>Difference in rate of treatment failure</th>
<th>Heterogeneity analysis (I²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All studies (10)</td>
<td>No significant difference (RR 0.87 [0.62, 1.22])</td>
<td>Moderate (46.6%)</td>
</tr>
<tr>
<td>Studies graded as good or fair (7)</td>
<td>No significant difference (RR 0.94 [0.61, 1.44])</td>
<td>High (62.2%)</td>
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<tr>
<td>Subgroup analysis of treatments:</td>
<td></td>
<td></td>
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<tr>
<td>Treatment with IV antibiotics (4)</td>
<td>No significant difference (RR 1.04 [0.51, 2.12])</td>
<td>High (50.9%)</td>
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<tr>
<td>Surgical intervention with DAIR (6)</td>
<td>No significant difference (RR 0.76 [0.42, 1.34])</td>
<td>Moderate (52.9%)</td>
</tr>
<tr>
<td>Implant removal (4)</td>
<td>No significant difference (RR 0.71 [0.45, 1.11])</td>
<td>Low (0.0%)</td>
</tr>
<tr>
<td>Anatomical sites:</td>
<td></td>
<td></td>
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<tr>
<td>Knee (3)</td>
<td>No significant difference (RR 0.85 [0.46, 1.58])</td>
<td>Low (0.0%)</td>
</tr>
<tr>
<td>Hip (4)</td>
<td>No significant difference (RR 0.81 [0.35, 1.88])</td>
<td>Low (0.0%)</td>
</tr>
<tr>
<td>Geographical areas:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA (3)</td>
<td>No significant difference (RR 0.62 [0.37, 1.02])</td>
<td>Low (0.0%)</td>
</tr>
<tr>
<td>Europe (6)</td>
<td>No significant difference (RR 0.93 [0.58, 1.48])</td>
<td>High (65.0%)</td>
</tr>
</tbody>
</table>

Publication bias
- There was no significant publication bias in the 10 included studies (Begg’s test p=0.107, Egger’s test p=0.998).
- We showed Funnel’s plot and Galbraith’s plot as below.

Conclusions
- Our pooled meta-analysis and subgroup analysis showed that a short course of antibiotics was as effective as a long course of antibiotics for treatment of PJI, regardless of the type and location of surgical intervention patients received.

Reference

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