Interactive Session:

How to optimise Oral Antibiotic Therapy

Alasdair MacGowan
You are asked to consult on a patient with Prosthetic Joint Infection

Two weeks previously, the patient had a first stage revision for a Right Hip Infection. All prosthetic material was removed and a spacer is now in place. Re-implantation is planned for 8-12 weeks.

In 2011, the patient, a 65 year old female (BMI 32) had a primary implant which was complicated by post-operative wound infection. Six months ago the patient re-presented with pain in the hip and a discharging ulcer on the lateral side of the thigh. The ulcer did not heal with antibiotics and dressings. An aspirate of the hip grew Staph epidermidis and five of the six tissues at the operation, when the prosthesis was removed, cultured the same organism.

The patient has been treated post operatively with vancomycin 1g 12hrly, plus rifampicin 600mg 24hr orally. Blood tests are: eGFR >90ml/min, LFTs normal, FBC normal, CRP 45mg/ml, pre-dose vancomycin levels 10-15mg/L.
What are your thoughts?
What are your thoughts?

a) I don’t believe in po therapy for PJI – continue the IVs and get a central line

b) Depending on the sensitivities of the organism, I would consider

1) cipro/levofloxacin plus rifampicin
2) co-trimoxazole plus rifampicin
3) doxycycline plus rifampicin
4) flucloxacillin plus rifampicin
5) another combination I use a lot
Iv oral switch therapy

• Variable opinions re acceptability of po antibiotics for PJI

• Historical approach - extended duration iv antibiotics

• No RCTS except for quinolone-rifampicin combinations

• Bejon et al, UK → 6 weeks iv before po switch
Hsieh et al Taiwan → 1 week iv then stop
Whittaker et al UK. → vanc x 2 weeks then stop ( + antibiotics in cement/spacer ).

Avon Orthopaedic Centre approach to antibiotic treatment of PJI: Microbiological Outcome analysis

- In 2006-725 patients identified who had a revision by 1 stage (n=19) or a 2-stage (n=6) for infected THR.
- Follow up duration for all cases = 24-36 months.
- 3 patients had died at time of follow up- without any further infective complications relating to their joint replacement.

Darley et al. J Antimicrobial Chemotherapy 2011
Interim analysis 2-year Outcome data.

- **1-stage revision surgery.**
- 5/6 had between 7-20 days iv antibiotics followed by 6-26 weeks oral antibiotics.
- 1 patient had 6 weeks oral antibiotics with no initial iv therapy.
- Case notes are unavailable for 2 patients.

**2-stage revision surgery.**
- 15/19 were treated with between 12 -21 days iv antibiotics followed by oral antibiotics for 4-25 weeks.
- 2/19 patients were treated with iv antibiotics for the whole duration.
- Two other patients had 28 days iv antibiotics prior to oral switch.
Results. 1 & 2-stage THR for infection.
2006-7

1-stage THR n=6
- relapse
- no relapse

2-stage THR n=19
- relapse
- no relapse

- iv only
- iv-oral switch
- oral exclusive
You review the sensitivities of the Staph epidermidis:

- Penicillin  R
- Flucloxacillin  R
- Erythromycin  R
- Clindamycin  R
- Ciprofloxacin  R
- Co-trimoxazole  R
- Doxycycline  R
- Rifampicin  R
- Fusidic acid  R
- Daptomycin  S
- Teicoplanin  MIC 4mg/L
- Vancomycin  MIC 1mg/L
- Linezolid  S
What additional sensitivities could you test?
What additional sensitivities could you test?

- Prishnamycin (synercid)
- Moxifloxacin MIC
- Fosfomycin MIC
- Minocycline MIC
- Rifampicin MIC
# S.epidermidis - full susceptibilities

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC (mg/L)</th>
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<tbody>
<tr>
<td>Penicillin</td>
<td>R</td>
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<tr>
<td>Flucloxicillin</td>
<td>R</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>R</td>
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<tr>
<td>Clindamicin</td>
<td>R</td>
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<tr>
<td>Ciprofloxacin</td>
<td>R</td>
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<tr>
<td>Co-trimoxazole</td>
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<td>Fusidic acid</td>
<td>R</td>
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<td>Daptomycin</td>
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<tr>
<td>Teicoplanin</td>
<td>MIC 4mg/L</td>
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<tr>
<td>Vancomycin</td>
<td>MIC 1mg/L</td>
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<tr>
<td>Linezolid</td>
<td>S</td>
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<tr>
<td>Synercid (pristinamycin)</td>
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<td>Moxifloxacin</td>
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<td>Fosfomycin</td>
<td>MIC 4 mg/L</td>
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<tr>
<td>Minocycline</td>
<td>MIC 0.12mg/L</td>
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What oral options would you choose?
What oral option would you choose?

a) Levofloxacin plus rifampicin - I don’t believe all these tests are relevant in chronic infection

b) Minocycline 100mg BD - Rifampicin is not needed, all metal work removed

c) Minocycline 100mg BD plus rifampicin 600mg OD - I think we need that extra antibacterial activity

d) Pristinamycin 500mg QDS - I like French drugs even if I can’t test them in the lab

e) Fosfomycin xg yhrly - I don’t know the right dose but it’s good stuff

f) Fosfomycin xg xhrly plus rifampicin - I’m worried about emergence or fosfomycin resistance

g) Another combination
How long would you treat?

a) Two weeks IV therapy enough?

b) For a total of 6-8 weeks?

c) Until two weeks before second stage procedure?

d) Up until second stage procedure?