2019 ASHP Midyear Clinical Meeting Roundtable/Poster Session Summary: Critical Care

Section of Clinical Specialists and Scientists Section Advisory Group on Emergency Medicine
This is a compilation of the Posters presented at the Critical Care Roundtable/Poster Session at the ASHP Midyear Clinical Meeting 2019 in Las Vegas, Nevada. Inclusion in this document does not imply endorsement by ASHP, the ASHP Section Advisory Group on Emergency Medicine, or its members.

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A retrospective comparison of the effectiveness and safety of intravenous olanzapine versus intravenous haloperidol for agitation in the intensive care unit

Michelle Wang, PharmD; George T. Abdallah PharmD, BCCCP; Kristen N. Knoph PharmD, BCPS; Parth Patel BSN, RN; Tuyen Yankama MPH; Ifeoma Mary Eche PharmD, BCPS, BCCCP, CACP

Department of Pharmacy at Beth Israel Deaconess Medical Center, Boston, MA
Assessing the use of activated prothrombin complex concentrates for reversal of oral factor Xa inhibitors at a level 1 trauma center

Lauren Bobby, PharmD, Evan Westlake, PharmD, Nathan Esplin, MD, Sarah Young, PharmD, Department of Pharmacy and Department of Neurosurgery, Allegheny General Hospital, Pittsburgh, PA

Introduction

Activated prothrombin complex concentrates (aPCC) are used at Allegheny General Hospital (AGH) for the reversal of oral factor Xa inhibitors, apixaban, and rivaroxaban. Clinical decision-making for activated prothrombin complex concentrates (aPCC) dosing and administration based on patient coagulation test results is challenging. There is a need to establish a dose for aPCC to reverse factor Xa inhibitors in patients with a normal INR.

Objectives

Primary safety: Efficacy of hemostatic complications in patients that received aPCC prior to hospital discharge.

Secondary efficacy: Improvement in length of stay (LOS), intensive care unit (ICU) LOS, and hospital mortality.

Methods

Prospective analysis of aPCC use for oral factor Xa inhibitors reversal at AGH from July 1, 2016 to June 30, 2019.

Results

Table 1: Baseline Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>All (n = 87)</th>
<th>ICH Patients (n = 17)</th>
<th>Non-ICH Patients (n = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>72.8 ± 12.7</td>
<td>71.9 ± 11.1</td>
<td>73.1 ± 12.8</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>43 (49.5)</td>
<td>6 (35.3)</td>
<td>37 (52.9)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>81.2 ± 22.6</td>
<td>83.4 ± 23.3</td>
<td>80.9 ± 21.2</td>
</tr>
<tr>
<td>INR</td>
<td>8.0 ± 6.0</td>
<td>8.0 ± 7.0</td>
<td>7.8 ± 5.1</td>
</tr>
<tr>
<td>aPCC dose (units/kg)</td>
<td>101.2 ± 28.9</td>
<td>121.9 ± 28.3</td>
<td>100.6 ± 29.3</td>
</tr>
<tr>
<td>aPCC dose (units/kg)</td>
<td>20.0 ± 3.0</td>
<td>20.0 ± 3.5</td>
<td>18.7 ± 3.1</td>
</tr>
<tr>
<td>INR below 1.5 (n, %)</td>
<td>12 (13.9)</td>
<td>7 (41.2)</td>
<td>5 (7.1)</td>
</tr>
<tr>
<td>INR at 15 min after 2 hours</td>
<td>3 (3.5)</td>
<td>3 (17.6)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Results - All Patients

<table>
<thead>
<tr>
<th>Group</th>
<th>All (n = 87)</th>
<th>ICH Patients (n = 17)</th>
<th>Non-ICH Patients (n = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary end point: thrombosis rate - n (%)</td>
<td>1 (1.3)</td>
<td>0 (0.0)</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Extremity or good hemostasis - n (%)</td>
<td>35 (97.0)</td>
<td>35 (97.0)</td>
<td>35 (97.0)</td>
</tr>
<tr>
<td>Mean length of stay - hours</td>
<td>136.4 ± 106.1</td>
<td>137.1 ± 105.8</td>
<td>140.2 ± 117.8</td>
</tr>
<tr>
<td>ICU length of stay - hours</td>
<td>71.6 ± 70.8</td>
<td>71.6 ± 70.8</td>
<td>70.6 ± 91.1</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>10 (11.6)</td>
<td>7 (41.2)</td>
<td>3 (4.3)</td>
</tr>
</tbody>
</table>

Discussion

ICH: aPCC improves safety and efficacy of factor Xa inhibitors. aPCC use is associated with a shorter length of stay in the intensive care unit and hospital. There was a statistically significant difference in the rate of thrombosis in the ICH group compared to the non-ICH group.

