Pharmacoeconomic analysis comparing the empiric utilization of cefepime versus piperacillin/tazobactam

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Abstract

Background: In the hospital setting, cefepime (CFP) and piperacillin/tazobactam (PTZ) are among the most commonly utilized antipseudomonal agents in the empiric treatment of nosocomial and healthcare-associated infections. Institutional preference of CFP or PTZ as the preferred antipseudomonal antibiotic varies. Recent literature suggests each may be associated with increased rates of harmful adverse effects including *Clostridiodes difficile* infection (CDI) and acute kidney injury (AKI). The objective of this study is to perform a pharmacoeconomic analysis comparing CFP versus PTZ for empiric antibiotic treatment in patients where *Pseudomonas aeruginosa* is a concern.

Methods: We performed a cost-utility analysis comparing vancomycin plus CFP (VCFP) and vancomycin plus PTZ (VPTZ) for empiric utilization in the hospital setting by creating a decision analytic model from the hospital perspective. Model variables were populated utilizing published clinical and economic data including incidence of AKI and CDI, their associated costs and mortality, and the cost of antibiotic therapy. Secondary and univariate sensitivity analyses tested the impact of model uncertainties and the robustness of our model. A willingness to pay (WTP) threshold of $0 was utilized.

Results: Results of our base-case model predicted that the use of CFP dominated PTZ as the empiric antipseudomonal agent, was less expensive ($7,690 vs. $9,331) and associated with a higher quality-adjusted life-year (QALY) (0.9193 vs. 0.9191) compared to the use of PTZ. Several variables had the potential to impact base case results. PTZ became cost-effective at our WTP threshold if VCFP nephrotoxicity rates increased to 17.3%, the VPTZ nephrotoxicity rates decreased to 28.5%, or if the cost of nephrotoxicity was less than $17,457. No other model variables, including incidence of CDI, impacted base case results.

Conclusion: Results of our model showed that VCFP dominated VPTZ for the empiric treatment of nosocomial infections. The model was sensitive to variation in VCFP and VPTZ nephrotoxicity rates.

Introduction

- *Pseudomonas aeruginosa* is one of the most common gram-negative bacterial causes of health care-associated infections
  - Accounts for approximately 10% of all nosocomial infections[1]
- In the hospital setting, cefepime (CFP) and piperacillin/tazobactam (PTZ) are the most frequently used anti-pseudomonal agents in an empiric therapy regimen for nosocomial and health care-associated infections[2]
  - Commonly utilized in combination with vancomycin for empiric coverage of methicillin-resistant *Staphylococcus aureus* (MRSA)
    - Vancomycin + cefepime (VCFP)
    - Vancomycin + piperacillin/tazobactam (VPTZ)
- The Centers for Disease Control and Prevention (CDC) lists third/fourth-generation cephalosporins, including CFP, among the antibiotics at highest risk for causing *Clostridiodes difficile* infection (CDI)[3]
- Studies have found a significantly higher incidence of acute kidney injury (AKI) among patients receiving VPTZ as compared to those receiving VCFP[4-6]
- Although both CFP and PTZ are effective against *P. aeruginosa,* adverse effects such as CDI and AKI could result in longer hospital stays, increased healthcare costs, and decreased patient quality of life[4-10]

Methods

- *Study Design:* cost-utility analysis utilizing the creation of a decision analytic model
- *Objective:* compare VCFP versus VPTZ for empiric antibiotic treatment in patients where *Pseudomonas aeruginosa* is a concern
- *Perspective:* analysis performed from the hospital perspective
- *Primary Analysis:* incremental cost/quality adjusted life years (QALYs)
- *Secondary Analyses:* univariate sensitivity analyses and probabilistic sensitivity analyses with 10,000 Monte Carlo Simulations

