Piperacillin/Tazobactam (PTZ) Assessment Before and After Implementation of an Extended Infusion Dosing Regimen

Candice Leung, B.Sc.(Pharm); Ivy Chow, PharmD; Vincent H. Mabasa, PharmD

Background

- Piperacillin/Tazobactam (PTZ):
  - Bactericidal effects ↑ with time of concentration above MIC
- Traditional Dosing: 3.375g IV over 30 minutes Q6-8H
- Extended-Infusion: 3.375g IV infusion over 4 hours Q8H
- Five retrospective studies have compared the 2 regimens
  - Four studies showed similar mortality rates (two for in-hospital mortality, one for 14-day mortality, one for 30-day mortality)
  - One study found a SS difference in 30-day mortality
- Limitations of current literature:
  - Absence of ICU clinical outcome data except for one non-powered study; absence of Canadian data; not statistically powered studies except for one not solely focused on PTZ

Objectives

- To determine the clinical effects of PTZ dosing regimens within Burnaby Hospital's ICU
- To determine any differences in cost between dosing regimens

Methods

- **Design**: Single-center, retrospective cohort study
- **Inclusion criteria**: Adult (≥18 yo) ICU patients who received ≥48H of the traditional dosing (Jan. 1, 2011 – Jan. 10, 2013) or the extended-infusion dosing (May 11, 2013 – Dec. 31, 2015)
- **Exclusion criteria**: Organisms intermediate or resistant to PTZ; PTZ allergy/intolerance; comfort care; transferred patients with unknown or prior PTZ history at referring facility; received >24H of the other dosing regimen and/or interruption of PTZ regimen by >24H
- **Sample size**: 277 patients per cohort to achieve 80% power
- **Outcomes**:
  - **Primary**: In-hospital all-cause mortality
  - **Secondary**: Clinical success rate, hospital and ICU length of stay, number of PTZ units used, grams of PTZ used
- **Definitions**
  - **Clinical success**: normalization or trend to normalization of temperature (<37.5ºC), HR (60-100 bpm), RR (12-20/min), WBC (<11 x 10^9/L), neutrophils (<8 x 10^9/L), and/or noted improvement from electronic medical record charting

Figure 1. Study participant flow chart

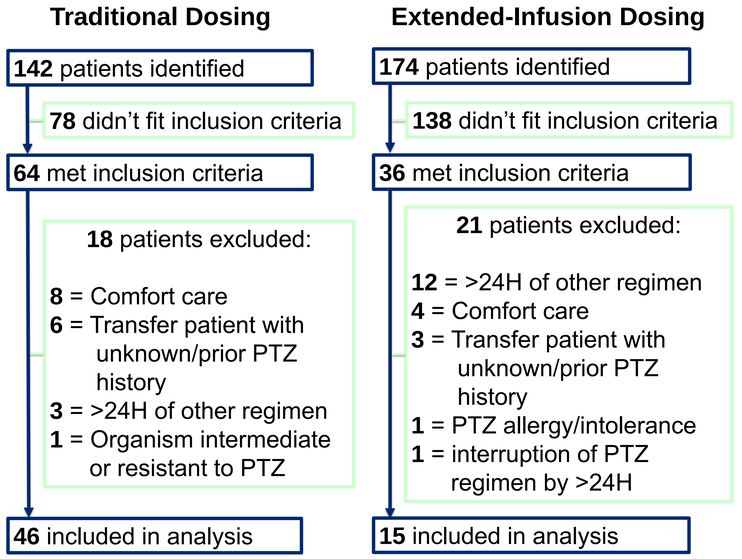

Table 1. Baseline Characteristics

	Traditional Dosing (N = 46)	Extended-Infusion (N = 15)
Age	69 ± 15.9	69.5 ± 14.2
Weight*	74.2 ± 27.2	70.8 ± 24.9
Male	31 (67%)	6 (40%)
eGFR (mL/min)	74 ± 39.2	82.3 ± 38.9
APACHE II score	23 ± 8.7‡	15.5 ± 4.9‡
Comorbidities		
Cancer	11 (23.9%)	0
Diabetes	11 (23.9%)	6 (40%)
Lung Disease	14 (30.4%)	8 (53.3%)
Microbiology		
Staphylococcus spp.	12 (23.1%)	1 (6.3%)
SPICE	7 (13.4%)	1 (6.3%)
Pseudomonas spp.	6 (11.5%)	4 (25%)
Source of Infection		
Lungs	26 (56.5%)	8 (53.3%)
Multiple	10 (21.7%)	6 (40%)
Abdomen	6 (13%)	1 (6.7%)
Blood	2 (4.3%)	0
Urinary tract	1 (2.2%)	0
Other	1 (2.2%)	0

*One patient in Traditional Dose group did not have weight reported
‡ Statistically significantly different

Table 2. Primary Outcome

	Traditional Dosing (N = 46)	Extended-Infusion (N = 15)	*P*-value
In-hospital all-cause mortality	23 (50%)	4 (26.7%)	NSS

Table 3. Secondary Outcomes

	Traditional Dosing (N = 46)	Extended-Infusion (N = 15)	*P*-value
Clinical success	11 (23.9%)	7 (46.7%)	N/A
Clinical failure excluding death	12 (26.1%)	4 (26.7%)	N/A
Hospital length of stay (days)	Median = 22 (range: 4 – 214)	Median = 46 (range: 5 – 161)	NSS
ICU length of stay (days)	Median = 16.5 (range: 4 – 101)	Median = 24 (range: 4 – 100)	NSS
PTZ units used per patient	29.4 ± 15.6	23.4 ± 19.3	N/A
PTZ used per patient (g)	99.8 ± 59.3	80.3 ± 67.5	N/A

Table 4. Cost Analysis

	Traditional Dosing	Extended-Infusion
Cost per patient per treatment	Mean = $114.22	Mean = $90.66

Discussion

- Majority of identified Tradition Dose patients did not fit inclusion criteria due to receiving less than 48 hours of PTZ
- Majority of identified Extended-Infusion patients did not fit inclusion criteria due to not having PTZ infused over 4 hours, or receiving less than 48 hours of PTZ
- No statistical differences in baseline characteristics with the exception of APACHE II scores, with higher scores seen in the Traditional Dose group
  - Higher APACHE II scores may explain higher mortality rate even if NSS
  - Unable to assess differences in comorbidities, microbiology, and source of infection due to small sample size
- No differences for in-hospital all-cause mortality, hospital, or ICU length of stay
  - However, difficult to make definitive conclusion due to the small sample size
- Unable to assess differences in clinical success/failure due to small sample size
- Mean savings of $23.56 per patient per treatment with the Extended-infusion

Limitations

- Retrospective study design
- Study was not adequately powered to reach statistical significance
- Temporal differences in treatment over study period
- Single-centre study

Conclusions

- Insufficient data from this study to conclude if there is a difference between the extended-dosing and traditional-dosing regimens in terms of clinical outcomes
- Reduced cost with the extended-infusion dosing regimen

Acknowledgements: Samar Hejazi, Nevena Rebić