Comparison of the Use of Extended and Intermittent Infusion Cefepime and Piperacillin/tazobactam in Non-critically Ill, Obese Patients

A collaboration between University of Minnesota, University of Minnesota Physicians and Fairview Health Services..

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BACKGROUND

- Beta-lactam antibiotics display time-dependent bactericidal activity
- Bactericidal activity is predicted by the free (unbound) antibiotic concentration above the minimum inhibitory concentration (fT>MIC)
- Obesity alters the pharmacokinetic and pharmacodynamic (PK/PD) properties of antibiotics: ↑ volume of distribution and ↑ clearance of drug[2]
- Cefepime and piperacillin/tazobactam can be administered by extended infusions (EI) over 4 hours to increase fT>MIC (Figure 1)
- EI provides a cost savings measure (piperacillin/tazobactam) and optimization of PK/PD to treat resistant organisms [1]
- Increasing rates of obesity in the US and worldwide indicate a need for more research into appropriate dosing and subsequent outcomes in obesity

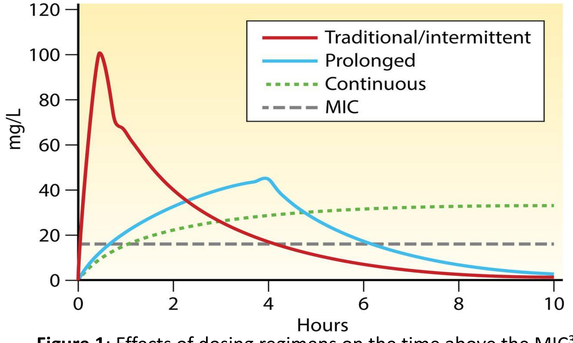

Figure 1: Effects of dosing regimens on the time above the MIC[3]

OBJECTIVES

- To determine if EI dosing of piperacillin/tazobactam and cefepime is associated with improved patient outcomes in non-critically ill patients with a BMI ≥ 30
- **Primary Outcome:** 30-day in-hospital, all-cause mortality
- **Secondary Outcomes:**
  - Hospital length of stay
  - Clinical success defined as time to resolution of fever, time to resolution of leukocytosis, and no escalation of therapy

METHODS

- Retrospective, single-center, comparative chart review study
- 1/2018-5/2018 intermittent infusion (II) data compared to 1/2019-5/2019 EI data
- **Inclusion Criteria:** Age ≥ 18; BMI ≥ 30; admitted to general medicine floor
- **Exclusion Criteria:** Received ≤ 2 doses of antibiotic; ICU admission; receipt of > 24h of II dosing in patients in the EI group
- All EI patients were given a loading dose over 30 minutes prior to EI dosing

Table 1. Antibiotic Dosing

Cefepime	II Dosing (30 min)	EI Dosing (4 hours)
Mild-moderate infections	1-2g every 8-12 hours	1-2g every 8-12 hours
Severe infections*	2g Q8H	2g Q8H
Piperacillin/tazobactam	**II Dosing (30 min)**	**EI Dosing (4 hours)**
Mild-moderate infections	3.375g every 6 hours	3.375g every 8 hours
Severe infections**	4.5g every 6 hours	4.5g every 8 hours

*meningitis, endocarditis, bacteremia, nosocomial pneumonia or sepsis
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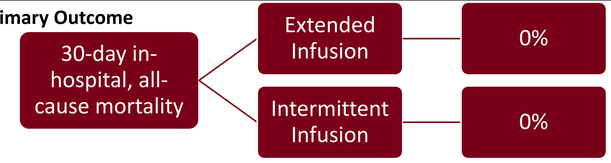
RESULTS

Table 2. Baseline Characteristics

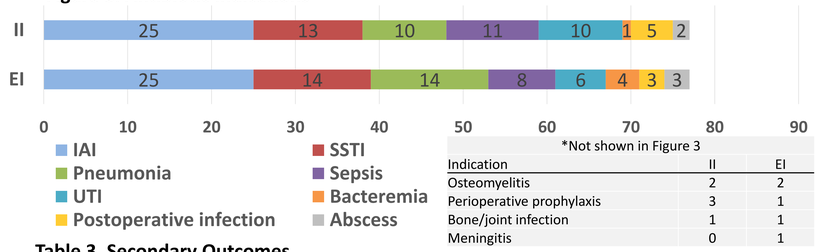
	II Group (n = 77)	EI Group (n = 71)	P-value
Age (years)	57.9 [34-94]	55.7 [23-86]	0.369
Sex (% female)	53.2% (41)	58.6% (41)	0.585
BMI (kg/m^2)	36 [30-50.9]	36.4 [30-58.1]	0.961
SCr (mg/dL)	1.25 [0.21-7.76]	1.17 [0.4-8.21]	0.636
Temp (°F)	99.6 [96.5-104.8]	99.1 [96.2-103.4]	0.094
WBC (cells/mm^3)	11.3 [1.7-31.2]	13.3 [1.2-28.7]	0.042

Figure 2. Primary Outcome



RESULTS (continued)

Figure 3. Antibiotic Indications



*Not shown in Figure 3

Indication	II	EI
Osteomyelitis	2	2
Perioperative prophylaxis	3	1
Bone/joint infection	1	1
Meningitis	0	1

Table 3. Secondary Outcomes

	II Group (n = 77)	EI Group (n = 71)	P-value
Hospital length of stay*	10.58 days [2-28]	9.74 days [2-37]	0.502
Time to temperature resolution if febrile	32.9 hours [4-133] N=22	30.8 hours [10-57] N=14	0.561
Time to resolution of leukocytosis if present	2.5 days [1-6.25] N=19	3 days [0.7-12] N=26	0.338
Treatment failure**	3	2	

*Excluding outlier of 78 and 104 days from II and EI, respectively **escalation to carbapenem

CONCLUSIONS

- No differences in primary or secondary outcomes were found with the use of EI infusion of piperacillin/tazobactam and cefepime when compared to II
- Small sample size limits ability to detect differences to support extended infusion of antibiotics as an effective dosing strategy in obese patients
- No other studies examine clinical outcomes of EI vs II in obese patients
- Next steps: assess use in obese, critically ill patients and system wide implementation

REFERENCES

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