

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.

For more information and resources on Emergency Care Pharmacy,
visit the ASHP Emergency Care Resource Center

<https://www.ashp.org/Pharmacy-Practice/Resource-Centers/Emergency-Care>

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

Beth Israel Deaconess Medical Center

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



Background

- Recent publications have demonstrated the effectiveness and safety of intravenous (IV) olanzapine for agitation in the emergency department, but limited data is available for its use in intensive care units (ICU)¹⁻⁴
- A pilot study at Beth Israel Deaconess Medical Center (BIDMC) suggested that IV olanzapine for agitation in the ICU was effective and had potential adverse effects⁵

Objective

To compare the effectiveness and safety of IV olanzapine to IV haloperidol for treatment of agitation in adult ICU patients

Methods

Primary Outcome

- Proportion of patients who achieve a Richmond Agitation and Sedation Scale (RASS) score of < 1 without the use of rescue drugs* within 4 hours of receiving IV olanzapine or IV haloperidol
- RASS is a validated and reliable method to assess sedation in the ICU

Secondary Outcomes

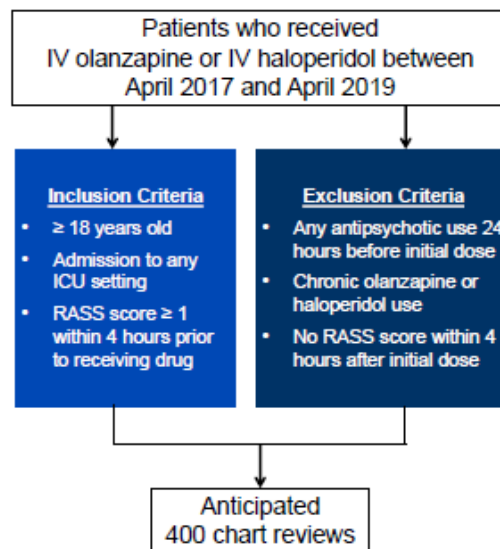
- Need for rescue drugs for agitation within 4 hours of initial drug administration
- Incidence of adverse events
- ICU length of stay

*Rescue drugs: antipsychotics and benzodiazepines

Methods

Study Design

- Retrospective, single-center, cohort analysis approved by BIDMC Institutional Review Board



Abbreviations

PMH	Past medical history	HR	Heart rate
SBP	Systolic blood pressure	BPM	Beats per minute
MAP	Mean arterial pressure	MS	Milliseconds

**QTc calculated based on Hodges formula

Data Collection

Baseline Characteristics

- Age
- Sex
- Height/weight
- Race
- Admission diagnosis
- Mechanical ventilation
- Active alcohol withdrawal
- Delirium
- Pertinent PMH
- Pertinent home drugs
- Deliriogenic drugs
- QTc prolonging drugs

Effectiveness Endpoints

- RASS scores 4 hours before and after initial dose
- IV olanzapine/haloperidol use 4 hours after initial dose
 - Initial dose (mg)
 - Total dose (mg)
- Rescue drugs* used within 4 hours after initial dose:
 - Frequency
 - Total dose (mg)
- Total dose (mg) of pertinent drugs used 4 hours before and after initial dose:
 - Antipsychotics
 - Sedatives
 - Analgesics
 - Phenobarbital
 - Valproic acid

Safety Endpoints

- Hypotension: SBP < 90 mmHg, MAP < 65 mmHg, new or increased pressor requirement
- Bradycardia: HR < 60 BPM
- QTc** prolongation: > 60 ms from baseline or > 500 ms
- Respiratory events: respiratory rate < 12 breath/min, O₂ sat < 90%, new non-invasive ventilation or intubation
- Somnolence: RASS ≤ -3

Statistics

- Categorical data:
 - Summarized: counts or percentages
 - Evaluated: chi-square or Fisher's Exact Test
- Continuous data:
 - Summarized: medians with interquartile ranges or means with standard deviations
 - Evaluated: T-test or Mann Whitney U Test
- 80% power and $\alpha = 0.05$
- Sample size calculation:
 - 192 patients (96 patients in each arm) to detect a 20% difference in the proportion of patients who achieved a RASS score of < 1

Disclosures

The authors have no disclosures 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