Conclusion

aPCC use is safe and effective for reversal of factor Xa inhibitors. Patients who experienced an ICH within 2 hours of the last dose of rivaroxaban or apixaban were more likely to have an ICH. aPCC use may be considered in patients with a normal INR and low INR.

References

Comparison of an anti-Xa versus aPTT guided management of heparin in patients requiring an Impella® percutaneous ventricular assist device

Justina Girgis, BS, PharmD; Sandra Rumyantsev, PharmD, BCCCP; Ifeoma Mary Eche PharmD, BCPS, BCCCP, CACP; George Abdallah, PharmD, BCCCP

Background
- An Impella® is a percutaneously inserted ventricular assist device that requires a heparin containing purge solution to prevent device thrombosis.
- Currently, there is no consensus regarding anticoagulation dosing and monitoring strategies.
- Retrospective data show that compared to aPTT, anti-Xa guided monitoring resulted in a faster time to goal anticoagulation and greater percentage of time within the desired goal range.
- In September 2019, Beth Israel Deaconess Medical Center (BIDMC) transitioned from an aPTT to anti-Xa guided management of heparin purge solutions for Impella support.

Objective
To compare the safety and effectiveness of anti-Xa versus aPTT guided monitoring of unfractionated heparin in patients requiring Impella® support.

BIDMC Updated Guidelines
- Impella® Support Required
  - Initial purge solution
    - Heparin 50 U/mL
  - Anti-Xa monitored every 6 hours
  - Goal anti-Xa 0.2 to 0.4 U/mL
  - Continue purge solution concentration 50 mL
  - Infuse additional IV heparin 5 U/kg/hr

Study Design
- Retrospective, single-center, cohort analysis at a tertiary academic medical center
  - Pre-Implementation (08/01/18 to 10/10/19)
  - Post-Implementation (10/11/19 to 03/31/20)

Methods

Data Collection
Baseline Characteristics
- Patient demographics
- Comorbidities
- Previous history of bleeding and thromboembolic events
- CHADS2VASc Score
- HASBLED Score
- Goal anti-Xa or aPTT
- Impella® indication
- Duration of Impella® support
- Not all inclusive
- Initial heparin purge concentration
- Anti-Xa or aPTT at the time of heparin or thromboembolic event
- Need for transfusions or blood products
- Use of concomitant antithrombotics
- Intensive care unit length of stay
- Hospital length of stay

Primary Endpoint
- Time to goal anticoagulation
- At least two consecutive aPTT or anti-Xa values within goal range

Secondary Endpoints
- Percentage of time at goal anticoagulation
- Major and non-major clinically significant bleeding while on heparin
- As defined by the International Society on Thrombosis and Haemostasis
- Thromboembolic events:
  - Device thrombosis
  - Systemic thrombosis
  - In-hospital mortality

Statistics
- Categorical data:
  - Summarized: Counts and percentages
  - Evaluated: Chi-square or Fisher’s Exact Test
- Continuous data:
  - Summarized: Means with interquartile ranges or means with standard deviations
  - Evaluated: Mann Whitney U Test

Clinical Implications
The results of this study will provide data comparing outcomes between two monitoring strategies, and add to the limited data available on anticoagulation strategies with Impella® devices.

