Poster #: 2442

Outcomes in ESBL Bacteremia Empirically Treated with Piperacillin/tazobactam or Carbapenems

Reeba John, PharmD[1] • Peter Colley, PharmD, BCPS-AQ ID, AAHIVP[1] • Hoa Nguyen, MD, MS, PhD[2] • Mezgebe Berhe, MD, MPH[1]

[1]Baylor University Medical Center - Dallas, TX; [2]Department of Quantitative Sciences, Baylor Scott and White Health, Dallas, TX

Reeba John, PharmD
Baylor University Medical Center
Department of Pharmacy
3500 Gaston Avenue
Dallas, TX 75246

Reeba.John@BSWHealth.org

Introduction

- Increasing prevalence of extended spectrum beta lactamase (ESBL) organisms is concerning due to worse outcomes and limited treatment options[1,2]
- ESBL organisms are inherently resistant to penicillins, cephalosporins and monobactams
- Beta lactam/beta lactamase inhibitors (BLBLI) such as piperacillin/tazobactam (PTZ), have reported *in vitro* activity but may lack clinical efficacy against ESBL infections, potentially due to[3,4]:
  - Inoculum effect
  - Production of multiple ESBL types
- Carbapenems (CBPs) are considered the drugs of choice for ESBL infections[5-8]
  - Increased use contributes to carbapenem resistant *Enterobacteriaceae*
- Studies have shown inconsistent clinical outcomes regarding the use of PTZ versus a carbapenem for treatment of ESBL bacteremia which leads to controversy over appropriate empiric therapy for suspected cases[5-8]

Objective

Primary

To evaluate hospital mortality during admission in patients with ESBL bacteremia who were empirically treated with PTZ vs a CBP

Secondary

To evaluate hospital length of stay, ICU length of stay and rates of recurrent ESBL bacteremia

Methods

Study Design: Multicenter, retrospective chart review of patients admitted to Baylor Scott & White Hospitals in the Northern Division

Time Frame: January 1, 2014 – September 22, 2017

Patients were identified using clinical surveillance software (MedMined, BD, Franklin Lakes, NJ). Patient data collected from the electronic medical record (Allscripts, Chicago, IL)

Inclusion Criteria	Exclusion Criteria
• Positive ESBL blood culture identified by rapid molecular assay (Verigene, Nanosphere Inc., Northbrook IL) • Administration of at least one dose of empiric PTZ or a CBP (meropenem or ertapenem) • 1st episode of bacteremia only	• Age <18 years • Pregnancy • Prisoners • Received PTZ ≥ 24 hours after positive ESBL blood culture • Did not receive a CBP as definitive therapy

Results

Figure 1. Enrollment

Table 1. Baseline Characteristics

Characteristic	Empiric PTZ N=66	Empiric CBP N=51	p-value
Age (mean, SD), years; range: 21-94	67.9 (14.1)	64.9 (14.9)	0.266
Gender (female)	31 (47%)	31 (60.8%)	0.191
Prior Hospitalization	17 (25.8%)	16 (31.4%)	0.539
Previous Antibiotic Therapy	14 (21.2%)	9 (17.6%)	0.815
Nursing Home/LTCF Residence	7 (10.6%)	6 (11.8%)	0.99
History of Diabetes Mellitus	29 (43.9%)	25 (49%)	0.709
History of (+) non-blood ESBL Cx	8 (12.1%)	13 (25.5%)	0.088
Frequent ED Visits	4 (6.1%)	5 (9.8%)	0.500
Admission to ICU	25 (37.9%)	20 (39.2%)	0.99
Septic Shock	12 (18.2%)	8 (15.7%)	0.807
Mechanical Ventilation	1 (1.5%)	2 (3.9%)	0.579
CVC	0	1 (2%)	0.436
In-dwelling/chronic foley	6 (9.1%)	0	0.035
Hemodialysis	4 (6.1%)	1 (2%)	0.385
Devices	0	6 (11.8%)	0.006
Percutaneous Tube	2 (3%)	2 (3.9%)	0.99
Immunosuppression	7 (10.6%)	7 (13.7%)	0.775
Time to identification of ESBL (mean, SD), hrs	22.5 (9.5)	25.1 (12.4)	0.197
Suspected Source of Bacteremia			0.34
Urinary	48 (72.2%)	37 (72.5%)	
Intra-abdominal	14 (21.2)	8 (15.7%)	
Respiratory	1 (1.5%)	0	
Other/unkown	3 (4.5%)	6 (11.8%)	
Organism			0.291
E. Coli	59 (89.4%)	42 (82.4%)	
Klebsiella spp.	7 (10.6%)	9 (17.6%)	

CVC = central venous catheter, Cx = culture, ED = emergency department, ICU = intensive care unit, LTCF = long term care facility, SD = standard deviation

