Clinical Presentation, Etiology and Outcome of Infective Endocarditis in University Hospital of Toulouse, France, 2010-2012

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ABSTRACT

Background: Since the 1980s, many studies have shown that the profile of infective endocarditis (IE) significantly changed over the past decades. However, little data are available on the characteristics of IE in recent years. The aim of this retrospective study was to describe the population and outcomes of patients with IE in University Hospital of Toulouse over the 5-year period 2010-2012.

Methods: A retrospective observational study was conducted. Data of patients included in the study were obtained from hospital charts.

RESULTS: The study population included 93 patients with IE, of whom 23% were men. The median age of patients at the time of diagnosis was 63 years. Of the patients, 69% had diabetes mellitus and 77% had a history of heart disease. The most common predisposing factor was a prosthetic valve (63%). The incidence of IE was 3.2 cases per 100,000 patient-years. The mean duration of follow-up was 1.2 years. The overall mortality rate was 23%.

DISCUSSION: The results of this study suggest that the profile of IE has changed over the past decades, with an increase in the number of cases, especially among patients with diabetes mellitus and heart disease. The outcomes of patients with IE are still poor, with a high mortality rate.

REFERENCE

No significant differences between generic Vancomycin (VAN) Products from Europe and America in the Treatment of Methicillin-Resistant Staphylococcus aureus (MRSA) Experimental Endocarditis in Rabbits: a confirmatory study

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Background / Objectives

- Concerns have recently emerged about the potency and the quality of generic vancomycin (VAN) products approved for use in humans, based on experiments in a neutropenic mouse thigh infection model.
- We previously found no statistically significant differences between 6 generic VAN products from Europe and America, in the model of MRSA aortic valve endocarditis in rabbits. However, due to limited sample sizes per generic (n=10), and multiple comparisons, these experiments may have been underpowered to detect clinically significant differences.
- To confirm these results, we performed a face-to-face comparison of the 2 VAN generics that demonstrated the highest and the lowest bactericidal effect in our previous study, with additional experiments and increased sample sizes.

Methods

- Bacterial strain: S. aureus strain COL is a homogeneous, highly methicillin-resistant strain (VANMIC 1-1-1 g/ml).
- Antibiotic agents: VAN generics were bought from local drug purchasing companies and prepared following label instructions.
- Rabbit endocarditis model:
  - The protocol was in keeping with French legislation on animal experimentation and was approved by the Local Animal Use Committee.
  - To establish endocarditis, a polyethylene catheter was positioned across the aortic valve and 24 hours later, 1 ml of 0.9% saline containing ~4 x 10^7 CFU of COL, was injected intravenously.
  - 20 rabbits in each group were treated with one VAN generics from APP (USA), or Hospira (Spain), 80 mg/kg bid during 4 days. Rabbits were euthanized 12 h after the last VAN dose. Aortic valve vegetations and spleens were removed.
- Data analysis: Bacterial titers were expressed as log_{10} CFU per gram of tissue. Cultures yielding no growth were scored as sterile, and assigned a value of 1.7 log_{10} CFU. The two groups were compared using chi2 test for mortality rates and non-parametric Wilcoxon tests for titers of residual organisms in vegetations and spleens, with Bonferroni correction methods to estimate adjusted P-values.

In addition, we compared the rate of emergence of VAN-resistant subpopulations in rabbits treated with the 6 VAN generics previously tested, as previously reported (Rodríguez et al.). Briefly, the area under the VAN concentration versus the log_{10} CFU/mL curve (AUC) was calculated and the resistance frequency at each concentration was determined by dividing the number of CFU that grew in antibiotic-containing agar by the total population in antibiotic-free plates.

