



Institutional Repository - Research Portal

Dépôt Institutionnel - Portail de la Recherche

researchportal.unamur.be

RESEARCH OUTPUTS / RÉSULTATS DE RECHERCHE

Heparin Calibrated Anti-Xa Assays for the Measurement of Low Levels of Direct Factor Xa Inhibitors

Sabor, Lina; Raphaël, Mélanie; Dogne, Jean-Michel; Mullier, François; Douxfils, Jonathan

Published in:
Research and practice in thrombosis and haemostasis

Publication date:
2017

Document Version
Publisher's PDF, also known as Version of record

[Link to publication](#)

Citation for published version (HARVARD):
Sabor, L, Raphaël, M, Dogne, J-M, Mullier, F & Douxfils, J 2017, Heparin Calibrated Anti-Xa Assays for the Measurement of Low Levels of Direct Factor Xa Inhibitors. in Research and practice in thrombosis and haemostasis: Abstracts of the XXVI Congress of the International Society on Thrombosis and Haemostasis, July 8–13, 2017. vol. 1, pp. 1044, Berlin, Germany, 8/07/17.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

PB 2151 | Heparin Calibrated Anti-Xa Assays for the Measurement of Low Levels of Direct Factor Xa Inhibitors

L. Sabor¹, M. Raphaël², J.-M. Dogné², F. Mullier², J. Douxfils²

¹CHU UCL Namur, Namur Thrombosis and Hemostasis Center (NTHC), Université Catholique de Louvain, Hematology Laboratory, Yvoir, Belgium, ²University of Namur, Namur Thrombosis and Hemostasis Center (NTHC), Department of Pharmacy, Namur, Belgium

Background: Apixaban, edoxaban and rivaroxaban do not require frequent monitoring but an assessment of the intensity of anticoagulation may be required in emergent or elective surgery. Some experts reported that anti-Xa activity below 0.1 IU/mL using heparin calibrated chromogenic assays may assert the absence of clinically relevant (i.e. < 30 or < 50 ng/mL depending on the clinical situation) direct factor Xa levels. However, it is not clear if difference in response will depend on the anti-Xa agent and also on the chromogenic anti-Xa kit used to assess the anti-Xa activity.

Aims: To assess if a cut-off of 0.1 UI anti-Xa/mL is able to exclude apixaban, rivaroxaban or edoxaban concentration < 30 ng/mL or < 50 ng/mL using different heparin calibrated chromogenic anti-Xa kits.

Methods: Apixaban, edoxaban and rivaroxaban were added to normal pooled plasma at increasing concentrations ranging from 0 to 500 ng/mL. Anti-Xa activities were measured using

- (1) STA®-Liquid Anti-Xa (STA®LAX) on a STA-R Evolution Coagulometer,
- (2) Biophen®Heparin LRT (BP®LRT) on a STA-R Evolution coagulometer and
- (3) Hemosil®-Liquid Anti-Xa (IL®LAX) on a ACL-TOP 700 according to manufacturer recommendations.

Results: At 30 ng/mL of rivaroxaban, BP®LRT, STA®LAX and IL®LAX provided anti-Xa results >0.1 IU/mL. At 30 ng/mL of apixaban or edoxaban, BP®LRT and IL®LAX were below the cut-off but the STA®LAX was not. At a concentration of 50 ng/mL, only edoxaban with the BP®LRT kit showed an anti-Xa activity < 0.1 UI/mL.

