Pharmacy and Therapeutics Committee Update – September 27th, 2017 Meeting

The Pharmacy and Therapeutics Committee at Hendrick Medical Center is a Medical Staff Committee that meets the fourth Wednesday of each month with five physicians and one pharmacist serving as voting members. P and T is Medical Staff Committee. The current Chair of P and T is Kelly Palmere, M.D. (formerly Sunderland).

ePrescribing Meaningful Use Update
The most recent indicated HMC physicians are ePrescribing at discharge 21.8% of the time. The current goal is 10%.

CroFab Drug Utilization Review (DUR/DUE) and Recommendations:
From 9/13/16 through 9/12/17 HMC administered CroFab to 21 patients. The Unified Treatment Algorithm for the Management of Pit Viper Snakebite in the United States was utilized as the criteria for appropriate use. All 21 patients received the appropriate 4 to 6 vial initial dose of CroFab based on swelling that was more than minimal and/or elevated protime, decreased fibrinogen or platelets and/or any systemic signs of toxicity. If any of the aforementioned items were progressing then it was appropriate to repeat a 4 to 6 vial dose of CroFab. In patients in which swelling and tenderness were not progressing; the protime, fibrinogen and platelets were normal or clearly improving and with clinical stability and no neurotoxicity then it was deemed appropriate to take the “watchful waiting” approach to therapy. This meant not administering the maintenance dose of 2 vials every 6 hours x 3 doses. Six patients were assumed potential “watchful waiters” that did receive the full maintenance dose. Limited literature reports that 50% of patients in which watchful waiting is applied will need maintenance dosing at some point in the first 24 hours. In the same study zero patients who received maintenance dosing did not need further dosing based again off limited literature. The median dose is 12 vials. Recurrent thrombocytopenia will occur at a rate of 14% in the maintenance group compared to 56% in the watchful waiting group. A recent ACCP Critical Care Pharmacy Research Network poll conducted in October 2017 resulted in 8 hospitals stating they practice watch and wait. There were no hospitals that give maintenance doses across the board when criteria is met.

The expert consensus is one size does not fit all. Institutions that can provided critical care nursing and medical care are more equipped to adopt a watch and wait protocol after the initial dose of CroFab.

P and T Recommendation: no changes, no restrictions.

1. Physicians may use a watch and wait strategy.
2. Physicians may do the scheduled 2 vials every 6 hours x 3 doses.
3. Physicians may consult with Poison Control to discuss when to watch and wait.
**IV Acetaminophen Utilization – continued follow up:**

After a four quarter decrease IV APAP use has increased over the 3rd quarter of 2017.

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**Antimicrobial Stewardship Committee (AMS) Update: Utilization Reports through September 2017**

**Overall utilization** There was a slight increase in overall utilization for Hendrick Medical Center. Our September 2017 utilization uploaded to the Centers for Disease Control/NHSN indicates a Standardized Antimicrobial Administration Ratio (SAAR) of 1.188 without an assigned p-value but with a 95% Confidence Interval (CI). As we move forward with our reporting we hope to have a number around “1” without a significant p-value (defined as < 0.05) or a CI that includes 1 which would indicate not being statistically significant. In this case the SAAR 95% CI does not include “1” so the utilization of antibiotics at Hendrick Medical Center would be considered more than expected/needed per the CDC. If we were in the CMS reporting mode (to come) this would be a “ding”. We can run reports for individual antibiotics. The take home from this is assure the patient needs antibiotics. When in doubt consider expert consultation with an Infectious Diseases specialist.

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**DOT Trending by Year**

**Agent Breakdown**

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<th>Mar</th>
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Vancomycin and Linezolid Utilization

Anti-Pseudomonas utilization

Fluoroquinolones
**Antimicrobial Stewardship Education** Gregory K. Perry, PharmD, BCPS-

The Overuse of “Vosyn” (Vancomycin and Zosyn) in Diabetic Foot Infections

One stewardship goal is to decrease piperacillin/tazobactam utilization. The increase patient risk of nephrotoxicity with the combination of Vancomycin + piperacillin/tazobactam is well documented in the literature. One area where we see overutilization is in the cases of the diabetic foot ulcer. *Pseudomonas aeruginosa*, although frequently a commensal when found, is usually not pathogenic. Studies using antibiotics with antipseudomonal activity often yield similar results to antibiotics that do not have antipseudomonal activity.

The recommendation is patients admitted to HMC with a Diabetic Foot Infection in which Vancomycin + Piperacillin/Tazobactam is ordered should be considered for a change if the criteria below are not met (see table) to Vancomycin + Ceftriaxone (if ESBL and/or anaerobic coverage is not needed) or Vancomycin + ertapenem (if ESBL and/or anaerobic coverage is desired). The 2002 “SIDESTEP” study also supports this recommendation. The reason for this recommendation is the combination of Vancoc+Zosyn (Vosyn) substantially increases the risk of nephrotoxicity without a defined therapeutic need in most cases as it relates to coverage of *Pseudomonas aeruginosa*. Below is a study summary presented at IDWeek 2017.

**IDWeek 2017 Research**

**Risk Factors for Pseudomonas aeruginosa in Diabetic Foot Infections**

**Background:** Infectious Diseases Society of America guidelines for the management of diabetic foot infections (DFIs) suggest 15 different antibiotic treatment options for moderate-to-severe infections. All treatment options provide coverage for gram-positive cocci, and some provide coverage for gram-negative pathogens, including *Pseudomonas aeruginosa* (PSA). However, there is minimal guidance in determining which patients require anti-PSA therapy.