Disclosures
The authors of the presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

References
Efficacy and Safety of Anticoagulation Reversal Agents in Patients without Intracranial Hemorrhage

Amber M. Ooley, PharmD; Melissa Smith, PharmD, BCCCP

Department of Pharmacy – Hillcrest Hospital, Mayfield Heights, OH

Introduction

- The efficacy and safety of anticoagulation reversal agents in life-threatening bleeders outside of intracranial hemorrhage (ICH) and emergent surgery is not well understood. Similarly, there are no consistent recommendations on dosing of these agents for bleeding outside of ICH.
- The Cleveland Clinic Health System formulary includes the following reversal agents: 4-factor prothrombin complex concentrate (Kcentra®), activated prothrombin complex concentrate (FEIBA®), and idarucizumab (Praxbind®).
- To date, an in-depth look at the use of these agents in severe bleeding outside of ICH has not been conducted within the regional Cleveland Clinic hospitals.

Methods

- This was a retrospective chart review of adult patients who had an order for either 4F-PCC, aPCC, or idarucizumab between January 1, 2019, and June 30, 2019.
- Data was collected from three of the regional Cleveland Clinic trauma centers – Fairview Hospital (level I), Akron General Hospital (level I), and Hillcrest Hospital (level II).
- Patients were excluded if they did not receive a dose of one of the medications or if they received the agent for ICH.

Results

- 128 patients identified
- 75 excluded (6 did not receive dose, 69 received for ICH)
- 53 patients included for analysis

- **4F-PCC:** median 25.9 units/kg (range 9.5 – 50)
- **aPCC:** median 50 units/kg (range 10.9 – 58.1)
- **Idarucizumab:** 5 g IV x 1 (all)

- 4F-PCC (n=27) was the most commonly utilized agent, followed by aPCC (n=24) and idarucizumab (n=2), respectively. Dosing of all agents closely mirrored recommendations for dosing in ICH, with few exceptions.
- Therapy was deemed appropriate if the patient was hemodynamically unstable (SBP < 90 mmHg despite fluid resuscitation), or if the bleeding was causing acute clinical worsening requiring immediate intervention.
- Of 53 patients included in the analysis, only 2 had a documented in-hospital thromboembolic event after the administration of the reversal agent (3.7%). No patients were re-admitted to a Cleveland Clinic hospital within 90 days for a thromboembolic event.

Discussion/Conclusions

- The use of anticoagulation reversal agents at the three regional Cleveland Clinic trauma centers has increased in recent years, and approximately 42% of these orders appear to be used for non-life-threatening bleeding or non-emergent surgery.
- The total cost of the potentially inappropriate orders amount to nearly $90,000 over a 6 month period.
- Potential follow-up actions include increasing restriction criteria, as well as providing education to providers of all disciplines.

Disclosures

The authors of this study have no actual or potential conflicts of interest to disclose.

References

Evaluation of antipsychotic utilization for delirium treatment from the intensive care unit to hospital discharge

Khine Tun, PharmD; Matthew Hornsby, PharmD; Corey Goodwin, PharmD, BCPS, BCCCP

Department of Pharmacy, Carilion Roanoke Memorial Hospital, Roanoke, VA

Background

- Delirium is the common complication of patients admitted to the intensive care unit (ICU) and is associated with increased morbidity and mortality.1
- Prior studies have revealed unnecessary continuation of antipsychotic therapy at hospital discharge in patients who were initiated on them for delirium while in the ICU.2,3
- Inappropriate continuation results in the potential for serious short-term and long-term adverse effects.4
- The utilization pattern of antipsychotics for ICU delirium upon ICU and hospital discharge is unknown at our institution.

Objectives

- Primary: To assess the continuation rate of antipsychotics at each transition of care from ICU to hospital discharge.
- Secondary: To determine the appropriateness of antipsychotics at each transition of care from ICU to hospital discharge.

Methods

Study Design

- This was a retrospective cohort study from July 2018 to July 2019.

Setting and Population

- The project was conducted at Carilion Clinic Roanoke Memorial Hospital, a 763-bed tertiary care facility located in Roanoke, VA.
- The study was approved by the Carilion Clinic IRB.
- Inclusion Criteria: ≥18 years of age admitted to the ICU for at least 24 hours, at least one positive CAM-ICU assessment, received at least one dose of antipsychotics (chlorpromazine, haloperidol, olanzapine, risperidone and ziprasidone) for ICU delirium.
- Exclusion Criteria: Antipsychotic therapy prior to ICU admission, Data Collection
- Data was extracted from the electronic medical record at each transition of care.