Conclusions: Low (< 0.1 IU/mL) anti-Xa activity is not safe to exclude clinically relevant direct factor Xa levels and should be avoided. It can only inform if the drug is present or not. Chromogenic anti-Xa assays calibrated against the appropriate agent and using the appropriate

TABLE 1 Anti-Xa activities using STA®LAX on a STA-R Evolution Coagulometer, BP®LRT on a STA-R Evolution coagulometer and (3) IL®LAX on a ACL-TOP 700

| concentration (ng/mL) | anticoagulant | STA®LAX (UI/mL) | BP®LRT (UI/mL) | IL®LAX (UI/mL) |
|-----------------------|---------------|-----------------|----------------|----------------|
| 30 | Rivaroxaban | 0,19 | 0,12 | 0,08 |
| 30 | Apixaban | 0,09 | 0,03 | 0,04 |
| 30 | Endoxaban | 0,07 | 0,02 | 0,02 |
| 50 | Rivaroxaban | 0,45 | 0,34 | 0,16 |
| 50 | Apixaban | 0,17 | 0,10 | 0,07 |
| 50 | Endoxaban | 0,13 | 0,06 | 0,04 |

procedure remains the more accurate method to assess accurately low levels of direct FXa inhibitors.

PB 2152 | Efficacy of a Novel Contact Pathway Inhibitor, Ir-CPI, on in vitro Clotting Induced by PCI Catheter Segment

J. Douxfils¹, D. Gheldof¹, S. Derochette², J. Tassignon², C. Meinguet², M. Guyaux², J.-M. Dogné¹, E. Godfroid²

¹University of Namur, Pharmacy, Namur, Belgium, ²Bioxodes, Marche-en-Famenne, Belgium

Background: Ir-CPI, a protein derived from the tick *Ixodes ricinus* salivary, is a serine protease inhibitor of both factor XIa (FXIa) and FXIIa. In patients undergoing percutaneous coronary intervention (PCI), catheter thrombosis may occur as catheters trigger activation of FXII/FXI. **Aims:** The aim of this study was to evaluate the effect of Ir-CPI on in vitro clotting induced by PCI catheter segment.

Methods: Catheter segments were pressed flat, shaped into rings and placed around the perimeter of wells (96-well plate), leaving the center of the well unobstructed. To the wells were added serial dilution of Ir-CPI (until 10 µM) with normal pooled plasma (NPP) or plasmas deficient in FXI or FXII. After incubation at 37°C and addition of a CaCl₂ solution, clot formation was assessed by monitoring absorbance at 340nm. Time to reach one-half maximal absorbance (IC50) was defined as the clotting time. Thrombin generation test (TGT) was also assessed using catheter segment as trigger of the process. Positive inhibitory controls were used (fondaparinux, enoxaparin).

Results: Presence of the catheter reduced the clotting time of NPP; an effect reversed by the addition of Ir-CPI. At high concentrations (> 5µM), Ir-CPI allowed to overpass the clotting time without catheter. On TGT (Fig 1), catheter segments decreased lag time and time

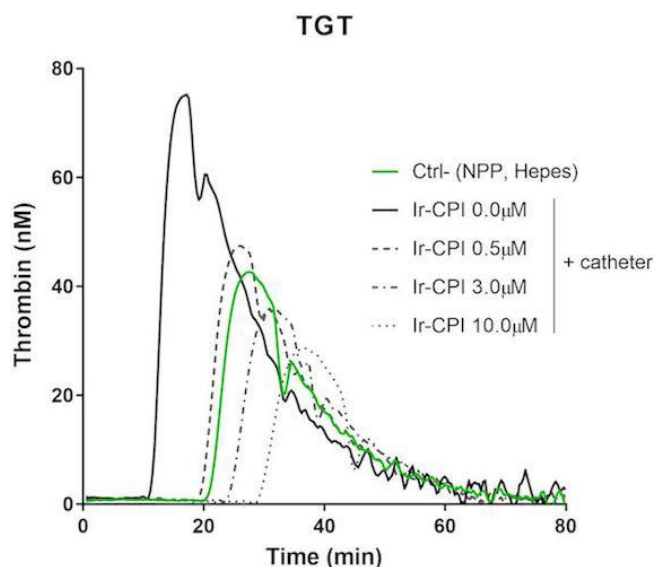


FIGURE 1 Effect of Ir-CPI on Thrombin Generation Time (TGT) in NPP exposed to PCI catheter segments