- Chen EW, Taylor DM, Knott JC, Phillips GA, Castle DJ, Kong DCM. Intravenous droperidol or olanzapine as an adjunct to midazolam for the acutely agitated patient: A multicenter, randomized, double-blind, placebo-controlled clinical trial. *Ann Emerg Med*. 2013; doi:10.1016/j.annemergmed.2012.07.118.
- Taylor DM, Yap CYL, Knott JC, et al. Midazolam-Droperidol, Droperidol, or Olanzapine for Acute Agitation: A Randomized Clinical Trial. *In: Annals of Emergency Medicine*. Vol 69; 2017; doi:10.1016/j.annemergmed.2016.07.033
- Cole JB, Moore JC, Dolan BJ, et al. A Prospective Observational Study of Patients Receiving Intravenous and Intramuscular Olanzapine in the Emergency Department. 2018; doi:10.1016/j.annemergmed.2016.08.009
- Mattar ML, Klein LR, Rivard RL, et al. A large retrospective cohort of patients receiving intravenous olanzapine in the emergency department. *Acad Emerg Med*. 2016;23(1):29-35; doi:10.1111/acem.12842
- Eche I, Eche I, Wang A, et al. (2018). A Retrospective Pilot Study Evaluating the Use of Intravenous Olanzapine for Agitation in the Intensive Care Unit. Manuscript submitted for publication.



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 concentrate (aPCC) is used at Allegheny General Hospital (AGH) for the reversal of oral factor Xa inhibitors, apixaban and rivaroxaban
- Coagulation factor Xa (recombinant), inactivated-zhzo received food and drug administration (FDA) approval for reversal of apixaban and rivaroxaban in 2018
- To date there are no studies to directly compare the two agents for safety and efficacy of oral factor Xa inhibitor reversal
- aPCC dosed at 20 units/kg is the approved reversal agent at our institution for oral factor Xa inhibitors for serious life-threatening bleeds
- Given cost and limited safety data regarding use of coagulation factor Xa (recombinant), inactivated-zhzo, outcomes associated with the use of aPCC continue to be evaluated at AGH

Objectives

Primary safety:

- Rate of thromboembolic complications in patients that received aPCC prior to hospital discharge

Secondary safety:

- Hospital length of stay (LOS), intensive care unit (ICU) LOS, in-hospital mortality

Secondary efficacy:

- Percent of patients that achieved hemostatic efficacy
- Compliance with institutional dosing guidelines

Methods

- Retrospective analysis of aPCC use for oral factor Xa inhibitor reversal at AGH from July 1, 2018- June 30, 2019

Inclusion Criteria

- Patient received at least one dose of aPCC for reversal of rivaroxaban or apixaban

Exclusion Criteria

- <18 years of age, incarcerated, pregnant, or received aPCC for hemophilia

- Data extraction per the electronic medical record
- Hemostatic efficacy defined per standards from study achieving FDA approval for factor Xa (recombinant), inactivated-zhzo (please see handout)
- Computed tomography (CT) scan interpretation of intracranial hemorrhage (ICH) performed by neurosurgeon

Results

Table 1: Baseline Characteristics

	All Patients (n = 77)	ICH Patients (n = 47)	Non-ICH Patients (n = 30)
Age – yr	76.0 ± 12.7	78.6 ± 12.9	72.1 ± 11.5
Male sex – no. (%)	43 (55.8)	25 (53.2)	18 (60.0)
Weight at time of admission – kg	91.2 ± 23.3	84.1 ± 22.4	102.3 ± 20.4
aPCC dose – units	1802.1 ± 399.3	1684.8 ± 399.5	1985.8 ± 327.9
aPCC dose – units/kg	20.1 ± 3.0	20.4 ± 3.5	19.7 ± 2.1
Below 18 units/kg – no. (%)	13 (16.9)	8 (17.0)	5 (16.7)
Above 24 units/kg – no. (%)	3 (3.9)	3 (6.4)	0 (0.0)
Oral Factor Xa Inhibitor (%)			
Apixaban	47 (61.0)	31 (66.0)	16 (53.3)
Rivaroxaban	30 (39.0)	16 (34.0)	14 (46.7)
Indication for anticoagulation – no. (%)			
Atrial fibrillation	62 (80.5)	40 (85.1)	22 (73.3)
Venous thromboembolism	11 (14.3)	4 (8.5)	7 (23.3)
Other	4 (5.2)	3 (3.9)	1 (3.3)
Anticoagulation restart before discharge			
No. (%)	5 (6.5)	0 (0.0)	5 (16.7)
Apixaban – no. (%)	4 (80.0)	0 (0.0)	4 (80.0)
Days after aPCC administration	5.6 ± 5.5	0 (0.0)	5.6 ± 5.5
Glasgow Coma Scale on admission		13.1 ± 3.1	

Plus-minus values are mean ± SD.

