A Retrospective Cohort Study for Heparin Infusion Initiation and Monitoring Quality Improvement

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BACKGROUND

- In recent years, there has been increased popularity in the use of direct oral anticoagulants (DOACs) for atrial fibrillation and venous thromboembolism (VTE) due to the lack of need for frequent monitoring associated with warfarin. This is supported in the 2016 CHEST Guidelines for VTE and the 2012 CHEST Guidelines for Atrial Fibrillation.[1, 3, 4]
- However, unfractionated heparin (UFH) remains an important anticoagulant during inpatient use owing to its' favorable pharmacokinetic/pharmacodynamic properties (i.e., quick onset/offset, ease of monitoring, easily reversible).[2, 6, 7]
- Activated partial thromboplastin time (aPTT) and more frequently, anti-factor Xa assays are used as methods of monitoring for UFH. [6, 7] DOACs do not require monitoring but their mechanisms of action lead to inhibition of factor Xa, altering the anti-factor Xa assay results.[1, 5]
- When switching from a DOAC to a parenteral anticoagulant (e.g., heparin), the manufacturer suggests that the parenteral anticoagulant be initiated at the time of the next DOAC dose.
- During transition from DOAC to continuous UFH, the use of anti-factor Xa assays can lead to falsely elevated levels due to lingering DOAC effects. Thus, it is more appropriate to use an aPTT assay in these cases.[2,3]
- Currently, within the Saint Luke's Health System (SLHS), the time of previous DOAC administration is unknown, leading to inappropriate timing of initiation of continuous UFH infusions and monitoring.

STUDY PURPOSE

- The purpose of this study is to evaluate the appropriateness of continuous UFH infusion initiations in patients with recent DOAC exposure prior to admission and the appropriateness of monitoring during admission within SLHS.

STUDY DESIGN

- A retrospective single center electronic medical record review was performed on patients with recent DOAC exposure initiated on a continuous UFH infusion during the time period from September 1, 2018 to April 30, 2019.

STUDY POPULATION

- **Inclusion Criteria:**
  - Patients on DOAC therapy prior to admission
  - Patients receiving continuous UFH infusion within 12 hours after last known dose of apixaban or within 24 hours of last known dose of rivaroxaban
  - Patients initiated on an acute coronary syndrome (ACS), venous thromboembolism (VTE) or atrial fibrillation (Afib) continuous UFH infusion order sets
- **Exclusion Criteria:**
  - Unknown time of last dose of home DOAC
  - Patient was on anticoagulant other than apixaban or rivaroxaban

STUDY ENDPOINTS

- **Primary Endpoint:**
  - Number of patients admitted to SLHS with recent DOAC exposure (<12 hours for apixaban, <24 hours for rivaroxaban) and inappropriately initiated on continuous UFH infusion
- **Secondary Endpoint:**
  - Number of patients with recent DOAC exposure (<72 hours) initiated on continuous UFH infusion with inappropriate monitoring (i.e., use anti-factor Xa assay instead of aPTT)

RESULTS

- **Primary Endpoint:**
  - n = 42 patients met the study criteria
  - 9.5% (n = 4) DOAC were inappropriately initiated on continuous UFH infusion
    - None of these patients exhibited signs of bleeding
- **Secondary Endpoints:**
  - 59.5% (n = 25) were inappropriately monitored during continuous UFH infusion
    - Of these, 44% (n = 11) had a supra-therapeutic (>0.7 IU/mL) anti-factor Xa assay
    - Of these, 25% (n = 5) had a critical (>1.1 IU/mL) anti-factor Xa assay

CONCLUSION

- During the study period, the incidence of inappropriate continuous UFH infusion initiation was infrequent (9.5%, n = 4).
- The incidence of inappropriate monitoring during continuous UFH infusions were noteworthy (59.5%, n = 25), which led to incorrect adjustments of the infusion rates.
- Adverse outcomes were not observed.
- This study indicates a need for further investigation into a larger patient population over a longer period of time.
- SLHS continuous UFH infusion order sets have been modified to provide aPTT monitoring in patients with recent DOAC exposure to facilitate more appropriate monitoring.

SELECTED REFERENCES

1. Macedo KA, Tatarian P, Eugenio K. Influence of direct oral anticoagulants on anti-factor Xa measurements utilized for monitoring heparin. *Annals of Pharmacotherapy.* 2018;52:e154-e159.
2. Centeno EH, Militello M, Comes MP. anti-factor Xa assays: What is their role today in antithrombotic therapy?. *Cleveland Clinic Journal of Medicine.* 2019;86:e417-e425.
3. Faust AC, Kanyer D, Wittkowsky AK. Managing transitions from oral factor Xa inhibitors to unfractionated heparin infusions. *ASHP.* 2016;73:e2037-e2041.
4. Antithrombotic Therapy for VTE Disease: CHEST Guidelines and Expert Panel Report. *CHEST.* 2016;149:3.15-352.
5. Douxfils J, Ageno W, Samama C, et. al. Laboratory testing in patients treated with direct oral anticoagulation: a practical guide for clinicians. *Journal of Thrombosis and Haemostasis.* 2017;16(2):209-219.
6. Hirsh J, Warkentin TE, Shaughnessy SG, et al. Heparin and low-molecular-weight heparin: mechanisms of action, pharmacokinetics, dosing, monitoring, efficacy and safety. *CHEST.* 2001; 119(Suppl 1):64S-94S.
7. Whitman-Purves E, Coons JC, Miller T, et al. Performance of Anti-Factor Xa Versus Activated Partial Thromboplastin Time for Heparin Monitoring Using Multiple Nomograms. *Clinical and Applied Thrombosis/Hemostasis.* 2017;24(2): 310-316.

AUTHORS' DISCLOSURES

- The authors have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interested in the subject matter.