Aspirin for secondary prevention of VTE after warfarin prophylaxis is discontinued

Compared with placebo, ongoing low-dose daily aspirin substantially reduced the risk of recurrence of VTE in people who had already completed 6 to 18 months of oral anticoagulation, with no increased risk of major bleeds.

Overview: People who experience an episode of VTE are offered treatment with an anticoagulant drug for a period afterwards. Deciding the duration of treatment needs a balance to be struck between the risk of VTE recurring and the increased risk of bleeding associated with the drug treatment. The risk of recurrence of VTE after thromboprophylaxis ceases is particularly high in people with so-called 'unprovoked' VTE: that is, VTE in the absence of an antecedent and transient major clinical risk factor (for example surgery, trauma, substantial immobility and pregnancy or puerperium, or treatment with oral contraceptives or hormone replacement therapy).

Current advice: NICE advises that people with confirmed proximal deep vein thrombosis or pulmonary embolism, who do not have active cancer, should be offered 3 months' treatment with a vitamin K antagonist (such as warfarin). Treatment beyond 3 months should be offered to people with an unprovoked pulmonary embolism and may be considered in people with unprovoked deep vein thrombosis, taking into account the risk of VTE recurrence and of bleeding.

New evidence: The WARFASA randomised controlled trial (Becattini et al, 2012) assessed whether aspirin prophylaxis could reduce VTE recurrence in 402 adults who had had their first unprovoked deep vein thrombosis or pulmonary embolism and who had completed 6 to 18 months' treatment with a vitamin K antagonist (target INR 2.0–3.0). About two-thirds had received prophylaxis for longer than 6 months. They were randomised to receive aspirin 100 mg daily or placebo for a median of about 2.5 years.

VTE recurred in 6.6% of the aspirin-treated group per year, compared with 11.2% of the placebo group (hazard ratio 0.58, 95% confidence interval 0.36 to 0.93, p=0.02). There were no fatal bleeding events, and non-fatal major bleeding occurred in 1 person in each group. Bleeding that did not meet the criteria for major bleeding but that needed medical intervention occurred in 3 people in each group.

This study suggests that low-dose aspirin may be an effective option for ongoing prophylaxis after initial prophylaxis with a vitamin K antagonist such as warfarin, with a low risk of serious bleeding (although the authors note this risk might be higher in a real-world situation). It has some limitations: the results cannot be applied to people with cancer, clinically significant thrombophilia or a bleeding event during anticoagulant therapy, because these were among the study's exclusion criteria. In addition, it did not have sufficient statistical power to detect a difference in rates of death or events such as myocardial infarction or stroke. A combined analysis is planned of WARFASA and a similar trial, the ASPIRE study, which has now closed after recruiting more than twice as many people as WARFASA. This may provide more and better evidence on this question.

Commentary: Platelets have a key role in arterial thrombus formation and antiplatelet agents have a recognised role in secondary thromboprophylaxis. However, the role of aspirin in primary prevention of VTE remains controversial and is surprisingly under-investigated in secondary prevention of VTE. This study suggests an approximate 40% risk reduction for recurrent VTE.
in patients treated with aspirin after unprovoked VTE compared with placebo. Standard intensity warfarin and the newer oral anticoagulants are associated with a risk reduction of more than 80%. Although aspirin may appear inferior to oral anticoagulants in these indirect comparisons, one might consider using aspirin in patients with a higher bleeding risk or who are deemed unsuitable for oral anticoagulants or on the grounds of affordability. If the results of this study are reproduced in the ASPIRE study, aspirin may find that it has a new role in prevention of VTE recurrence”. – Dr Will Lester, Haematology Consultant Queen Elizabeth Hospital and Birmingham Women’s Hospital and Honorary Senior Clinical Lecturer in the School of Clinical and Experimental Medicine, College of Medical and Dental Sciences, University of Birmingham.

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