Figure 1: Impact on Coagulation

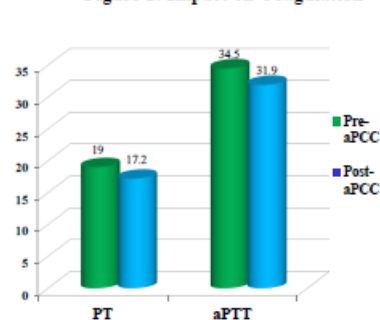


Table 2: Results – ICH Patients

	(n = 47)
Surgical intervention required – no. (%)	0 (0.0)
Post-aPCC hematoma expansion – no. (%)	5 (10.6)
Post-aPCC stable CT – no. (%)	42 (89.4)
Time after aPCC to follow-up CT – no. (%)	
< 12 hours	34 (72.3)
12 to 24 hours	10 (21.3)
> 24 hours	1 (2.1)
None performed	2 (4.3)

Table 3: Results – All Patients

	All (n = 77)	ICH (n = 47)	Non-ICH (n = 30)
Primary end point: Thromboembolic events – no. (%)	1 (1.3)	0 (0.0)	1 (3.3)
Excellent or good hemostasis – no. (%)	60 (77.9)	42 (89.3)	18 (60.0)
Hospital length of stay – hours	138.5 ± 106.1	131.7 ± 98.8	149.2 ± 117.6
ICU length of stay – hours	71.2 ± 78.8	71.5 ± 70.8	70.6 ± 91.1
In-hospital mortality	10 (13.0)	7 (14.9)	3 (10.0)

Plus-minus values are mean ± SD.

Conclusion

- aPCC is safe to use to reverse oral Factor-Xa inhibitors given the low rate of thromboembolic complications
- Post-aPCC imaging shows aPCC is effective at establishing excellent or good hemostasis following intracranial hemorrhage
- Patients experienced an average stay of approximately 3 days in the ICU and 6 total days in the hospital following a life-threatening bleed requiring aPCC to reverse an oral Factor-Xa inhibitor, whether it was an ICH or not
- Rounding aPCC dosing to the nearest vial size may need reassessed due to the number of patients receiving doses less than 18 units/kg
- Our institutional practices utilizing aPCC for reversal of oral factor Xa inhibitors appear to be safe and effective

Discussion

- The trial that gained FDA approval for coagulation factor Xa (recombinant), inactivated-zhzo was a multicenter, prospective, open-label, single-group study
- Key exclusion criteria of this approval trial included:
 - ICH in a patient with a score of less than 7 on the Glasgow Coma Scale, an estimated hematoma volume of more than 60 cc, or expected survival of less than 1 month
- The outcome results of this approval trial included:
 - Good or excellent hemostasis was achieved in 204/248 (82%) patients
 - ICH patients (135/168) 80%
 - Thromboembolic complications included 34/352 (9.7%) patients
 - Mortality rate was (49/352) 14%
- Given the efficacy of aPCC seen at our institution we recommend continuing the use of aPCC for reversal of oral factor Xa inhibitors

References

- FEIBA [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; 2013.
- N Engl J Med, 2019; 380:1326-1335.
- Thromb Haemost 2012; 108: 217-224.

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

Beth Israel Deaconess Medical Center

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

George Abdallah, PharmD, BCCCP

Department of Pharmacy, Beth Israel Deaconess Medical Center, Boston, MA



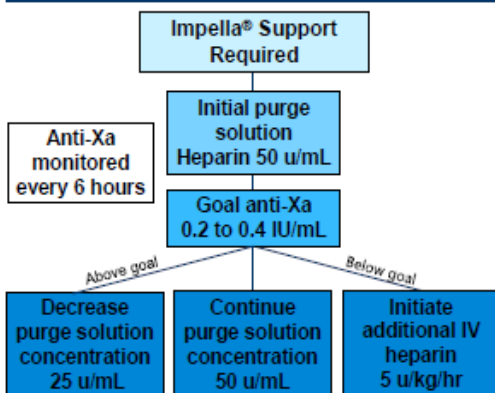
Background

- 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.

