Analysis of Seizure Activity with Cefepime Use in a Large Metropolitan Teaching Hospital

R. Staudt, G. Caliendo, V. Adams, P. Saunders-Hao

Department of Pharmacy, The Mount Sinai Medical Center, New York, NY

Rachel Staudt, Pharm.D.
PGY-2 Transplant Pharmacy Resident
The Mount Sinai Medical Center, NY, NY
Rachel.Staudt@mountsinai.org
Phone: 212-241-1833
Fax: 212-426-5110

Background

- Cefepime is a fourth generation cephalosporin antibiotic with broad spectrum activity against Gram-positive and Gram-negative bacteria.
- Cefepime is primarily renally cleared.
- Adverse effects of cefepime include gastrointestinal upset, rash, transaminitis, and rarely blood dyscrasias.
- In June 2012 the Food and Drug Administration (FDA) issued a drug safety communication to health care professionals regarding the risk of nonconvulsive status epilepticus (NCSE) in patients receiving cefepime.
  - NCSE can take several forms and broadly refers to prolonged seizure activity in the absence of major motor signs.
  - NCSE primarily occurred in patients with renal dysfunction who did not receive proper dosage adjustments for cefepime.
  - In most cases, seizures were reversible and resolved after discontinuation of cefepime and/or initiation of hemodialysis.
  - Based on 59 case reports between 1996 and February 2012.

Objectives

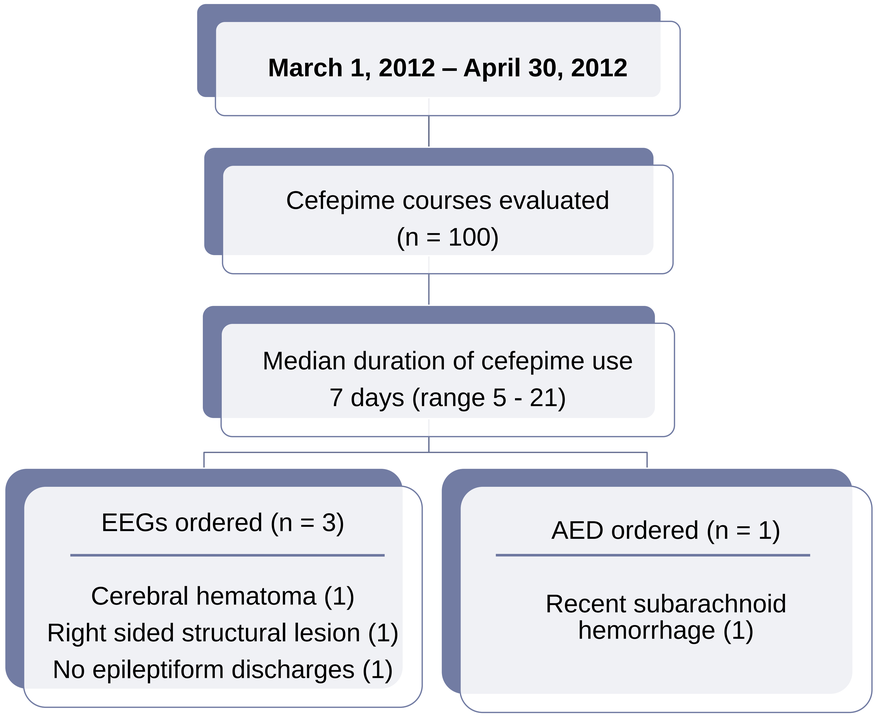
Primary: Assess the incidence of nonconvulsive status epilepticus in patients receiving cefepime.
Secondary: Evaluate if cefepime was properly dose adjusted for renal dysfunction.

Methods

- Single center, retrospective chart review assessing the use of cefepime in 100 adults who received cefepime for a minimum of 5 days from March 1, 2012 through April 30, 2012.
- Seizure activity was identified through orders for an electroencephalogram (EEG) or new antiepileptic drug (AED) during or within 7 days of cefepime exposure.
- The following data was collected:
  - Duration of cefepime therapy
  - Cefepime dose and frequency
  - Patient age
  - Calculated creatinine clearance (CrCl)
  - Orders for an EEG
  - Orders for a new AED
- EEG results were reviewed for evidence of NCSE.
- Each patient's course of cefepime therapy was assessed for seizure activity as well as appropriateness of dose for renal function.
- Cefepime dose was reassessed for appropriateness in any patient having a change in serum creatinine (SCr) ≥ 50% from baseline.

Results

Primary Outcome



Secondary Outcomes

- 51 of 100 patients had a CrCl < 60 ml/min/m^2, 11 of 100 patients were on hemodialysis
- Inappropriate cefepime dosing was identified in 13 patients.
  - 11 patients were receiving subtherapeutic doses
  - 2 patients were receiving supratherapeutic doses
- 10 patients had a change in SCr ≥ 50% from baseline, 9 patients received appropriate dose adjustments

Dosing Recommendations Based on Renal Function Estimated CrCl (ml/min)			
> 50	30 – 50	10 – 30	< 10 or Hemodialysis
1-2 g q 8h	1-2 g q 12h	1-2 g q 24h	0.5-1 g q 24h

Conclusion

- Cefepime use was not associated with nonconvulsive status epilepticus in this retrospective chart review.
- Cefepime dosing was appropriate in the majority of patients based on renal function.
- For patients with changing renal function, the cefepime dose was appropriately adjusted.

Recommendations

- A memo detailing the results of this Medication Use Evaluation, including dosing recommendations, was sent to all pharmacists with the following recommendations:
  - Assess the appropriateness of cefepime orders for indication as well as dose.
  - For patients with unstable renal function, alert the provider to the recent FDA warning and consider the risks versus benefits of administering cefepime.

Discussion

- This chart review included 100 adults, 51 of which had impaired renal function and were at risk for occurrence of NCSE. This is a small sample size in which to identify a rare side effect.
- A larger sample size including only patients with renal dysfunction would be better suited for assessing the true incidence of NCSE.
- This trial did not assess for changes in mental status. NCSE occurs in the absence of major motor signs and often presents as altered mental status or decreased responsiveness.
- Altered mental status is a nonspecific clinical sign and is difficult to assess in a retrospective chart review. However, exclusion of this symptom may have resulted in under estimation of the incidence of NCSE within this study.

References

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The authors have nothing to disclose