Definitions

- ICU delirium: at least one positive Confusion Assessment Method for the ICU (CAM-ICU) documented during ICU stay
- Inappropriate continuation of antipsychotics (transfer from ICU to hospital discharge): no documentation of delirium diagnosis on discharge summary while antipsychotics were listed as discharge medications

Baseline Characteristics (n = 150)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean</td>
<td>61 (16.1)</td>
</tr>
<tr>
<td>Sex, male (%)</td>
<td>62 (61.3)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>130 (86.7)</td>
</tr>
<tr>
<td>African American</td>
<td>20 (13.3)</td>
</tr>
<tr>
<td>ICU services, n (%)</td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>86 (57.3)</td>
</tr>
<tr>
<td>Surgical/trauma</td>
<td>64 (42.7)</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>112 (74.6)</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>15 (10.1)</td>
</tr>
<tr>
<td>Neurological or psychiatric disorders</td>
<td>87 (57.8)</td>
</tr>
<tr>
<td>Risk factors:</td>
<td></td>
</tr>
<tr>
<td>APACHE II, mean (SD)</td>
<td>16 (6.5)</td>
</tr>
<tr>
<td>Opioid administration, n (%)</td>
<td>125 (83.5)</td>
</tr>
<tr>
<td>Benzodiazepine administration, n (%)</td>
<td>121 (80.6)</td>
</tr>
<tr>
<td>Mechanical ventilation, n (%)</td>
<td>99 (65.1)</td>
</tr>
<tr>
<td>Duration of mechanical ventilation, median (IQR)</td>
<td>4 (5)</td>
</tr>
</tbody>
</table>

Hospital length of stay [days], median (IQR) 8 (9)

Antipsychotic Utilization from ICU to Hospital Discharge

| Patients initiated on antipsychotics in the ICU | 150 |
| Patients transferred from ICU to hospital floors | 141/150 (94%) |
| Patients continued on antipsychotics from ICU to hospital floors | 69/141 (49%) |
| Inappropriately continued | 28/69 (41%) |
| Patients continued on antipsychotics from ICU to hospital discharge | 22/141 (16%) |
| Inappropriately continued | 10/22 (46%) |

Antipsychotic Regimen Administration in ICU

<table>
<thead>
<tr>
<th>Antipsychotic administered, n</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>99</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>51</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>24</td>
</tr>
<tr>
<td>Risperidone</td>
<td>10</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>6</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>1</td>
</tr>
</tbody>
</table>

Frequency, n

| Schedule | 92 |
| Administered as needed | 77 |

Summary

- The continuation of antipsychotics for the management of ICU delirium during transitions of care was common.
- Antipsychotic therapy for ICU delirium was inappropriately continued: 41% of the patients when transferred from the ICU to the hospital floor, 46% of the patients transferred from the ICU to hospital floor and continued upon hospital discharge.
- Importantly, about 15% (1096) of patients continued on antipsychotics from ICU to hospital discharge were inappropriately prescribed with antipsychotics upon hospital discharge.
- Our study finding highlights the importance of regular assessment of antipsychotic use in patients with ICU delirium, particularly during transitions of care.
- There is a need for educational efforts to the providers in order to minimize patient harm by reducing inappropriate continuation of antipsychotic agents during transitions of care.

Disclosure

Authors of this presentation have no financial or personal relationships with commercial entities that may have a direct interest in the material of this presentation. Names: Khine Tun, Corey Goodwin, Matthew Hornsby.

References

Enzyme immunoassay versus automated immunoassay in the diagnosis of heparin-induced thrombocytopenia

Alexandra Adler, PharmD¹, Robert D. Willim, MD, I. Mary Eche, PharmD BCPS BCCCP CACP¹
1. Department of Pharmacy 2. Department of Pathology
Beth Israel Deaconess Medical Center, Boston, MA

Background

- Heparin-induced thrombocytopenia (HIT) can be diagnosed by detection of antibodies against platelet factor 4 (PF4).
- Previously we used the enzyme immunoassay (EIA) for patients with suspected HIT. This assay has a reported sensitivity of 98-99%, however, it has a low specificity of 65%. Additionally, there is a long turnaround time due to batching.
- The automated latex immunoturbidimetric assay (LIA) is a new diagnostic assay with better sensitivity (97%) and specificity (94%). Additionally, the test results in ~1 hour.
- Our institution adopted the use of LIA in place of EIA for the diagnosis of HIT.