**Methods:**

This single-center retrospective case-control study included patients hospitalized between October 2013-September 2015. Adult patients admitted with a DFI were identified using a combination of ICD-9 codes for diabetes with complications and cellulitis. The primary outcome was identification of risk factors associated with PSA DFIs. A multivariable model using logistic regression was constructed, and a receiver operator characteristic (ROC) curve was generated to assess the sensitivity and specificity of the model.

**Results:** 262 patients were included and 12 (4.6%) patients had cultures with PSA. Multivariable analysis yielded six risk factors for PSA DFIs (see table). ROC construction yielded an area under the curve of 0.895.

**Conclusion:** The incidence of PSA from DFIs is low. A model with excellent performance characteristics demonstrated that risk factors for PSA DFIs include age > 65, BMI ≥ 35, former or current smoker, history of lower extremity bypass procedure, and cardiovascular disease. Future validation of these factors could help stewardship programs reduce unnecessary antibiotic utilization.

<table>
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<th>Risk Factor for PSA DFI</th>
<th>Odds Ratio (95% confidence interval)</th>
<th>P</th>
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<tr>
<td>Age &gt; 65 years</td>
<td>5.94 (1.40-25.28)</td>
<td>0.016</td>
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<tr>
<td>Body mass index ≥ 35 kg/m²</td>
<td>7.53 (1.73-32.81)</td>
<td>0.007</td>
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<tr>
<td>Former or current smoker</td>
<td>9.27 (1.06-81.54)</td>
<td>0.045</td>
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<tr>
<td>History of a lower extremity bypass procedure</td>
<td>9.63 (1.52-61.15)</td>
<td>0.016</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>5.28 (1.22-22.86)</td>
<td>0.026</td>
</tr>
<tr>
<td>Severe infection</td>
<td>4.50 (0.97-20.95)</td>
<td>0.055</td>
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Background
Evaluating options for venous thromboembolism (VTE) prophylaxis in critically ill patients is challenging. Renal failure, bleeding risk, and thrombocytopenia can limit available pharmacotherapy options. Per the package insert, Fondaparinux is contraindicated in severe renal dysfunction (SRD). In one study published this month, fondaparinux was used in critically ill patients with SRD at an extended dosing regimen with the addition of monitoring antifactor Xa levels for VTE prophylaxis.

Methods
This study was a prospective, single arm, interventional study. Patients were enrolled from two academic hospitals of the Detroit Medical Center. Only ICU patients with an estimated creatinine clearance less than 30 ml/min were enrolled. These included patients with acute kidney injury or end-stage renal disease. Fondaparinux was given at a dose of 2.5 mg subcutaneously every 48 hours. Peak and trough antifactor Xa levels were monitored. Ultrasound was used at baseline and study completion to assess for deep vein thrombosis (DVT). Bleeding complications were also recorded.

Results
Thirty-two patients received a median of 4 doses of fondaparinux. Fondaparinux peak and trough antifactor Xa levels were 0.36 ± 0.18 mg/L and 0.17 ± 0.11 mg/L (mean ± SD), respectively. These levels are similar to those in patients with normal renal function receiving conventional once-daily dosing. No lower extremity DVTs or suspected VTE events occurred. Two patients (6%) had significant bleeding events.

Conclusion
The authors concluded: “In critically ill patients with SRD, an extended interval fondaparinux dosing regimen of 2.5 mg every 48 hours for VTE prophylaxis achieved peak and trough anti–factor Xa levels similar to those reported in noncritically ill patients with normal renal function receiving once-daily fondaparinux.”

Discussion
This study may help with the decision making process of using VTE prophylaxis in a patient with a high risk of VTE but also with a history of heparin induced thrombocytopenia. Limitations of this study include small sample size. Also the bleeding incidence of 6% was not compared against a placebo group. Therefore this study cannot be generalized to all patient in ICU. However, if a patient presents with unique characteristics of high clotting risk, renal dysfunction, and the need to avoid heparin, this option could be considered.

Test Your Knowledge: Bob Wray, RPh, MBA, Pharmacy Financial Coordinator

NDC Primer

Quiz: Which of the following numbers are equivalent to the fictitious NDC 00515-0123-01?
A. 00515012301
B. 515012301
C. 0515-123-1
D. 0051512301

Dissecting an NDC code
An NDC is always an 11 digit number but sometimes leading zeros are omitted. The first 5 digits are the labeler code (e.g. Mylan), the middle 4 are the product code (e.g. furosemide 40mg tablets) and the last two are the package code (e.g. unit dose box of 100). If leading zeros are omitted from the middle (from the product or package code) the NDC must be segmented or the location of the omitted zeros is unclear.

It is common for the same drug to have different NDCs including Unit of Sale (the flat or carton NDC), Inner Pack (an NDC for an unsalable package contained inside the unit of sale item) and Unit of Use NDCs (e.g. the NDC on a single vial or on a unit dose tablet).

Remember that at Hendrick, we almost always use the Unit of Sale NDC as primary with the others included as secondary if needed. The Unit of Use NDCs are related to the barcodes on products vended from Pyxis machines. Similarly, the Talyst database uses the Unit of Sale NDC (and/or the wholesaler’s catalog number) as primary and must also contain the Unit of Use NDC so that the scanner recognizes the unit dose barcodes.

Test Your Knowledge Answer:
Quiz answer A, B, and C but not D.