Dabigatran etexilate

Management of bleeding complications for patients taking this medication

Dabigatran etexilate is an oral direct thrombin inhibitor. It has been approved by the FDA for use in atrial fibrillation, following a study published in 2009 which suggested it was as efficacious and had a better safety profile than warfarin, in terms of bleeding risk. [1] Dabigatran is a small molecule that shows low plasma protein binding. It is excreted predominantly through renal clearance mechanisms, and does not affect cytochrome P450 drug metabolizing enzymes. These characteristics result in a predictable pharmacokinetic profile, which allows for a fixed dose regimen without the need for routine coagulation monitoring.

For a patient on dabigatran who experiences severe or life threatening bleeding, management will be challenging due to the lack of a specific reversal agent for this medication. Plasma administration will be ineffective in reversing the effect of the drug. The thrombin time (TT) will be prolonged if there is dabigatran in the plasma sample. (The thrombin time will also be prolonged if heparin is present in the sample, or if serum fibrinogen concentration is low). The activated partial thromboplastin time (aPTT) is relatively insensitive within the range of plasma concentration of dabigatran used at normal doses, but may be helpful in providing a qualitative indication of anticoagulant activity in overdose situations. The prothrombin time (PT) typically shows poor correlation to the plasma concentration of dabigatran. The University of Washington coagulation laboratory has a modified thrombin time, ordered as a direct thrombin inhibitor test, which is available 24/7 and can be used to assess dabigatran concentration in the plasma. If the patient has ingested a dose of the medication within 2 hours of presentation, oral charcoal may be of use. The half life of dabigatran in a patient with normal renal clearance is 12 hours. Thus dialysis may be useful. Dialysis has been determined to remove 62% of the drug at 2 hours and 68% at 4 hours. Data to suggest that agents such as recombinant factor VIIa or prothrombin complex concentrates may be of benefit in stopping bleeding exists in in-vitro or animal models only. Whether these agents will be of use to the bleeding patient on dabigatran is currently unknown.[2]

References:

1. Connolly SJ, Ezekowitz MD, Yusuf S, et al; the RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139-1151.

2. Van Ryn J, Stangler J, Haertter S, et al. Dabigatran etexilate- a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity. Thromb Haemost 2010;103: 1-11.

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