The intensity of the effect (IE) was calculated as the difference between the AUCs of the control and treated groups by the following formula: IE = AUC_treatment - AUC_control

Results

<table>
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<tr>
<th>Comparison of the VAN generics who had the lowest and the highest bactericidal activity in the previous study (20 rabbits/group)</th>
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<tr>
<td>Controls (n=10)</td>
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<td>----------------</td>
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<tr>
<td>Median [25, 75] (SD)</td>
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<tr>
<td>Vegetations (0%)(10%)(50%)</td>
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<td>Spleen (10%)(50%)</td>
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- No significant differences between the VAN generics with the highest (Hospira) and the lowest (APP) bactericidal activity, even after increasing the sample sizes, in terms of:
  - Organism titers in vegetations, and in spleens
  - Proportions of spleen and vegetations sterilized

- No significant differences in terms of resistance selection under treatment between 5 VAN generics approved for use in Europe and America (Alaron, APP, Hospira, Mylan, Sandos and Tira):

  This holds true even for generic VAN products found sub-optimal in the neutropenic in vivo model

- In this stringent MRSA endocarditis model, additional investigations found no significant differences in the in vivo bactericidal activity of generic VAN products currently in use in Europe and America even after increasing sample sizes, and testing for resistance selection after VAN generics exposure.

- Limitations:
  - We could not compare generic VAN products with the innovator, as Eligilbwrap had its production stopped in 2005
  - These are not non-inferiority studies (sample sizes required not realistic)

Comments

- In this stringent MRSA endocarditis model, additional investigations found no significant differences in the in vivo bactericidal activity of generic VAN products currently used in Europe and America, even after increasing sample sizes, and testing for resistance selection after VAN generics exposure.

References


Multicenter Experience of the Effectiveness and Safety with Ceftaroline Fosamil (CPT) Therapy

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Abstract (Updated)

Background: Ceftaroline fosamil (CPT) is an oral fluoroquinolone approved for the treatment of community-acquired pneumonia (CAP) and skin and skin structure infections (SSSI). The objective of this multicenter experience was to evaluate the safety and efficacy of CPT in patients with CAP and SSSI.

Methods: A multicenter, retrospective study of patients treated with CPT in the delivery system from January 1, 2013, to June 30, 2013, was conducted. Patients were included if they were treated with CPT for CAP or SSSI. The primary endpoint was the proportion of patients with clinical and microbiological cure at follow-up visit. Secondary endpoints included safety, tolerability, and resistance patterns.

Results: A total of 100 patients were enrolled in the study. Patients with CAP were predominantly male (75%) and the median age was 60 years. The most common pathogens were Streptococcus pneumoniae (35%) and Staphylococcus aureus (25%). The overall clinical and microbiological cure rates at follow-up were 78% and 73%, respectively. Resistance to CPT was observed in 2% of patients.

Conclusion: CPT is an effective and safe treatment option for patients with CAP and SSSI. Further studies are needed to evaluate the long-term efficacy and safety of CPT in these patient populations.
Characterization of Patients with Methicillin-Resistant Staphylococcus aureus (MRSA) Infective Endocarditis (IE)

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Introduction

- Methicillin-resistant Staphylococcus aureus (MRSA) accounts for up to 1/3 of all patients with IE.
- Vancomycin (VAN) has been the preferred treatment for MRSA IE.
- Recent MRSA guidelines have provided a roadmap for management.
- Changes in the duration of therapy have not been systematically quantified.
- We describe the clinical course in patients with MRSA IE treated with VAN and allow 8-1 year followup.

Methods

- Study Design:
  - A retrospective cohort study was conducted at the Detroit Medical Center.
  - Consecutive adult patients treated for MRSA IE with VAN for 8-1 year followup were collected from 2008 to 2011.
- Medical records were reviewed for demographics, comorbidities, antimicrobial therapy, microbiology culture, clinical outcomes, and vancomycin parameters through the last available visit.

Outcome Assessment:

- VAN treatment failure: persistent bacteremia (7 days or VAN or death by MRSA within 30 days of the initial event)
- Length of hospital stay (LOS)
- Use of subsequent therapy (i.e., unnecessary blood cultures to the day of discharge for blood cultures)

Microbiological Assessment:

- VAN minimum inhibitory concentration (MIC) were determined by broth microdilution using Clinical Laboratory Standards Institute standardized reference procedures.
- VAN (0.5) was selected for vancomycin MIC cut-offs for S. aureus and MRSA, based on previous literature.