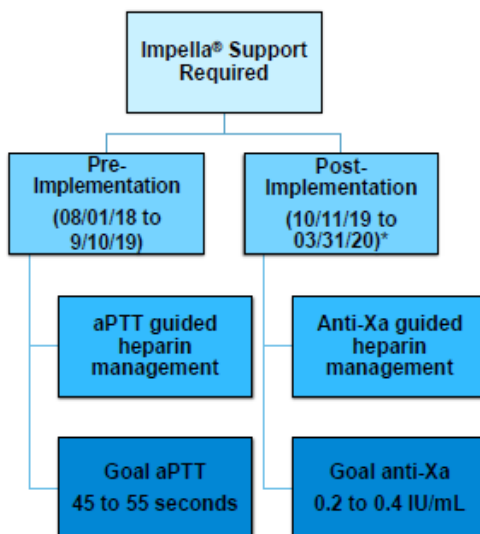
BIDMC Updated Guidelines



Methods

Study Design

- Retrospective, single-center, cohort analysis at a tertiary academic medical center



*One month wash-out period

Inclusion Criteria	<ul style="list-style-type: none"> Age ≥ 18 years old Requiring Impella® support On heparin anticoagulation Monitored using aPTT or anti-Xa
Exclusion Criteria	<ul style="list-style-type: none"> Pregnancy Impella® support for < 24 hours Known coagulation disorder

Data Collection

Baseline Characteristics*

- Patient demographics
- Comorbidities
- Previous history of bleeding and thromboembolic events
- CHADS₂/VAS_C Score
- HASBLED Score
- Goal anti-Xa or aPTT
- Impella® indication
- Duration of Impella® support
- Initial heparin purge concentration
- Anti-Xa or aPTT at the time of bleed or thromboembolic event
- Need for transfusions or blood products
- Use of concomitant antiplatelets
- Intensive care unit length of stay
- Hospital length of stay

*Not all inclusive

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
- Disposition

Statistics

- Categorical data:
 - Summarized: Counts and percentages
 - Evaluated: Chi-square or Fisher's Exact Test
- Continuous data:
 - Summarized: Medians 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

- Impella Program Protocols & Tools. Protected PCI Community. Abimed®. Available at: <http://www.protectedpci.com/>. Accessed, August 2019.
- Myat A, Patel N, Tehrani S, Banning AP, Redwood SR, Bhatt DL. Percutaneous Circulatory Assist Devices for High-Risk Coronary Intervention. JACC: Cardiovascular Interventions. 2015;8(2):229-244.
- A. Sleg, B. A. Mardis, C. R. Mardis et al., "Developing an anti-Xa-based anticoagulation protocol for patients with percutaneous ventricular assist devices," ASAIO Journal, vol. 61, no. 5, pp. 502-508, 2015.
- B. Reed, R. DiDomenico, J. Allender et al., "Variability in anticoagulation practices with the Impella percutaneous ventricular assist device: a survey of high-volume centers," The Journal of Heart and Lung Transplantation, vol. 37, no. 4, pp. S310-S311, 2018.
- Rihal CS, Naidu SS, Givertz MM, et al. 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care. Journal of the American College of Cardiology. 2015;65(19):e7-e26.



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

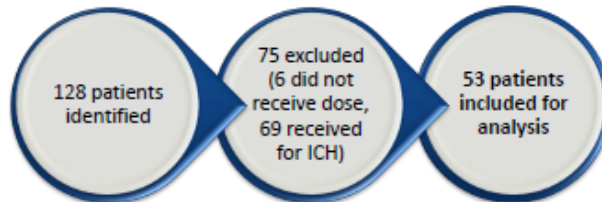
Introduction

- The efficacy and safety of anticoagulation reversal agents in life-threatening bleeds 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 II), 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



• **4F-PCC:** median 25.9 units/kg (range 9.5 – 50)

• **aPCC:** median 50 units/kg (range 10.9 – 58.1)

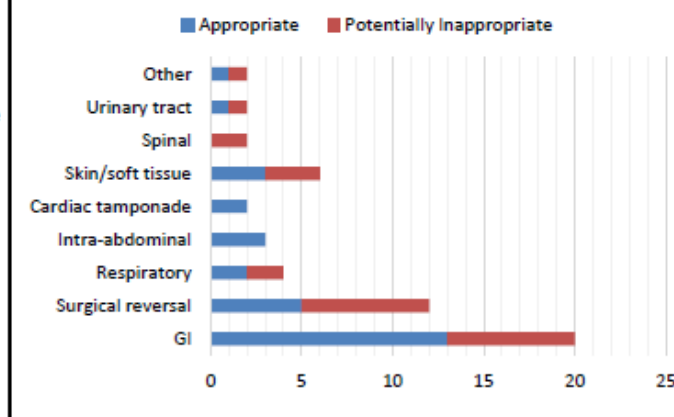
• **Idarucizumab:** 5 g IV x 1 (all)

- 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.