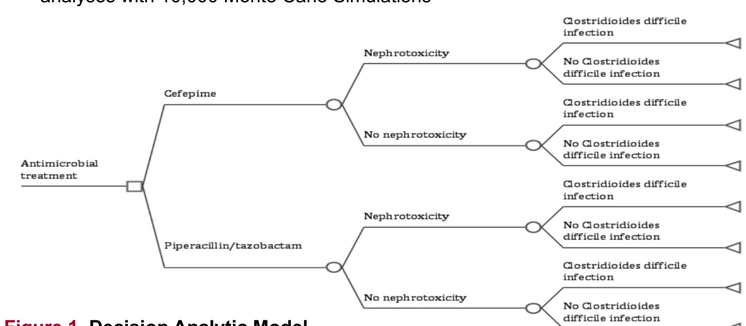

Figure 1. Decision Analytic Model

Table 1. Decision Analytic Model Variables

Variable	Base-Case Value	Range
COSTS		
Cefepime (per day)[11]	29	1-100
Piperacillin-tazobactam (per day)[11]	44	1-100
Antibiotic duration (days)[12]	7	1-21
AKI[13]	11,453	0-50,000
CDI[14,15]	6,698	0-50,000
PROBABILITIES		
Cefepime		
Nephrotoxicity (+vancomycin)[16-20]	0.14	0-0.29
CDI[7]	0.07	0-0.36
Piperacillin-Tazobactam		
Nephrotoxicity (+vancomycin)[16-20]	0.35	0-0.65
CDI[7]	0.03	0-0.24
UTILITIES		
Quality-adjusted life years		
CDI[21]	0.42	0-1
Nephrotoxicity[22,23]	0.7	0-1
Survival[24,25]	0.92	0.5-1

Results

Table 2. Cost-effectiveness of VCFP versus VPTZ Treatment Strategies*

Strategy	Cost, $	Incremental Cost, $	Effect (QALY)	Incremental Effect (QALY)	Incremental C/E (ICER)
Base case (Cost/QALY)			**QALY**		
Cefepime	7,690		0.91928		
Piperacillin/ tazobactam	9,331	1,641	0.91906	-0.00022	Dominated

**Calculations for cost-effectiveness were performed by taking the incremental cost (difference between costs of compared strategies) divided by the incremental effectiveness (difference between the effectiveness of the compared strategies)*

- **Univariate sensitivity analyses:** Piperacillin/tazobactam became cost effective at our WTP threshold of $0 if:
  - VCFP nephrotoxicity rate ↑ from 14% to 17.3%
  - VPTZ nephrotoxicity rate ↓ from 35% to 28.5%
  - Cost of nephrotoxicity was less than $17,457

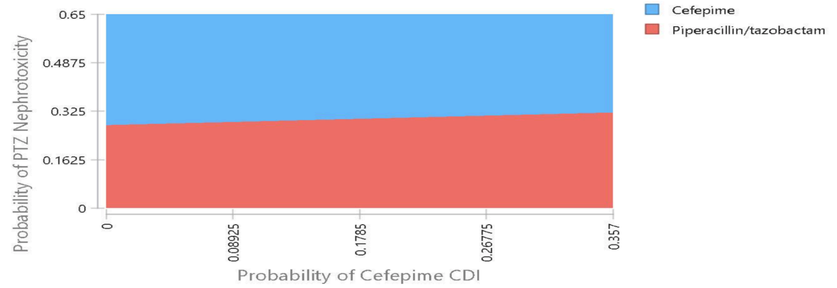

Figure 2. Sensitivity Analysis Comparing Variations in VCFP CDI incidence with VPTZ Nephrotoxicity Incidence

Conclusion

- Our model suggests that VCFP was cost-effective when compared with VPTZ for the empiric therapy of nosocomial and healthcare-associated infections where *P. aeruginosa* is a concern
- The model was sensitive to variation in VCFP and VPTZ nephrotoxicity rates
- While the extent of differences between regimens will continue to be analyzed and further high-quality information will likely emerge, results of our analysis provide decision makers with additional information on which to base their decision for the choice of preferred antipseudomonal β-lactam therapy

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