

# RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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## Comparing dabigatran and rivaroxaban

Two emerging anticoagulants look set to finally make significant in-roads into clinical practice in areas that have long been dominated by warfarin and enoxaparin.

Rivaroxaban is an oral agent that competitively and reversibly inhibits activated Factor Xa. Dabigatran is a competitive reversible antagonist of thrombin. While both appear to offer potential advantages over the current commonly-used anticoagulants such as warfarin and enoxaparin, the efficacy of the two drugs in relation to each other has not yet been tested.

Recently an indirect comparative analysis has been performed, using existing published and unpublished data from studies comparing either dabigatran or rivaroxaban with enoxaparin in elective orthopaedic surgery (total hip and knee replacements). The random effects meta-analysis technique was used to calculate pooled relative risks (RRs) for various outcomes, including risk for all venous thromboembolism (VTE), which included deep venous thromboembolism, non-fatal pulmonary embolism, and all-cause mortality, as well as haemorrhagic events (major and clinically relevant non-major bleeds).

The adjusted indirect comparison suggested that rivaroxaban was superior to enoxaparin for the prevention of venous thromboembolism (RR 0.56, 95% CI 0.43-0.73,  $P < 0.0001$ ), but this was accompanied by a trend for increased haemorrhage (RR 1.26, 95% CI 0.94-1.69,  $p = 0.13$ ). Dabigatran was not superior to enoxaparin for prevention of VTE (RR 1.12, 95% CI 0.97-1.29,  $P = 0.12$ ), and did not influence haemorrhage risk (RR 1.10, 95% CI 0.90-1.35,  $P = 0.32$ ). Adjusted indirect comparison suggested that rivaroxaban was superior to dabigatran in preventing VTE, RR 0.50 (95% CI 0.37-0.68), but that rivaroxaban might also be associated with a trend towards increased haemorrhage RR 1.14 (95% CI 0.80-1.64).

While both drugs have been separately compared to the efficacy of warfarin for preventing stroke induced by atrial fibrillation, and both appear to be non-inferior (and probably more effective) compared to conventional warfarin management, there has been no direct comparison between rivaroxaban and dabigatran in this setting. An indirect comparison of these studies using currently available published data unfortunately may not provide clear answers either, as the rivaroxaban study (ROCKET-AF) enrolled significantly sicker patients than the equivalent rivaroxaban study (RE-LY) and was run as a blinded trial (whereas RE-LY was not blinded).

There is no compelling reason to switch patients already stable on warfarin. Factors apart from efficacy, such as cost, and further clinical experience in patients with poor renal function, will also play a part in dictating future clinical direction.

This E-Bulletin is based on work by Greg Roberts, Senior Research Pharmacist, RGH

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