Demographics/Characteristics

Median age, yr (range)	80 (45 - 96)
Female, n (%)	30 (55.6)
Median weight, kg (range)	79 (46 - 163.2)
Concomitant antiplatelet therapy, n (%)	26 (48)
Anticoagulant, n (%)	
Warfarin	25
Apixaban	19
Rivaroxaban	6
Dabigatran	2

Reversal Indications



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

- Cannon JW, Khan MA, Raja AS, et al. Damage control resuscitation in patients with severe traumatic hemorrhage: A practice management guideline from the Eastern Association for the Surgery of Trauma. In: *Journal of Trauma and Acute Care Surgery*. Vol 82. Lippincott Williams and Wilkins; 2017:605-617.
- Raval AN, Cigarroa JE, Chung MK, et al. Management of patients on Non-Vitamin K antagonist oral anticoagulants in the acute care and periprocedural setting. *Circulation*. 2017;135(10):e604-e633
- Engelbart JM, Zepeski A, Galet C, Polloent B, Skeets DA, Faine BA. Safety and effectiveness of Factor Eight Inhibitor Bypassing Activity for direct oral anticoagulant-related hemorrhage reversal. *Am J Emerg Med*. 2019;37(2):214-219.
- Milling TJ, Clark CL, Feronti C, et al. Management of Factor Xa inhibitor-associated life-threatening major hemorrhage: A retrospective multi-center analysis. *Am J Emerg Med*. 2018;36(3):396-402.

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 (aripiprazole, haloperidol, olanzapine, quetiapine, 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 floors): negative CAM-ICU within 24 hours before transfer to hospital floors
- Inappropriate continuation of antipsychotics upon hospital discharge: no documentation of delirium diagnosis on discharge summary while antipsychotics were listed as discharge medications

Results

Baseline Characteristics (n = 150)

Age, mean (SD)	61 (16.1)
Sex: male, n (%)	92 (61.3)
Race, n (%)	
White	130 (86.7)
African American	20 (13.3)
ICU services, n (%)	
Medical	86 (57.3)
Surgical/trauma	64 (42.7)
Comorbidities, n (%)	
Hypertension	112 (74.6)
Cerebrovascular accident	15 (10)
Neurological or psychiatric disorders	87 (58)
Risk factors	
APACHE II, mean (SD)	16 (6.9)
Opioid administration, n (%)	125 (83.3)
Benzodiazepine administration, n (%)	121 (80.6)
Mechanical ventilation, n (%)	99 (66)
Duration of mechanical ventilation, median (IQR)	4 (5)
ICU length of stay [days], median (IQR)	8 (9)
Hospital length of stay [days], median (IQR)	14 (13)

Antipsychotic Regimen Administration in ICU

Antipsychotic administered, n	
Haloperidol	98
Quetiapine	51
Olanzapine	24
Risperidone	16
Ziprasidone	6
Aripiprazole	1
Frequency, n	
Once	92
Scheduled	77
Administered as needed	47

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% (10/69) of patients continued on antipsychotics from ICU to hospital floors 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 effort to the providers in order to minimize patient harm by reducing inappropriate continuation of antipsychotic agents during transitions of care.

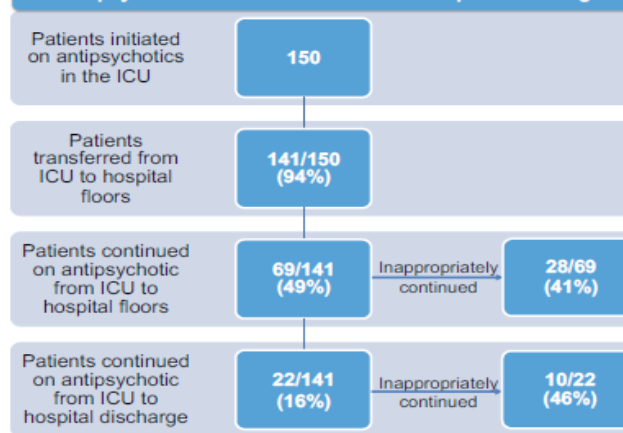
Disclosure

Authors of this presentation have the following 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:
Names: Khine Tun, Corey Goodwin, Matthew Hornsby

