

# Utilising anti-Xa for monitoring therapeutic heparin during COVID-19



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#### INTRODUCTION

- Patients with COVID-19 in intensive care have a high incidence of thrombotic events such as strokes, pulmonary embolism, cutaneous and alveolar micro-thromboses.<sup>1</sup>
- COVID-19 can lead to **abnormalities of coagulation parameters** which can affect the monitoring methods used for heparin.<sup>1</sup>
- ▶ It has been found that APTTr monitoring for heparin in COVID-19 patient could lead to the use of higher doses of heparin and bleeding complications.¹
- Anti-Xa monitoring led to a reduced number of dose adjustments and length of time to reach therapeutic anticoagulation compared to APTTR.<sup>2</sup>
- Anti-Xa monitoring for heparin in COVID-19 patient has been found to be a more accurate method for monitoring heparin dosing than APTTr in COVID-19 patients.<sup>1,2</sup>

#### **AIMS & OBJECTIVES**

- ► To analyse and compare APTTr versus anti-Xa during therapeutic heparin monitoring in critical care patients with COVID-19
- To assess compliance with a new anti-Xa heparin monitoring protocol using the following standards (expected 100%). COVID-19 positive patients in critical care prescribed heparin:
  - 1. Should have an **Anti-Xa level test 5-7 hours after starting the infusion (target 6 hours)**
  - 2. Should have the correct dose alteration in response to the Anti-Xa levels
  - 3. Should have received an adjustment of the heparin infusion rate within 2 hours of the Anti-Xa level result

### **METHODS**

Ethical approval was not required for this project as the anti-Xa innovation was classified as service evaluation and improvement. The audit was logged following the standard Trust governance procedure.



Anti Xa Vs APTTr comparison study

- ➤ Anti-Xa levels and APTTr were requested on each blood sample taken for routine monitoring of therapeutic heparin between April and December 2020 inclusive.
- ➤ A retrospective cohort analysis of unfractionated heparin anti-Xa levels and APTTr was performed on data extracted from the electronic clinical information system for critical care (Philips ICCA)
- ► The reference ranges used were ≥0.5 to <0.8 and ≥1.5 to <2.5 respectively.
- Only results for patients who also tested positive for COVID-19 by PCR were included for analysis
- ▶ Results were mapped against the respective dosing titration protocols to determine whether the result dictated an increase, decrease or no change in the heparin rate



Unfractionated heparin titration protocol audit

- ► Audit data were collected for all patients retrospectively identified as having received heparin and with a positive COVID-19 PCR in critical care from April to June 2020 inclusive using Phillips ICCA and ICE.
- ➤ The audit tool was piloted on 2 patients and minor adjustments made
- Scanned copies of the paper heparin charts were retrieved from the patient management system (Careflow EPR)

## **RESULTS**

From April 2021 to June 2021 inclusive, records of 13 patients were audited against the required standards (Figure 1). The 13 patients had 59 anti-Xa results reported. Only 38 of these had a time documented against the subsequent action taken by the nurse. One patient was excluded from standard 1 as there was no infusion initiation time recorded

482 paired samples (anti-Xa and APTTr processed from the same tube) were reported for 24 patients with confirmed COVID-19 infection on a therapeutic heparin infusion April 2021 to December 2021 inclusive (Figure 2). The mean number of samples per course of treatment was 20.

Standard 3: 100% should have received an adjustment of the heparin infusion rate within 2 hours of the Anti-Xa level result (n=38)

Standard 2: 100% should have the correct dose alteration in response to the Anti-Xa levels (n=59)

Standard 1: 100% should have an Anti-Xa level test 5-7 hours after starting the infusion (n=12)



1.8 Notable disparity -Using Agreement between Anti-Figure 1: Performance Xa and APTTr: no change anti-Xa no change needed to 1.6 against audit standards heparin rate; using APTTr, needed to heparin rate dose increase needed. 1.4 Figure 2: Paired tests on individual blood samples. 1.2 (Therapeutic range –APTTr: 1.5-2.5; Anti-Xa: 0.5-0.8) **Anti-Xa** 8.0 0.6 0.4 0.2 1.5 0.5 4.5 2.5 3.5 **APTTr** 

- ➤ 55% of paired samples resulted in conflicting advice regarding dose amendments depending on whether Anti-Xa or APTTr was used
- ➤ 35% of samples were in range for Anti-Xa whilst using APTTr suggested increasing the dose
- 6% of paired samples recommended opposite actions, using Anti-Xa a dose reduction; APTTr a dose increase

## **CONCLUSIONS**

- The project found a higher discordance rate (55%) than reported in the literature (49%)<sup>2</sup>.
- The higher discordance rate potentially highlights the decreased reliability of APTTr due to COVID-19 and suggests that the use of APTTr monitoring would have led to significantly higher rates of heparin in COVID-19 patients.
- ► The audit demonstrated that although 100% adherence was not achieved for any of the standards, there is a high level of adherence to the new guideline in critical care.
- ► The audit has highlighted that the process of result acknowledgement needs to be improved regardless of whether it necessitates a change in rate or not.

# REFERENCES

- Adie SK, Farina N. Impact of COVID-19 on monitoring of therapeutic unfractionated heparin [published online ahead of print, 2020 Aug 19]. *Journal of Thrombosis and Thrombolysis*. 2020;1-3. <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7437961/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7437961/</a>. (accessed 14/11/21).
- 2. Whitman-Purves E, Coons JC, Miller T, DiNella JV, Althouse A, Schmidhofer M, Smith RE. Performance of Anti-Factor Xa Versus Activated Partial Thromboplastin Time for Heparin Monitoring Using Multiple Nomograms. Clin Appl Thromb Hemost. 2018; 24(2):310-316.

## **CORRESPONDANCE**

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