An Analysis of the Use of Ampicillin for Urinary Tract Infections Caused By Vancomycin-resistant Enterococcus

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INTRODUCTION
- Enterococci are gram-positive, facultatively anaerobic organisms found in the gastrointestinal tract.
- In a 2008 report from the National Healthcare Safety Network (NHSN), Enterococcus spp. comprised 12% of antimicrobial-resistant pathogens associated with healthcare-associated infections (HAI).
- Specifically, Enterococcus spp. were the 3rd most common cause of catheter-associated UTI and 23% of these organisms were VRE, primarily E. faecium.
- Unfortunately, few agents exist which provide adequate enterococcal activity
- Aminopenicillins may be a treatment option based on their pharmacokinetic profile. Single 1 gm doses of IM ampicillin produce peak urine concentrations of 1500 to 3300 mcg/mL, possibly exceeding the MIC of resistant isolates.
- Clinical data highlighting aminopenicillin activity is limited, but a recent report revealed a 100% cure rate for ampicillin resistant enterococcal UTI.

OBJECTIVE
- Describe clinical and microbiological outcomes in patients with VRE UTIs treated with intravenous ampicillin.

METHODS
- Retrospective chart review evaluating patients who received ampicillin therapy for VRE UTI from January 2000 through August 2010.
- Eligibility criteria
  - Age ≥ 18 years
  - Urine culture growing > 10^3 CFU/mL VRE
  - receipt of ampicillin within seven days of the positive culture
  - receipt of an antimicrobial possessing activity against VRE or demonstrated a mixed urinary tract infection with ≥ 2 organisms
- Conclusions
  - Treatment of VRE UTI with AMP resulted in high clinical and microbiological cure rates with low rates of relapse. AMP should be considered as a viable treatment option for patients with VRE UTI.

TREATMENT RESPONSE
- Clinical cure was defined as:
  - Infection resolution upon completion of treatment without receiving additional antimicrobial therapy for the UTI.
  - Subjects receiving ampicillin treatment as an inpatient, responded to therapy, and discharged on oral amoxicillin or amoxicillin without readmission due to VRE UTI.
- Cure criteria
  - Receipt of an antimicrobial possessing activity against VRE for an unrelated infection
- Microbiologic cure was determined in subjects with repeat urine cultures negative for VRE or to newer agents complicate treatment. Based on high urinary concentrations of ampicillin (AMP) which may exceed minimal inhibitory concentration (MIC) of resistant isolates, Shands at the University of Florida (SUF) implemented a policy of AMP as first line therapy for VRE UTI. This study describes the efficacy of this recommendation.

RESULTS
- Median age was 65.9 yrs, 76% had an indwelling catheter. E. faecium (91%) was the predominant pathogen, and median Charlson score was 6.
- Organism persistence or relapse occurred in 6.5% (6/46) patients. Median dose and duration of AMP were 4 gm/day and 4.25 days, respectively. Six patients who failed therapy responded to alternative VRE therapy. Three infection related deaths occurred but none due to VRE UTI.
- Cure rate in patients with a Foley catheter was 85% (41/48). Cure rate in subset of patients with catheter exchange or removal was 97% (33/34).
- Cure rate in patients with catheter retention was 57% (6/11).
- All cause mortality during hospitalization was 16% (11/70). Infection related mortality was 4% (3/70); none related to VRE UTI.
- Microbiologic cure occurred in 90% patients.

LIMITATIONS
- Retrospective, descriptive analysis.
- Small patient population
- Receipt of concomitant antimicrobial agents for treatment of other diseases processes may have affected outcome.
- Geographic variability in organism susceptibility
- Poor documentation of systemic disease

CONCLUSIONS
- In our knowledge this is largest case series examining the efficacy of aminopenicillins for treatment of VRE UTI.
- Clinical and microbiologic cure reached 90%.
- Due to the frequency of VRE infections in catheterized patients and limited treatment options, the aminopenicillins may serve as a reasonable alternative for clinical care while preserving agents with VRE activity for use at other sites.

BIBLIOGRAPHY
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