EVALUATION OF EXTENDED-INFUSION DOSING OF PIPERACILLIN-TAZOBACTAM IN ADULT PATIENTS INFECTED WITH PSEUDOMONAS AERUGINOSA

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BACKGROUND

Recent studies have illustrated through simulations that prolonged infusions of beta-lactam antibiotics may have clinical benefits that include mortality as well as length of stay. Piperacillin-tazobactam has been a major focus in these studies because of its broad-spectrum coverage and utility in the empiric treatment of infections. By extending the infusion period over 4 hours, the bactericidal ability of piperacillin-tazobactam can be maximized to effectively target pathogens that are both susceptible and moderately susceptible to piperacillin-tazobactam[1].

On July 1, 2013, Stony Brook University Hospital, an academic level 1 trauma center in Stony Brook, NY, implemented a new dosing protocol for all patients receiving piperacillin-tazobactam. The protocol requires that all patients on piperacillin-tazobactam receive 4.5g to be infused over 4 hours. Dosing interval would be adjusted in consideration of renal function. The goal of this protocol was to maximize the time that free serum concentrations of drug exceeds the MIC of the organism[2]; which has been proven as an effective practice in recent literature to reduce duration of hospital stay and improve rates of mortality.[1-4] This study evaluates the clinical efficacy of this extended-infusion protocol for patients at our institution with culture-confirmed infections with Pseudomonas aeruginosa.

SBUH's Extended Infusion Protocol for Piperacillin-Tazobactam

- CrCl > 20mL/min: 4.5g every 8 hours, infused over 4 hours
- CrCl < 20mL/min: 4.5g every 12 hours, infused over 4 hours
- Hemodialysis: 4.5g every 12 hours, infused over 4 hours
  - 750mg supplement following hemodialysis

OBJECTIVES

- Evaluate the efficacy of the newly standardized extended-infusion piperacillin-tazobactam administration protocol compared to non-standardized methods used prior to July 2013 at Stony Brook University Hospital.
- Compare the overall length of hospital stay and mortality for inpatients with confirmed Pseudomonas infections treated with piperacillin-tazobactam before and after the implementation of the extended-infusion dosing protocol.

METHODS

- Retrospective chart review of inpatients at Stony Brook University Hospital with positive cultures for *Pseudomonas Aeruginosa* and treatment with at least one dose of piperacillin-tazobactam.
  - **Pre-protocol Group:** received treatment between July 1, 2009 to July 1, 2012
  - **Post-Protocol Group:** received treatment between July 1, 2013 and July 31, 2014.
- Inclusion Criteria:
  - Patients who received at least 1 dose of piperacillin-tazobactam
  - Positive culture for *Pseudomonas aeruginosa*
  - Age over 18
  - Absolute neutrophil count >1000cells/mm^3
- Exclusion Criteria:
  - Patients in the emergency department
  - Pediatric patients under age 18
  - Patients with cystic fibrosis
  - *Pseudomonas* cultures susceptible to piperacillin-tazobactam

RESULTS

- Data analysis shows a decrease in the length of hospital stay for patients who received treatment after the initiation of the new extended-infusion dosing protocol for piperacillin-tazobactam.
  - Average length of stay prior to the protocol was 41.13 days, and fell to 29.75 days after protocol initiation.
  - Percent difference shows a 27.67% reduction in length of stay with the extended-infusion protocol.
- Patients enrolled in final data analysis were infected with strains of *Pseudomonas aeruginosa* sensitive to piperacillin-tazobactam, which accounted for 40.625% of the total study population.
  - Pre-Protocol Group: 37.2% enrollment
  - Post-Protocol Group: 49.8% enrollment
- There was a 41.96% reduction in the average number of doses administered per hospital visit (27.05 to 15.70).
- There was a 43.44% reduction in the average number of doses administered per patient following the implementation of the new extended infusion protocol (28.96 to 16.38).

CULTURES

BASELINE CHARACTERISTICS

TOTAL STUDY POPULATION

	Pre-Protocol 7/1/2009 to 7/1/2012	Post-Protocol 7/1/2013 to 7/31/2014
Total Patients	571	218
Men	338	135
Women	233	83
Average Age	70.1	73.51
Total Number of Cultures	651	245
Number of Sensitive Cultures (%)	**242 (37.2%)**	**122 (49.8%)**

SENSITIVE CULTURES ONLY

	Pre-Protocol 7/1/2009 to 7/1/2012	Post-Protocol 7/1/2013 to 7/31/2014
Total Patients	226	117
Men	136	74
Women	90	43
Average Age	66.3	68.8

PRELIMINARY RESULTS

	Pre-Protocol 7/1/2009 to 7/1/2012	Post-Protocol 7/1/2013 to 7/31/2014
Enrolled	242	122
Average Age	61.9	66.0
Average Number of Doses per Visit	27.05	15.70
Average Number of Doses per Patient	28.96	16.38
Number of Cultures	706	301
# Sputum Cultures	350	115
# Urine Cultures	185	90
# Blood Cultures	40	17
# Other Cultures	131	79
Average Length of Stay (Days)	**41.13 (1-300)**	**29.75 (2-167)**
Length of Stay - Percent Reduction	**27.67%**	

CONCLUSION

From July 1, 2009 to July 1, 2012, 571 patients have received piperacillin-tazobactam for an infection with Pseudomonas aeruginosa over the course of 651 patient encounters at Stony Brook University Hospital; of these, 242 cases had susceptible cultures that were evaluated. From July 1, 2013 until July 31, 2014, 218 patients have been prescribed piperacillin-tazobactam for Pseudomonas aeruginosa over the course of 248 patient encounters under the new SBUH extended-infusion protocol; of which, 122 cases had susceptible cultures that were evaluated. Preliminary data analysis indicated that the average length of stay prior to the initiation of the protocol was 41.13 days, and fell to 29.75 days after initiation of the protocol; resulting in a percent reduction of 27.67%. Further analysis of mortality outcomes will be completed. Thus far, the extended-infusion protocol has helped to standardize the administration of piperacillin-tazobactam at SBUH for both prescribers and pharmacy staff. Preliminary results also indicate the potential for the reduction of costs and ease of labor following the implementation of this new protocol. The results from this preliminary data analysis demonstrate the potential benefits for our institution for improving patient outcomes by administering piperacillin-tazobactam over a 4 hour infusion.

References

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Disclosures

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