Evaluation of the Management of Extended-Spectrum Beta-Lactamase (ESBL) Enterobacteriaceae Infections

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Abstract

Introduction: Intravenous carbapenem is the standard for hospitalized patients with extended-spectrum β-lactamases (ESBL)-producing organisms. This study was performed to determine the appropriateness of treatment regimens within our network.

Methods: All patients admitted to our network between January 1, 2014 and December 31, 2015 with a positive culture for an ESBL-producing pathogen identified by microbiology were enrolled. Empiric and definitive treatment was considered appropriate (TA) or inappropriate (TI) based on organism susceptibilities. Therapy, organism susceptibilities, and demographic data were collected. Data were entered into SPSS for statistical analysis using Chi-square and Student’s T test.

Results: A total of 172 patients with an ESBL infection were enrolled. The majority of patients had a urinary source (79%) with 27% of patients also having bacteremia. Twenty-two percent (n=36) of patients received TA empiric therapy. However, 86% of patients received TA definitive therapy. TA patients’ length of IV antimicrobial therapy was significantly longer compared to TI definitive therapy (TA 6.7 ± 5.5 vs TI 3.5 ± 2.0, p<0.001). A total of 26% (15) patients had treatment failure. A significant number of bacteremic patients (40%) who failed therapy, died during this hospitalization. A total of 65% of patients were discharged with an Infectious Diseases (ID) consult.

Conclusion: Treatment of infections caused by ESBL-producing organisms in hospitalized patients is difficult. There is a need for further education in community hospitals regarding the management of infections caused by ESBL-producing organisms.

Introduction

Extended spectrum β-lactamase producing Enterobacteriaceae (ESBL-E) resistant to broad-spectrum cephalosporins have become a dominant concern for anti-infective treatement worldwide.

Observational data with ESBL K. pneumoniae have demonstrated greater than two-fold increase in treatment failures and death at both 7 and 21 days [2].

Intravenous carbapenem antibiotics are the gold standard for treating ESBL-E pathogens. For ESBL-producing pathogens, the CDC recommends laboratory reporting as resistant, all penicillins, cephalosporins, and monobactam regardless of M/C.

The goal of this retrospective review was to determine which treatment regimens were used in these patients and their appropriateness based on patient outcomes.

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Materials & Methods

• Retrospective electronic medical record review.
• Patients with a positive ESBL-E culture were identified from the Microbiology laboratory at our Health system for the Omaha metro area only, and were admitted to a CHI Health hospital between January 1, 2014 and December 31, 2015.
• Exclusion criteria included patients < 19 years of age or inadequate follow-up within the first week of treatment including death (before susceptibilities), hospice care, treatment refusal, DNR/DNI status, or transfer to an outside hospital.
• Therapy was divided into empiric (prior to antimicrobial susceptibilities) and definitive (after antimicrobial susceptibilities) and was considered appropriate (TA) or inappropriate (TI).
• Intravenous carbapenem and oral fosfomycin were considered TA definitive therapy for complicated and uncomplicated ESBL-E infections.
• Oral definitive therapy was considered TA or TI based on antimicrobial susceptibilities.
• Duration of therapy of 7-14 days was considered appropriate for uncomplicated infections, with extension up to 28 days for complicated or non-responsive infections.

• Patient outcomes were defined as clinical success (resolution of fever (≤37 °C for ≥ 1 day) and normalization of white blood cell count and negative blood cultures without any recurrence during the follow-up period [1].
• Clinical failure was defined as recurrent fever and abnormal WBC count, and/or blood culture positive with the same organism ≥ 7 days after initial blood culture results, but before completion of antimicrobial therapy or death.
• Data were entered into statistical software (SPSS ver 24; IBM Inc.) and results analyzed.

• Results

A total of 172 patients with an infection caused by an ESBL-producing organism were enrolled during the study period.

The majority of these patients (82%) were from healthcare-associated infections within CHI Health system.

A total of 55 (31%) were from patients living in skilled nursing facilities.

The majority (79%) of organisms cultured were from a urinary source with 27% of patients also having bacteremia.

A total of 17 (10%) patients expired.

E. coli was the most common (78%) ESBL-infecting organism followed by K. pneumoniae (15%).

Seventy-eight percent (n=136) of patients received TI empiric therapy.

However, only 14% of patients received TI definitive therapy based on antimicrobial susceptibilities.

Infectious Diseases (ID) was consulted for 65% of total patients enrolled.

A significant number of bacteremic patients who failed therapy also died (n=6, 40%). Bacteremic patients who died were hospitalized significantly shorter compared to patients without bacteremia who died (6.0 ± 3.2 vs 13.3 ± 7.9 days, p<0.021).

All 17 (10%) patients who died, received TA therapy.

Table. Study Results

<table>
<thead>
<tr>
<th>Bacteremia (%)*</th>
<th>Therapy</th>
<th>Duration of IV therapy (d)**</th>
<th>Definitive Therapy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TA</td>
<td>TI</td>
<td>Carbapenem</td>
</tr>
<tr>
<td></td>
<td>95</td>
<td>3</td>
<td>72</td>
</tr>
<tr>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Appropriate Definitive Therapy (n=148)</th>
<th>Inappropriate Definitive Therapy (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age (y) (mean ± SD)</td>
<td>66.8 ± 11.4</td>
<td>67.2 ± 11.5</td>
</tr>
<tr>
<td>Female (%)</td>
<td>62</td>
<td>63</td>
</tr>
<tr>
<td>Admitted from nursing home (%)</td>
<td>35</td>
<td>17</td>
</tr>
<tr>
<td>ID consult (%)*</td>
<td>82</td>
<td>31</td>
</tr>
<tr>
<td>Concomitant diabetes (%)</td>
<td>36</td>
<td>29</td>
</tr>
<tr>
<td>Chronic kidney disease (%)</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>Bacterial isolate from healthcare setting (%)</td>
<td>65</td>
<td>42</td>
</tr>
</tbody>
</table>

Conclusions

• In this retrospective review of ESBL-E infections, ID consultation was shown to result in more appropriate therapy with appropriate duration.

• A formal ASP led by an ID clinician to address widespread use of carbapenem in the management of resistant infections such as those caused by ESBL-E.

References


Available: Appropriate Definitive Therapy (n=148)

UTI (%) | 79
Bacteremia (%)* | 93
Duration of IV therapy (d) (mean ± SD) | 9.7 ± 7.5
LOS (d) (mean ± SD) | 7.8 ± 5.9
Definitive Therapy (%) | 6.9 ± 7.1
Duration of antimicrobial treatment (d) (mean ± SD) | 11.6 ± 6.7
Definitive Therapy (%) | 10.9 ± 4.2
Carbapenem | 72
Fosfomycin | 3
Cephalosporins | 0
Fluoroquinolones | 9.4
Piperacillin-tazobactam | 2
Doxycycline | 2
TMP-SMZ | 4.7
Amoxicillin-clavulanate | 0.6
Ceftriaxone | 2
Ceftazidime | 2
| 2
ID=Infectious Diseases; UTI=urinary tract infection; N=total cases; LOS=length of hospital stay; TMP-SMZ=trimethoprim-sulfamethoxazole; *p<0.05; **p<0.01