Table 2. Outcomes

Primary Outcome	Empiric PTZ (N = 66)	Empiric CBP (N = 51)	p-value
Hospital Mortality (%)	2 (3%)	4 (7.8%)	0.401
Secondary Outcomes			
Hospital LOS (mean, SD), days	7.9 (6.1)	7.1 (5.9)	0.882
ICU LOS (mean, SD), days	4.4 (4.7)	3.4 (3.3)	0.392
Recurrent ESBL Bacteremia (N (%))	5 (7.6%)	4 (7.8%)	0.99

LOS = length of stay

Graph 1: Minimum Inhibitory Concentration (MIC) of PTZ

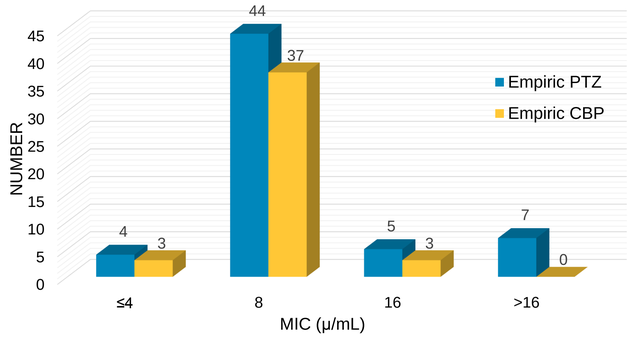

Table 3. Study Critique

Strengths	Limitations

• Multicenter design
• Moderate sample size
• Extensive assessment of baseline characteristics, including
  • Severity of illness on presentation
  • Risk factors for ESBL
	• Retrospective design
	• Lack of applicability to settings that do not utilize rapid diagnostic testing capable of identifying ESBL resistance
	• Role of empiric antibiotics other than PTZ or CBPs were not assessed
	• Did not collect data regarding polymicrobial bacteremia
	• Inherent prescriber bias for each agent

Discussion

- Both groups were well-matched at baseline with respect to markers for severity of illness and history of a positive non-blood ESBL culture
- There was no difference in hospital mortality between empiric PTZ vs. a CBP for suspected ESBL bacteremia identified by rapid molecular assay
- To our knowledge, this is the first study that has evaluated comparative effectiveness of these agents in the setting of rapid diagnostic testing for resistance markers, as opposed to ESBL identification using traditional culture and susceptibility methods
- These findings are consistent with a majority of previously published literature which demonstrate that there is no difference in appropriate empiric therapy versus a CBP[5-8]
  - Limitations:
    - Definition of “appropriate” empiric therapy
    - Evaluation of empiric antibiotics were not the only focus of these studies

Conclusion

- Avoidance of CBPs may be considered until evidence for ESBL infection is identified via rapid diagnostics (if available)
- Further study is warranted to confirm the role of PTZ in suspected ESBL infections and the associated role of rapid diagnostics in antimicrobial stewardship efforts

References

1. Thaden JT, Fowler VG, Sexton DJ, Anderson DJ. Increasing incidence of extended spectrum B-lactamase producing Escherichia coli in community hospitals throughout the southeastern united states. Infect Control Hosp Epidemiol. 2016 Jan; 37(1): 49-54.
2. Endimiani A, Luzzaro F, Brigante G et al. Proteus mirabilis bloodstream infections: risk factors and treatment outcome related to the expression extended-spectrum beta-lactamases. Antimicrob Agents Chemother 2005 Jul;49(7):2598-605.
3. Hoban DJ, Lascols C, Nicolle LE et al. Antimicrobial susceptibility of Enterobacteriaceae, including molecular characterization of extended-spectrum beta-lactamase-producing species, in urinary tract isolates from hospitalized patients in North America and Europe: results from the SMART study 2009–2010. Diagn Microbiol Infect Dis. 2012; 74:62–7
4. Paterson DL, Bonomo RA. Extended-spectrum beta-lactamases: a clinical update. Clin Microbiol Rev 2005;18: 657–86.
5. Vardakas KZ, Tansarli GS, Rafailidis PI, Falagas ME. Carbapenems versus alternative antibiotics for the treatment of bacteraemia due to Enterobacteriaceae producing extended-spectrum B-lactamases: a systematic review and meta-analysis. J Antimicrob Chemother. 2012 Dec; 67(12): 2793-803.
6. Shiber S, Yahav D, Avni T, Leibovici L, Paul M. B-lactam/B-lactamase inhibitors versus carbapenems for the treatment of sepsis: systematic review and meta-analysis of randomized controlled trials. J Antimicrob Chemother. 2015; 70: 41-47.
7. Ng TM, Khong WX, Harris PNA et al. Empiric piperacillin-tazobactam versus carbapenems in the treatment of bacteraemia due to extended-spectrum-beta-lactamase-producing enterobacteriaceae. PLoS One. 2016 Apr 22; 11(4):e0153696.
8. Tamma PD, Han JH, Rock C et al. Carbapenem therapy is associated with improved survival compared with piperacillin-tazobactam for patients with extended-spectrum B-lactamase bacteremia. Clin Infect Dis. 2015 May 1; 60(9): 1319-25.

Disclosure

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

All authors: Nothing to disclose