Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

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Objective

• Characterize the potential patient comfort and clinical advantages of a partial oral antimicrobial treatment strategy on patient outcomes when compared to long historical standard of care for the routine management of infective endocarditis
Background

- Patients with left-side infective endocarditis generally require 6 weeks intravenous therapy

- Highly complex management with increased potential for complications

- Clinical safety and efficacy of oral antibiotic therapy for treatment of endocarditis remains limited

Previous Trials:
- Dworkin (1989)
- Mzabi (2016)
- Iversen (2013)
Methods

• Nationwide investigator-initiated, randomized, unblinded, multicenter, non-inferiority study from Iversen et al.

• Primary Outcome
  – Composite of all-cause mortality, unplanned cardiac surgery, clinically evident embolic events or relapse of bacteremia with the primary pathogen from randomization through 6 months after antibiotic treatment was completed

• Intent-to-treat analysis
Methods

Inclusion Criteria

• Left sided endocarditis based on Duke criteria
• Infected with Streptococci, *E. faecalis*, *S. aureus*, Coagulase negative staphylococci
• CRP dropped to <25% of peak or <20mg/L, and WBC <15x10^9/L during antibiotic treatment
• Echocardiography within 48hrs of randomization, without signs of abscess

Exclusion Criteria

• BMI > 40
• Concomitant infection requiring intravenous antibiotics
• Suspicion of reduced absorption of oral treatment due to abdominal disorder
• Reduced compliance

Oral Regimens:

- **Amoxicillin 1g four times daily**
- **Linezolid 600mg twice daily**
- **Dicloxacillin 1g four times daily**
- **Moxifloxacin 400mg daily**

Rifampicin or fucidic acid
## Results

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Intravenous treatment (n=199)</th>
<th>Oral treatment (n=201)</th>
<th>Hazard Ratio (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Outcome</td>
<td>24 (12.1)</td>
<td>18 (9.0)</td>
<td>0.72 (0.37 to 1.36)</td>
<td>0.40</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>13 (6.5)</td>
<td>7 (3.5)</td>
<td>0.53 (0.21 to 1.32)</td>
<td></td>
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<tr>
<td>Unplanned cardiac surgery</td>
<td>6 (3.0)</td>
<td>6 (3.0)</td>
<td>0.99 (0.32 to 3.07)</td>
<td></td>
</tr>
<tr>
<td>Embolic event</td>
<td>3 (1.5)</td>
<td>3 (1.5)</td>
<td>0.97 (0.20 to 4.82)</td>
<td></td>
</tr>
<tr>
<td>Relapse of the positive blood culture</td>
<td>5 (2.5)</td>
<td>5 (2.5)</td>
<td>0.97 (0.28 to 3.33)</td>
<td></td>
</tr>
</tbody>
</table>
Results

• A total of 400 patients randomized from July 15th, 2011 to August 30th, 2017
  – 160 (80% of patients treated as outpatient)
  – Transition to oral occurred on about day 17
  – Median LOS: 19 days IV group vs 3 days oral group (p<0.001)
Discussion

Critique

- Study population/medications
- Strict inclusion criteria
- Inclusion of few antibiotic resistant organisms
- Discharge following switch to oral therapy was not mandatory
- Further investigation and standardization may be necessary

Considerations

- A shift from initial intravenous to oral antibiotic treatment was non inferior to continued intravenous therapy
- Transition to oral therapy and shortened inpatient stays as a result may have positive health outcomes
Key Takeaways

• Initial intravenous therapy for at least 10 days with early transition to oral therapy may be considered for medically stable patients with left sided endocarditis resulting from a susceptible gram positive organism
  – Outpatient oral therapy may provide greater patient comfort
  – Potential for reduced healthcare costs and risk of infection associated with prolonged hospitalization

• Selection of oral antibiotics based on culture results with appropriate bioavailability and penetration into cardiac tissue prior to transition of therapy is important

• Compliance to regimen and close outpatient follow-up remains imperative to ensure resolution of primary infection
A 42-year-old male admitted to your institution is empirically initiated on Vancomycin 1,250mg IV every 12 hours for suspected left native valve endocarditis. An echocardiogram confirms the presence of a vegetation and blood cultures taken on admission have revealed methicillin-susceptible *S. aureus*. As a result, the patient is then switched to Cefazolin 2g IV every 8 hours and has since completed a total of 14 days of intravenous therapy. At this time, the patient remains medically stable and the provider subsequently requests to discharge the patient with plan to finish out a total course of 6 weeks of antibiotics on an outpatient basis. Which of the following regimens may be most appropriate to consider for continued management of his MSSA endocarditis?

a) Doxycycline 100mg by mouth twice daily PLUS rifampin for 4 weeks  
b) Cefazolin 2g IV every 8 hours for 6 weeks  
c) Dicloxacillin 1000mg four times daily PLUS rifampin for 4 weeks  
d) Trimethoprim-Sulfamethoxazole 160/800mg by mouth twice daily PLUS rifampin for 4 weeks