References

- Devlin JW, Skrobik Y, Gélinas C, et al. Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. *Crit Care Med*. 2018;46(9):e825-e873.
- Kram BL, Kram SJ, Brooks KR. Implications of atypical antipsychotic prescribing in the intensive care unit. *J Crit Care*. 2015;30(4):814-818.
- Marshall J, Herzig SJ, Howell MD, et al: Antipsychotic utilization in the intensive care unit and in transitions of care. *J Crit Care* 2016; 33:119–124.
- Hale GM, Kane-gill SL, Groetzinger L, Smithburger PL. An Evaluation of Adverse Drug Reactions Associated With Antipsychotic Use for the Treatment of Delirium in the Intensive Care Unit. *J Pharm Pract*. 2016;29(4):355-60.

Antipsychotic Utilization from ICU to Hospital Discharge



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

Beth Israel Deaconess Medical Center

Alexandra Adler, PharmD¹, Robert D. Willim, MD², 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 85%. 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
EIA	Detect the presence of antibodies against PF4/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

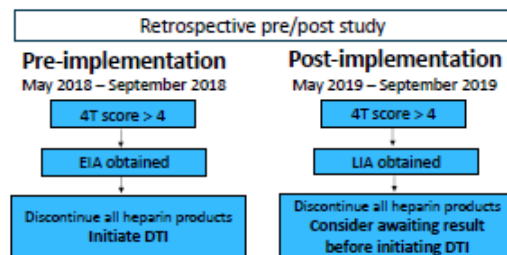
* SRA – Serotonin release assay

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

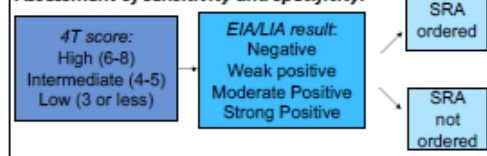
Study Design



Data Collection

- Baseline data:**
- Demographic (age, gender, weight, height, race)
 - Dose, route, duration, and type of anticoagulant
 - Indication for anticoagulation
 - Primary team (medicine, surgery, critical care)
 - Active hematology consult
 - 4T score

Assessment of sensitivity and specificity:



Assessment of outcomes:

- Appropriateness of immunoassay order
- Time to result of immunoassay
- Appropriateness of SRA order
- Time to switching to alternative anticoagulant
- Dose, route, duration of alternative anticoagulant (if initiated)

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

Statistics

- Preliminary sample size: ~160 patients
- Fisher's exact test or chi-square test will be used for categorical data
- Continuous variables will be analyzed using Wilcoxon-rank sum or Student's t-test
- Sensitivity, specificity, positive predictive value, and negative predictive value will be reported with 95% confidence intervals
- Pre-test probability will be calculated with respect to SRA status

Clinical Implications

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

Limitations

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

Disclosures

The authors have no disclosures 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

- Linkins LA, Dans AL, Moores LK, et al. Treatment and prevention of heparin-induced thrombocytopenia: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. Feb 2012;141(2 Suppl):e495S-530S.
- Cuker A, Arepally GM, Chong BH, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia. Blood Adv. 2018;2(22):3360-3392.
- Instrumentation_Laboratory. HIT-Ab(PF4-H) 0020014600. 2017; Insert Sheet. Available at: <https://www.instrumentationlaboratory.com/us/en/hemosil-reagents?scrollto=title-container-5>. Accessed 04/21/17, 2017.
- Warkentin TE, Sheppard JI, Linkins LA, Arnold DM, Nazy I. Performance characteristics of an automated latex immunoturbidimetric assay [Hemosil(L)(R)] HIT-Ab(PF4-H)] for the diagnosis of immune heparin-induced thrombocytopenia. Thrombosis research. May 2017;153:108-117.
- Althaus K, Hron G, Strobel U, et al. Evaluation of automated immunoassays in the diagnosis of heparin induced thrombocytopenia. Thromb Res. 2013;131(3):e85-90.



