Assessing Clinical Cure of Empiric Piperacillin-Tazobactam for ESBL Urinary Tract Infections (ACCEPT – UTI)

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Background

- Gram-negative bacteria that produce extended spectrum beta-lactamase (ESBL) enzymes present a serious threat to public health.[1]
- Carbapenems are generally accepted as the drug of choice for ESBL infections, but empiric over-utilization risks the development of carbapenem resistance.[2]
- Literature supports use of carbapenems over piperacillin-tazobactam (TZP) for ESBL bacteremia, but data is limited for urinary tract infections (UTIs).[3]

Purpose

- The objective of this study was to compare early clinical outcomes of patients treated empirically with TZP vs. carbapenems for ESBL UTIs.

Methods

- Multicenter, retrospective evaluation of patients at five Methodist Le Bonheur Healthcare adult hospitals between January 1, 2016 and June 30, 2021.

Inclusion	Exclusion
• Age ≥18 years • Urine culture positive for ESBL organism • Presence of symptoms OR leukocytosis† • Received ≥ 48 hours of empiric antibiotic therapy with either TZP or a carbapenem	• Polymicrobial urinary culture (≥ 3 isolates) • TZP or carbapenem initiated ≥ 48 hrs after culture collected • Other concomitant source of infection • Urinary ESBL isolate resistant to empiric antibiotic of choice

†Qualifying symptoms include: dysuria, polyuria or urgency, hematuria, costovertebral angle/flank tenderness, suprapubic or abdominal pain, or hypotension (systolic blood pressure < 90 or MAP < 65). Leukocytosis defined as WBC > $12x10^3/mm^3$.

Primary Outcome

Clinical success defined as:
- Temperature resolution (T > 36 and < 38 ˚C) within 48 hrs AND
- Resolution of symptoms or leukocytosis (WBC < $12x10^3/mm^3$) within 48 hrs AND
- Absence of readmission for ESBL cystitis or pyelonephritis within 6 months

Secondary Outcomes

- Hospital & ICU length of stay (LOS)
- Time to clinical resolution (resolution of symptoms & temperature)
- In-hospital all-cause mortality
- 30-day all-cause mortality

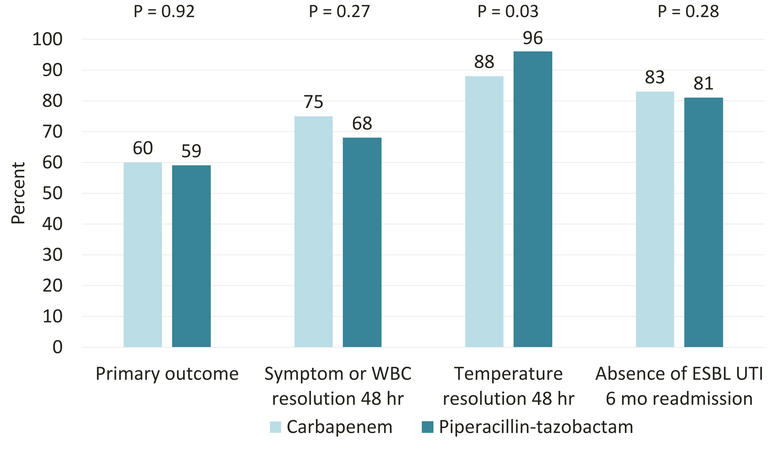
Results

Table 1. Baseline characteristics

Characteristic	Carbapenem (n = 100)	TZP (n = 123)	P value
Female	69 (69)	75 (61)	0.21
Caucasian	49 (49)	65 (54)	0.49
Age, median (IQR) years	71 (61, 81)	68 (57, 81)	0.52
Symptoms documented	71 (71)	93 (76)	0.44
Urologic abnormalities	37 (37)	37 (30)	0.28
Immunocompromised	12 (12)	20 (16)	0.37
ESBL Bacteremia	27 (27)	28 (23)	0.47
Severity of Illness			
ICU Admission	14 (14)	31 (25)	0.04
CCI, median (IQR)	2 (1, 4)	3 (2, 5)	0.62
APACHE II, median (IQR)	29 (18, 32)	23 (17, 29)	0.19
UTI Classification			
Uncomplicated cystitis	15 (15)	15 (12)	0.54
Complicated cystitis†	61 (61)	73 (59)	0.80
Pyelonephritis	24 (24)	35 (29)	0.29
Catheter-related	23 (23)	22 (18)	0.34
Causative Organism			
E. coli	81 (81)	92 (75)	0.27
K. pneumoniae	16 (16)	27 (22)	0.26
P. mirabilis	6 (6)	7 (6)	0.92

Characteristics reported as n (%) unless otherwise stated
CCI = Charlson Comorbidity Index
†Complicated cystitis defined as those who were pregnant, had anatomical or functional urinary tract abnormalities, had concurrent immunocompromising diseases or medications, and those with sepsis or septic shock

Figure 1. Clinical success outcomes



Results

Table 2. Primary outcome for select subgroups

Subgroup§	Carbapenem	TZP	P value
Bacteremia	12/27 (44.4)	16/28 (57.1)	0.92
ICU admission	5/14 (35.7)	21/31 (67.7)	0.04
Uncomplicated cystitis	10/15 (66.7)	12/15 (80.0)	0.68
Complicated cystitis	37/61 (60.7)	44/73 (60.3)	0.96
Pyelonephritis	13/24 (54.2)	17/35 (48.6)	0.34
Catheter-related	15/23 (65.2)	13/22 (59.1)	0.67
History recurrent UTI±	17/33 (51.5)	18/30 (60.0)	0.50

±Recurrent UTI defined as two separate culture-proven episodes of acute bacterial cystitis or pyelonephritis and associated symptoms within six months or three episodes within one year
§Outcomes reported as n (%)

Table 3. Secondary outcomes

Outcome	Carbapenem (n = 100)	TZP (n = 123)	P value
Hospital LOS, days†	38.9 (21.2, 51.7)	40.3 (24.5, 56.9)	0.53
ICU LOS, days†	7.0 (5.1, 10.7)	6.8 (4.7, 9.2)	0.12
Time to clinical resolution, days†	2.2 (1.0, 3.5)	1.8 (1.0, 3.0)	0.51
Antibiotic changed after 48 hrs§	3 (3.0)	3 (2.4)	1.00
In-hospital all-cause mortality§	4 (4.0)	3 (2.4)	0.72
30-day all-cause mortality§	38.9 (21.2, 51.7)	40.3 (24.5, 56.9)	0.53

†Outcomes reported as median (IQR)
§Outcomes reported as n (%)

Conclusion

- Results suggest no difference in clinical outcomes for ESBL UTIs treated empirically with TZP compared to carbapenems.
- There was no difference in outcomes based on UTI classification, suggesting that TZP is a viable option for more severe infections.
- Clinicians should consider using TZP as a carbapenem-sparing option for UTIs caused by pathogens susceptible to TZP.

References

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Disclosures

The authors of this presentation have nothing 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