Dabigatran: How to Manage Bleeding, Surgery and Overdose - Full Clinical Guideline - DERBY

Reference no.: CG-T/2014/165

1. Introduction

Dabigatran is a Direct Oral Anticoagulatnt which acts as a direct thrombin inhibitor. It is indicated for the treatment and secondary prevention of Venous Thromboembolism, and the prevention of stroke in non-valvular atrial fibrillation. Bleeding is a recognised complication.

2. Aim and Purpose

This document describes how to manage bleeding and surgery in patients taking Dabigatran; or who have taken an overdose of Dabigatran.

3. Definitions, Keywords

PT – Prothrombin Time; APTT – Activated Partial Thromboplastin Time; INR – International Normalized Ratio; TT – Thrombin Time; eGFR – estimated Creatinine Clearance; FBC – Full Blood Count

4. Bleeding.

- **Stop dabigatran.** Document the time of the last dose.
  - Dabigatran has peak levels 2 – 3 hours after ingestion
  - It is predominantly renally excreted (80%).
  - GFR > 80ml/min: half-life 13 hours.
  - GFR 30 - 50: half life 18 hours.
  - GFR < 30: half life 22 – 35 hours
  - Dabigatran **is** dialyzable
  - If taken within 2 hours consider activated charcoal. Dabigatran is dialysable

- **Check the Prothrombin Time (PT), APTT, Thrombin Time (TT), eGFR and FBC**.
- **Use the Cockcroft Gault formula to calculate the Creatinine Clearance.**

- **The Thrombin Time is sensitive to Dabigatran. If the TT is normal the Dabigatran level is likely to be very low.**

- **The APTT may be prolonged by dabigatran but gives only a rough estimate of the level of anticoagulation. In some patients the APTT is normal at therapeutic levels.**
- **Consider other causes of abnormal PT and/or APTT**.
- **The PT is insensitive to dabigatran.**
- **Fibrinogen results may be falsely low with dabigatran.**

Management should be individualised according to the severity and location of the bleed, as below:

Minor bleeding:
Local haemostatic measures (where possible).
Consider tranexamic acid orally (25 mg/kg TDS), IV (15mg/kg) and/or topically (e.g. mouthwash, nasal drops, applied directly to a bleeding point). Delay next dose of dabigatran, or discontinue.

Major bleeding:
Local haemostatic measures (where possible).
Give tranexamic acid IV (15 mg/kg) and/or topically (mouthwash, nasal drops, applied directly to bleeding point).
Give fluid replacement; maintain good urine output (dabigatran is 80% renally excreted).
Give blood product support as indicated by Hb, other coagulopathy, platelets (if count< 75 x 10^9/L or antiplatelet agents).
Consider haemodialysis.
In on-going life or limb threatening bleeding: Consider Idarucizumab (Praxbind):
Praxbind (2x2.5 g/50 mL) is administered intravenously as two consecutive infusions over 5 to 10 minutes each or as a bolus injection. Suggest discuss with on-call haematologist.

5. Surgery/interventional radiology procedures.

Risk of bleeding depends on:
Timing of last dose
Renal function
Type of surgery/procedure

Planned Surgery: Usual time to discontinue Dabigatran before surgery or invasive procedures for which anticoagulation needs to be stopped. (h = hours)

Renal function (CrCl, ml/min)	Estimated half-life (h)	Low bleeding risk (h)	High bleeding risk (h)
≥80	13	24	48
≥50 to <80	15	24–48	48–72
≥30 to <50	18	48–72	96

Emergency surgery:

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- GFR 30 - 50: half life 18 hours.
- GFR < 30: half life 22 – 35 hours
- Dabigatran **is** dialyzable
- If taken within 2 hours consider activated charcoal. Dabigatran is dialyzable

- **Check the Prothrombin Time (PT), APTT, Thrombin Time (TT), eGFR and FBC**.
- **Use the Cockcroft Gault formula to calculate the Creatinine Clearance.**

- **The Thrombin Time is sensitive to Dabigatran. If the TT is normal the Dabigatran level is likely to be very low.**

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- **Consider other causes of abnormal PT and/or APTT**.
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Risk of bleeding depends on:
Timing of last dose
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Type of surgery/procedure

Discuss delaying surgery:
- If > 12 hours delay possible – see table above for elective surgery.
- If 4 – 12 hours delay possible consider dialysis.
- If immediate surgery necessary consider Idarucizumab (Praxbind): Praxbind (2x2.5 g/50 mL) is administered intravenously as two consecutive infusions over 5 to 10 minutes each or as a bolus injection. Suggest discuss with on-call haematologist.

6. Overdose

- **Stop dabigatran.** Document the time of the last dose.
  - Dabigatran has peak levels 2 – 3 hours after ingestion
  - It is predominantly renally excreted (80%).
  - GFR > 80ml/min: half-life 13 hours.
  - GFR 30 - 50: half life 18 hours.
  - GFR < 30: half life 22 – 35 hours
  - Dabigatran **is** dialyzable
  - If taken within 2 hours consider activated charcoal. Dabigatran is dialyzable
  - Maintain BP and urine output (dabigatran is 80% renally excreted)
  - Monitor APTT and TT until normal

- **Check the Prothrombin Time (PT), APTT, Thrombin Time (TT), eGFR and FBC**.
- **Use the Cockcroft Gault formula to calculate the Creatinine Clearance.**

- **The Thrombin Time is sensitive to Dabigatran. If the TT is normal the Dabigatran level is likely to be very low.**

- **The APTT may be prolonged by dabigatran but gives only a rough estimate of the level of anticoagulation. In some patients the APTT is normal at therapeutic levels.**
- **Consider other causes of abnormal PT and/or APTT**.
- **The PT is insensitive to dabigatran.**
- **Fibrinogen results may be falsely low with dabigatran.**

If bleeding see bleeding protocol above.

7. References (including any links to NICE Guidance etc.)

Guideline on the management of bleeding in patients on antithrombotic agents: Makris, M et al, BCSH guideline, BCSH website, November 2012

Peri-operative management of anticoagulation and antiplatelet therapy. David Keeling, R. Campbell, Tait, Henry Watson on behalf of the British Committee of Standards for Haematology. First published: 07 October 2016 https://doi.org/10.1111/bjh.14344

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Straingier J, Rathgen K, Stahle H, et al. Influence of renal impairment on the pharmacokinetics and pharmacodynamics of oral dabigatran etexilate. Clin Pharmacokinet 2010;49:259-268.

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8. Documentation Controls

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