Outcomes:

- Logistic regression analysis was performed to identify risk factors for mortality and repeat infection.

Statistical Analysis:

- SPSS software (version 21, IBM Corp., Chicago, IL) was used to perform descriptive statistics, analyses using contingency tables, and distributional analysis.

Reference:

# Abstract

**Background/Objectives**

Staphylococcus aureus bacteremia has been the leading cause of infective endocarditis in Western Europe and Northern America. The objective of this study was to identify factors associated with infective endocarditis in patients presenting with Staphylococcus aureus bacteremia.

**Methods**

All adult patients in whom a SAB was observed between April 2009 and October 2011 in the 5 French University hospitals participating in the study were prospectively included.

- **SAB** was defined as blood culture-positive Staphylococcus aureus. Patients having catheterization were included.

**Results**

The factors associated with infective endocarditis in patients presenting with Staphylococcus aureus bacteremia were:

- **Diabetes mellitus**: Yes
- **Heart failure**: Yes
- **Hypertension**: Yes
- **Prior cardiac valve disease**: Yes
- **Prior hospitalization within 3 months**: Yes
- **Prior antibiotic treatment within 3 months**: Yes
- **Previous SAB**: Yes
- **Prior antibiotics treatment within 3 months**: Yes
- **Other**: Yes

**Discussion/Conclusions**

Endocarditis is a severe complication of SAB. Its frequency is high, even in case of non-endocarditis infection and in the absence of known predisposing condition.

- **Staphylococcal bacteremia** should be performed in most cases of SAB in order to detect IE as early as possible and thus improve its prognosis.

- **Exacerbation of predisposing conditions** was the result of any clinical or epidemiological factor that may explain why IE occurs in some cases of SAB. Genetic analysis in both the host and the infectious agent are under way.

- **Most SAB** are healthcare-related in tertiary hospitals in France. Every effort should be made to prevent this dreadful complication of medical progress.
Four Cases of Ceftaroline Salvage Therapy for Complicated Methicillin-Resistant Staphylococcus aureus Infections

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Abstract

Background: Treatment of severe MRSA infections with decreased susceptibility to daptomycin (DAP) and vancomycin (VAN) represents a significant challenge. We report four such patient cases of complicated MRSA infections treated with Ceftaroline, an 

Results

Patient 1

- A 16-year-old female with a past medical history of polydactylar and multiple surgical procedures was administered a total of 6 weeks of 
  Ceftaroline for treatment of septic arthritis when found to be bacteremic with MRSA. She was admitted and started empirically on 
  Ceftaroline while waiting for bacterial cultures to grow. After 3 days on Ceftaroline, the patient was switched to 
  Ceftaroline and remained negative. The patient was discharged on 6 weeks of Ceftaroline.

Patient 2

- A 19-year-old female with a past medical history of cerebral palsy and 
  ventilator dependence was found to have sepsis caused by 
  methicillin-resistant S. aureus. The patient was treated with 
  Ceftaroline for 10 days and remained negative. The patient was discharged on 6 weeks of Ceftaroline.

Patient 3

- A 16-year-old female with a past medical history of juvenile rheumatoid arthritis and 
  ventilator dependence was found to be bacteremic with MRSA. The patient was treated with 
  Ceftaroline for 10 days and remained negative. The patient was discharged on 6 weeks of Ceftaroline.

Patient 4

- A 15-year-old female with a past medical history of neurofibromatosis and 
  ventilator dependence was found to be bacteremic with MRSA. The patient was treated with 
  Ceftaroline for 10 days and remained negative. The patient was discharged on 6 weeks of Ceftaroline.

Conclusions

- These cases add to the growing clinical evidence supporting the use of Ceftaroline in the treatment of severe MRSA infections. Further investigations are required to better elucidate the role of Ceftaroline both as monotherapy and as an adjunctive agent in the treatment of severe MRSA infections.

References