Monitoring of Voriconazole levels at University Hospital

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Background

- Voriconazole is a second-generation azole antifungal drug. It is the preferred agent for treatment of aspergillosis and is also a treatment option for other fungi and refractory invasive fungal infections (1,2,4).
- There is significant variance in serum concentration of voriconazole between patients receiving similar dosing regimens (5). Voriconazole relies heavily on hepatic metabolism for drug elimination (3).
- A recent study evaluating the efficacy of voriconazole therapeutic drug monitoring in patients found that persistence or progression of invasive fungal infection was observed in a significantly higher proportion of patients with voriconazole trough concentrations < 1 mg/L, compared with patients with trough concentrations > 1 mg/L. (4).
Background

- This efficacy study also found that one-third of patients with trough levels > 5.5 mg/L after > 1 week of therapy had toxic encephalopathy (4). Other reports have also noted adverse neurologic effects (hallucinations, encephalopathy) with voriconazole levels > 6 mg/L (5,6).
- A retrospective review of 90 hospital courses at University Hospital 8/2003 – 5/2009 found that 12% of patients on voriconazole for at least 3 days had adverse effects. The majority of patients had hematologic malignancy or solid organ transplants (7).
- Marked variability of voriconazole levels can jeopardize patient outcomes and prolong hospital stays.
Background

AIM statement

- Our aim is to increase the amount of voriconazole levels ordered on patients hospitalized at University Hospital taking this medicine for 7 days or more by at least 10% by January 1\textsuperscript{st} 2011.
Team Members

- **CSE Participants:**
  - Jason Bowling, MD  Rachel Rivera, MD

- **UHS Pharmacy:**
  - Jim Lewis, PharmD  Susan Spencer  Michael Andersen RPh

- **Sunrise Information System specialists:**
  - Alton Powell, MD  Irene Puente MSN, RN

- **Microbiology laboratory:**
  - James Jorgensen, PhD  Kathleen Lawless MT(ASCP)  Norma Pena

- **Infectious Diseases:**
  - Thomas Patterson, MD

**Facilitator:**
- Amruta Parekh, MD, MPh
Need for monitoring of voriconazole levels

- Hem-Onc
- Transplant
- Medicine

- UH
- UH Clinics

- Training needed on how to collect specimens
- In progress

- No system in place to Monitor levels
- Sunrise access
- No reminder flag

- Pharmacy
- Sunrise
- Triggers
- Training

- Ordering level
- Monitoring
- Data Collection
- Obstacles

Fishbone Diagram: Voriconazole Project
Patient on voriconazole

- **vori >7 days?**
  - Yes: Need to Monitor vori levels
  - No: No need to monitor vori levels

Need to Monitor vori levels

- Check vori levels every 7 days

vori level less than 1?

- Yes: Adjust vori dose or call ID
- No: Continue checking levels

vori greater than 6?

- Yes: Hold vori and/or call ID
- No: Continue checking levels
Interventions

- Met with Sunrise committee to discuss need for Voriconazole level order set. Detailed report submitted.
- Met with Infectious Disease PharmD, Transplant PharmDs to discuss project and disseminate information to providers
- Formal presentation to Hem-Onc staff and fellows regarding this project, how and when to check levels
- Flow chart included in Hem-Onc fellows consult rotation packet
- Voriconazole order set created: Ordering voriconazole automatically triggers order for drug level to be drawn 7 days after the start date
Sunrise Implementation

**Purpose:** To improve patient safety and outcomes by maximizing the efficacy of the medication.

- **Request:** Automated order set that includes level to be checked 7 days after starting voriconazole.

- **Goal:** To use a combination of interventions including automated ordering of drug levels on Sunrise and targeted inservice education to appropriate providers on the importance of checking voriconazole levels as it relates to patient care and safety.
Prior Sunrise order

Allergies: Drug: PENICILLAMINE, Food: DAIRY PRODUCTS, WHEAT; Environment: CATS, DOGS, PERFUME

Requested By: Me, Other: 

Date: __.__, Time: __:__

Session

Type: Inpatient Orders

Reason:

Manual Entry, Searching for ...

Generic Lab Order Request

<table>
<thead>
<tr>
<th>Order</th>
<th>Cost</th>
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</thead>
<tbody>
<tr>
<td>Generic Nursing Order</td>
<td></td>
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<tr>
<td>Dialysis</td>
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</tbody>
</table>

Any generic nursing order requesting service from FOOD SERVICES must be placed as a DIET order. Generic nursing orders are not seen by Food Services personnel.

Generic Nursing Order

Generic Pharmacy Order
## Sunrise Order Set

<table>
<thead>
<tr>
<th>Order Set:</th>
<th>Voriconazole (Adult) Order Set</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Order Items</strong></td>
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<tr>
<td><strong>Pharmacy</strong></td>
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<tr>
<td>✔️</td>
<td>Voriconazole Inj</td>
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<tr>
<td>✔️</td>
<td>Voriconazole Oral Susp</td>
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<tr>
<td>✔️</td>
<td>Voriconazole Tab</td>
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<tr>
<td><strong>Laboratory</strong></td>
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<tr>
<td>✔️</td>
<td>Voriconazole Level</td>
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</tbody>
</table>
Metrics

- Number of patients on Vori for more than 7 days on whom levels were done from Jan-Dec 2010: 14
- Pre-intervention: 2 levels checked per month
- Post-intervention: 5 levels checked per month
# Metrics

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
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<tbody>
<tr>
<td>1</td>
<td>Time period Levels doi Pts with the</td>
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<tr>
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<td>5</td>
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</table>
Statistical Process Control Chart showing ratio of the number of patients on who levels of Vorix were done at 7 days.

Preintervention data

Postintervention Data

Intervention

Ratio of pts with levels done at 7 days/pts with therapy 7 days or more

CL

UCL

0.316

0.727
Return on Investment

- Cost of voriconazole level: $125
- # patients on voriconazole for 7 days or more in 2010: 30
- Total cost for 30 levels: $3750
- Prior review of UH patients on voriconazole: 12% with adverse effects, predominately abnormal LFTs and delirium
- 12% of 30 patients: 4 patients
- Based on AHRQ data:
  - 2008 Texas Teaching hospital: delirium mean LOS 7.0 days, charge $22,102; liver abnormalities, mean LOS 6.3 days, charge $46,043


http://hcupnet.ahrq.gov/
Return on investment

- If you take **lesser of mean charges** at $22,102
- Estimate you can avoid adverse effects in all 4 patients: $88408
- $88408 - $3750 (cost of levels for all 30 patients):
  - Savings of $84,658/year
  - Savings over 5 years: $423,290
- At **higher mean charge**:
  - Savings of $180,422/year
  - Savings over 5 years: $902,110
- This analysis only examines affect on toxicities. Obviously, there would be benefit to improving sub-therapeutic levels in more rapid improvement in invasive fungal infections, decreased morbidity and overall length of stay.
Future Directions

- Review new order set with Hematology-Oncology, Transplant, Infectious Disease services
- Continue monitoring number of levels checked at University Hospital
Voriconazole is commonly used in immunocompromised patients to treat aspergillosis, candidiasis and invasive fungal diseases.

- Great variability in voriconazole levels
- Subtherapeutic and supratherapeutic levels can lead to increased morbidity, mortality and length of hospital stay
- Patients on voriconazole for more than 1 week should have levels checked and doses adjusted as needed
- Order set on Sunrise exists that will automatically order a voriconazole level when the medication is ordered
- Continued monitoring of levels by Hem-Onc, Transplant, and Infectious Disease teams is essential to improve patient safety and outcomes
Questions?

Thank you