Test Detection method
IAA Detect the presence of antibodies against PF4/6-heparin complexes
LIA Uses a monoclonal antibody to compete with HIT antibodies
SRA* Detects the capability of the HIT antibodies to activate platelets in the presence of heparin
* SRA = serotonin-release assay

Objective

To compare the impact of the use of LIA versus EIA on the incidence of switching to alternative anticoagulant therapy such as a direct thrombin inhibitor (DTI).

Methods

Study Design

<table>
<thead>
<tr>
<th>Pre-implementation</th>
<th>Post-implementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 2018 - September 2018</td>
<td>May 2019 - September 2019</td>
</tr>
</tbody>
</table>

Assessment of sensitivity and specificity:

- 4T score: high (0-6) Intermediate (4-6) Low (3 or less)
- EIAIA results: Negative, Weak positive, Moderate, Positive
- 4T score: ordered, not ordered

Outcomes

- Primary outcome: Proportion of patients who were switched to an alternative anticoagulant
- Secondary outcome: Time from ordering the assay to initiating an alternative anticoagulant
- Cost: Total cost of management of suspected HIT
- Safety: Rates of bleeding and thrombosis due to alternative anticoagulant use

Limitations

- Single-center, retrospective analysis
- Comparing historical control creates risk for imbalance between the two groups
- 4T score calculation is based on historical data

Results from this study will validate the use of LIA instead of EIA for the diagnosis of HIT in our institution. Based on the fast turnaround time we can minimize the need to switch anticoagulants in patients with suspected HIT.

References

Evaluation of phytonadione prescribing practices
Courtney Olesky, PharmD; Lucy Stabke, PharmD.

New Hanover Regional Medical Center, Wilmington, North Carolina

Background
- American College of Chest Physicians and Surgical Critical Care recommend phytonadione to reverse oral vitamin K antagonists
- Dose and route are dependent on the presence of bleeding, time to surgical intervention, and the patient's international normalized ratio (INR)

Purpose
- Assess the safety and effectiveness of phytonadione dosing strategies

Study Design
- Single-center, retrospective observational cohort
- As a quality improvement project, IRB review was not required
- Study site: New Hanover Regional Medical Center teaching hospital
- Study period: April 1, 2018 to June 30, 2018

Inclusion
- Age ≥ 18 years
- Phytonadione administered

Exclusion
- Pregnancy
- Incarcerated

Endpoints
- Primary: Appropriateness of reversal of bleeding
- Secondary: INR reduction post-phytonadione dose

Definitions
- Appropriateness of reversal: In accordance with the CHEST guidelines
- Appropriate dose and route based on indication and INR

Results

Baseline Characteristics
- All N = 45
- Active bleeding N = 18
- Emergent surgery N = 12
- Supra-Tx INR N = 12

- Age, y**
  - Mean: 75.61
  - Range: 63-87
- SOFA**
  - Mean: 3.80
  - Range: 2-10

Anticoagulation therapy:
- Warfarin
  - Mean: 42.3
  - Range: 3.2%
- Heparin
  - Mean: 8.4%
  - Range: 0-21.02

Supra-Tx INR
- Mean: 10.2
  - Range: 6-16

Emergency bleeding (N = 12)
- INR > 5
  - Mean: 10.2
  - Range: 6-16

Discussion
- Twelve patients (86%) were appropriately reversed for emergent surgery
- Six patients (50%) were appropriately reversed for Supra-Tx INR and no bleeding
- Three adverse reactions (N = 2) occurred post-phytonadione administration
- A patient developed a hematoma after intramuscular injection of phytonadione for Supra-Tx INR

Conclusions
- Phytonadione was safe and effective for anticoagulation reversal
- Results will lead to a re-evaluation of the anticoagulation reversal order set
- Identified need for order panel and education for safe reversal without bleeding

References

At authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

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