Time to Clinical Stability in Patients with Ventilator-Associated Pneumonia due to Methicillin-Resistant Staphylococcus aureus Treated with Linezolid versus Vancomycin: Results from the IMPACT-HAP Study

Senen Pena, Kendra Thompson, Himabindu Boja, Andrea Reyes, Ibrahim Elkhawas, Ane Uranga Echeverria, Timothy L. Wiemken, Julio Ramirez, Paula Peyran
Division of Infectious Diseases, University of Louisville, Louisville, KY

ABSTRACT

Background: Time to clinical stability (TCS) is a well-defined early clinical outcome in hospitalized patients with community-acquired pneumonia, but it has not been evaluated in patients with VAP. The objective of this study was to compare TCS in patients with MRSA VAP treated with linezolid (Lin) versus vancomycin (Van).

Methods: This was a multicenter, retrospective, observational study of patients with MRSA VAP treated with Lin or Van. Non-consecutive patients requiring intensive care were enrolled from five academic institutions in the USA. VAP was defined according to CDC criteria. MRSA VAP was considered when MRSA was isolated from a tracheal aspirate or bronchoalveolar lavage. A patient was considered to reach clinical stability the day the following four criteria were met: 1) Aflebre for 24 hours, 2) Decrease in WBC >100%, 3) Improving of PaO2/Fio2 ratio >200 mmHg, and 4) Systolic blood pressure >90 mmHg. TCS for linezolid and vancomycin were compared using the Chi-Squared and Student’s t-tests.

Results: A total of 50 patients treated with Lin and 50 patients treated with Van were evaluated. The population of Lin treated patients, 64% reached clinical stability, compared to 70% of the population of Van treated patients (P=0.671). Mean number of days to clinical stability was 5.8 days (SD 3.0) for patients treated with Lin, versus 7.2 days (SD 3.7) for patients treated with Van (P=0.040).

Conclusions: In patients with MRSA VAP, early TCS is achieved for patients treated with Lin when compared to Van. The number of days for patients to reach clinical stability can be used as an early clinical outcome in patients with VAP.

INTRODUCTION

• Time to clinical stability (TCS) is a well-defined early clinical outcome in hospitalized patients with community-acquired pneumonia (CAP). Several guidelines for the management of patients with CAP have established criteria to define when a patient has reached clinical stability.1,2 White blood cell count (WBC), temperature, and respiratory symptoms are within the criteria commonly used.

• On the contrary, few studies have been published evaluating TCS in patients with ventilator-associated pneumonia (VAP).3-5 Clinical resolution has been described to be between 3 and 10 days depending on the cohort of patients being evaluated. Patients with VAP due to methicillin-resistant Staphylococcus aureus (MRSA) have a longer time to resolution when compared with patients with VAP due to methicillin-susceptible Staphylococcus aureus (MSSA) or Haemophilus influenzae.6 The presence of AODS (Acute respiratory distress syndrome) also delays clinical resolution.7

• In the field of clinical research on CAP, TCS has been used as a clinical outcome to compare effectiveness of intravenous antibiotics.8 It can be hypothesized that those antibiotics with better activity against the etiologic organism will produce a faster clinical response and early time to clinical stability. None of the published data on VAP has evaluated the impact of antibiotic treatment in TCS.

• The objective of this study was to compare TCS in patients with VAP due to MRSA treated with linezolid versus vancomycin.

RESULTS

• A total of 50 patients treated with linezolid and 50 patients treated with vancomycin were evaluated.

• Baseline characteristics of the study population are shown in Table 1.

• The study flow is shown in Figure 1.

• Kaplan-Meier curves for TCS is shown in Figure 2. For those patients who reached clinical stability, the mean number of days to reach clinical stability was 5.8 days (SD 3.0) for patients treated with linezolid, versus 7.2 days (SD 3.7) for patients treated with vancomycin (P=0.040).

• The percentage of patients who met the study definition for clinical stability for each criterion is shown in Figure 3.

• This study shows that in patients with VAP due to MRSA, earlier TCS is achieved for patients treated with linezolid when compared to vancomycin.

• The TCS for both study groups is within the range reported in the literature. The number of days for patients to reach clinical stability can be used as an early clinical outcome when comparing different antibiotics for therapy of VAP.

• Prior studies evaluating the clinical course of patients with VAP have used similar parameters such as a temperature, PaO2/Fio2 ratio, CRP, and Pseudomonas aeruginosa.8-10 In these studies, a fixed predetermined value was selected to define improvement. For example temperature ≤38 °C, WBC ≤10,000, PaO2/Fio2 ratio ≤250, or negative micro results. Measuring these criteria practically defines the time when the patient is almost back to baseline. This is in accordance with our study where some of the criteria used define an improvement (and not resolution) from the prior day.

• The number of days for patients to reach clinical stability can be used as an early clinical outcome in patients with VAP.

REFERENCES


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ACKNOWLEDGMENTS

Table 1: Characteristics of the study population

<table>
<thead>
<tr>
<th>Patient Description</th>
<th>Age, median (IQR)</th>
<th>WBC, median (IQR)</th>
<th>PaO2/Fio2, median (IQR)</th>
<th>Clinical stability, median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA VAP Lin</td>
<td>65 (18)</td>
<td>9 *10^9 (5 *10^9)</td>
<td>190 (110)</td>
<td>6 (3)</td>
</tr>
<tr>
<td>MRSA VAP Van</td>
<td>78 (18)</td>
<td>8 *10^9 (5 *10^9)</td>
<td>190 (110)</td>
<td>6 (3)</td>
</tr>
</tbody>
</table>

Figure 1: Study flow

Figure 2: Kaplan-Meier curves for TCS for both study groups