

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

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



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of Endocarditis

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 <15x10⁹ /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

Rifampicin or
fucidic acid

Dicloxacillin 1g
four times daily

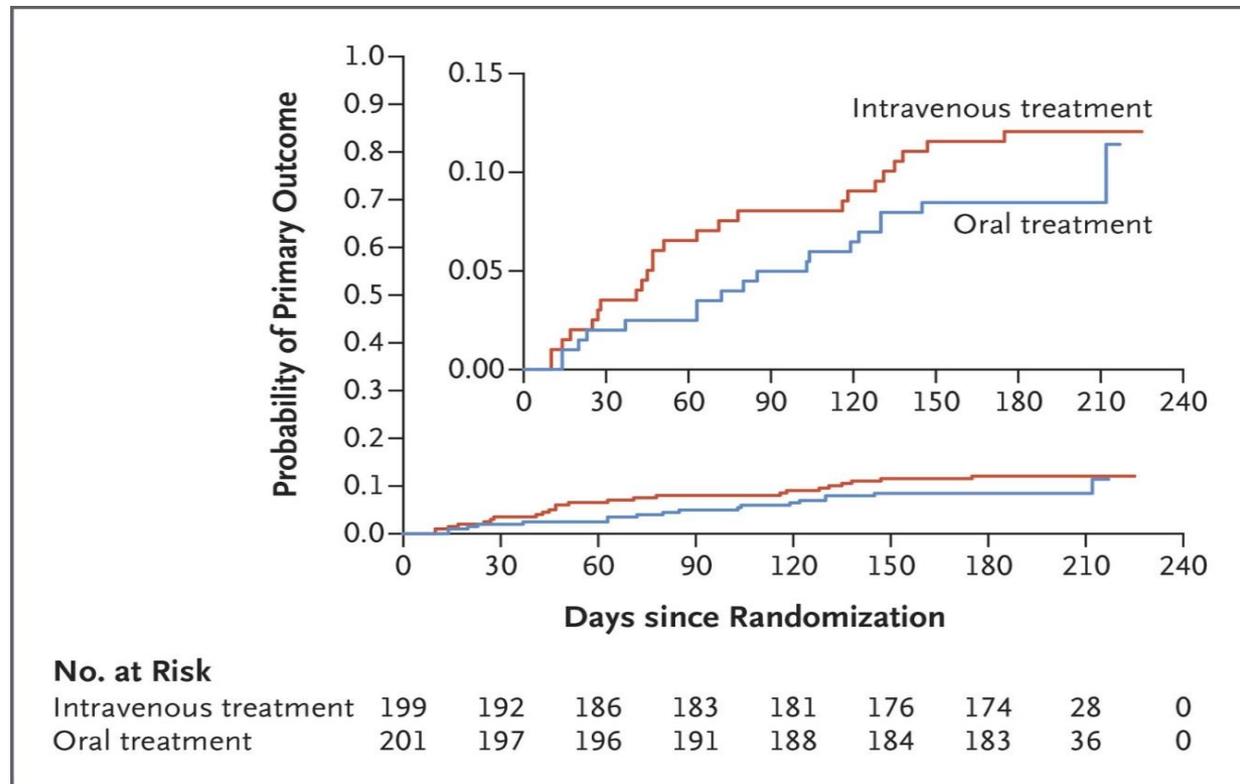
Moxifloxacin
400mg daily

Results

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

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

Post-Assessment

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