Evaluation of phytonadione prescribing practices

Courtney Olesky, PharmD; Lucy Stanke, 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

- Design: Single-center, retrospective observational cohort
- As a quality improvement project, IRB review was not required
- Study Site: 855-bed Regional Referral Community Teaching Hospital
- Study Period: April 1 to June 30, 2019

Inclusion

- Age \geq 18 years (yr)
- Phytonadione Administered

Exclusion

- Pregnancy
- Incarcerated

Endpoints

- Primary**
- Appropriateness of reversal of bleeding
- Secondary**
- INR reduction post-phytonadione dose
 - Prevalence of adverse effects associated with phytonadione use

Definitions

- Appropriateness of reversal** Appropriate dose and route based on indication and INR according to the CHEST guidelines

Results

Baseline Characteristics	ALL N = 45	Active Bleeding N = 18	Emergent Surgery N = 15	Supra-Tx INR N = 12
Age, yr*	73 \pm 11	73 \pm 12	73 \pm 8.2	72 \pm 12.2
Male**	22 (48.9)	8 (44.4)	12 (80)	2 (16.7)
Anticoagulation with warfarin**	42 (93.3)	18 (100)	13 (87)	11 (91.6)
Anticoagulation for atrial fibrillation**	31 (68.9)	11 (61.1)	11 (80)	9 (75)
Hemoglobin, g/dL*	10.6 \pm 2.3*	10.1 \pm 2.5	11.7 \pm 3.3*	10.2 \pm 2.1

Supra-Tx INR = supra-therapeutic INR without bleeding; *mean \pm SD; **n (%); n = 44; n = 14

Active Bleeding Dosing Strategy Summary

Type of Bleed	INR Range	Dose	n (%)
Head	< 2	10 mg IV	2 (11.1)
	2 – 2.9	10 mg IV	2 (11.1)
Gastrointestinal Tract	< 2	5 mg IV	1 (5.6)
	2 – 4.99	2.5 mg PO 5 mg PO	1 (5.6) 1 (5.6)
	5 – 7.49	3 mg IV 5 mg PO 10 mg IV	1 (5.6) 1 (5.6) 3 (16.7)
Skin	2 – 4.99	5 mg PO	1 (5.6)
	> 10	10 mg IV	1 (5.6)
Nose	7.5- 9.99	1 mg IV	1 (5.6)
	> 10	5 mg PO 10 mg IV	1 (5.6) 1 (5.6)
Hepatic	5 – 7.49	10 mg IV	1 (5.6)

Emergent Surgery Dosing Strategy Summary

Dose, n (%)	
2.5 mg PO	4 (26.7)
5 mg PO	4 (26.7)
10 mg IV	4 (26.7)
10 mg PO	2 (13.3)
10 mg SQ	1 (6.7)
Multiple Doses, n (%)	
	1 (5.6)

Supra-Tx INR Dosing Strategy Summary

INR Range	Dose	n (%)
2 – 2.99	10 mg IV	1 (8.3)
5 – 7.49	5 mg PO	1 (8.3)
7.5 – 9.99	10 mg PO	2 (16.7)
>10	2.5 mg PO	1 (8.3)
	5 mg PO	4 (33.3)
	10 mg PO	1 (8.3)
	10 mg SQ	1 (8.3)
	10 mg IM	1 (8.3)

INR Reduction Post-Phytonadione

	Active Bleeding N = 18	Emergent Surgery N = 15	Supra-Tx INR N = 12
Baseline INR*	6.1 \pm 4.4	2.0 \pm 1.6	11.2 \pm 3.9
Repeat INR ordered, n (%)	18 (100)	12 (80)	12 (100)
INR at 24-hr*	1.7 \pm 0.8	1.7 \pm 0.7**	4.0 \pm 4.9
INR < 1.5 at 24-hr, n (%)	10 (58.8)	6 (50)	4 (33.3)

*mean \pm SD; **n = 12

Discussion

- Twelve patients (80%) were appropriately reversed for emergent surgery
- Six patients (50%) were appropriately reversed for Supra-Tx INR with 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 review of the anticoagulant reversal order set
- Identified need of order panel and education for INR reversal without bleeding

References

- Holbrook A, et al. Evidence-based management of anticoagulant therapy. *CHEST*. 2012; 141(2).
- Surgical Critical Care. Warfarin reversal guidelines. Available at www.surgicalcriticalcare.net/Guidelines/Warfarin%20Reversa%202017.pdf.