Protein Z-dependent protease inhibitor W303X mutation in venous thrombosis: response to Gonzalez-Conejero et al

In reply to the study by Gonzalez-Conjero et al, we found their results on 218 Spanish White patients very interesting. As suggested in their article, there does indeed appear to be an ethnic bias and possible founder affect with regard to the W303X mutation in thrombosis patients. The frequency of both the Factor V Leiden mutation and the prothrombin 20210A variant also varies within White populations. The allelic frequencies for the factor V Leiden mutation in White subpopulations ranges from <1% to 8.5% (Zivelin et al, 1997) and appears to be absent or in very low frequencies in non-European White people and totally absent in other ethnic groups (Rees et al, 1995). The 250 patients and 250 control subjects used in our study (Van de Water et al, 2004) were European White people of whom >90% were of northern European origin (McKinnon et al, 1997) with a strong influence from UK immigration. In our study we also identified another stop codon mutation (R67X) in three of our thrombosis patient cohort (n = 250). It is unfortunate that Gonzalez-Conjero et al. did not extend their study to include the R67X mutation within the ZPI gene as well. Further studies of ZPI mutations in thrombosis patient populations are required, especially those in patients of northern European background, to evaluate the role of protein Z-dependent protease inhibitor in haemostasis and thrombosis.

Paul Harper

Department of Haematology, Auckland City Hospital, Auckland, New Zealand.
E-mail: paulh@adhb.govt.nz

References


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Bone marrow biopsy in thrombocytopenic or anticoagulated patients

Bone marrow aspiration and trephine biopsy are performed in an estimated 10 000 patients each year in the UK (Bain, 2004). A recent postal survey of members of the British Society for Haematology suggested that these procedures are generally safe, with adverse events being reported in only one per 1000 procedures (Bain, 2003, 2004). However, while complications

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are rare, they may be serious, and fatal outcomes have been reported (Le Dieu et al, 2003; Morley & Makris, 2003; Bain, 2004). The most frequently reported serious adverse event is bleeding. Patients with thrombocytopenia or receiving anticoagulant therapy with heparin or warfarin are likely to be at increased risk of bleeding following bone marrow biopsy but the optimal management of these patients at the time of the procedure is uncertain.

Following the recent death of an Australian patient, who experienced a massive retroperitoneal haemorrhage after bone marrow aspirate and trephine biopsy was performed during warfarin therapy with an International Normalised Ratio (INR) of 1.9, an email survey was conducted of members of the Australasian Society of Thrombosis and Haemostasis and the Hematology Society of Australia and New Zealand, to document current approaches to performing bone marrow biopsy among thrombocytopenic or anticoagulated patients. Recipients of the survey were also asked whether written informed consent was routinely obtained prior to bone marrow biopsy.

A total of 104 of more than 400 persons on the Societies’ mailing lists responded to the survey. Most responses were from Australian or New Zealand haematologists but replies were also received from Cambodia, Singapore and the UK.

The results are summarised in Table I. Most respondents indicated that they did not routinely transfuse platelets prior to bone marrow biopsy in thrombocytopenic patients. Approximately 20% stopped or reversed warfarin prior to biopsy, 10% performed a biopsy irrespective of the INR, and the remainder performed a biopsy as long as the INR was ‘acceptable’. Approximately two of three respondents routinely obtained written informed consent prior to bone marrow biopsy.

This survey demonstrated a broad range of practices among haematologists who perform bone marrow biopsy in thrombocytopenic or anticoagulated patients. The widespread practice of performing a biopsy without platelet support or during warfarin therapy suggests that most haematologists do not consider thrombocytopenia or anticoagulation to be important risk factors for bleeding following bone marrow biopsy.

Our survey has several limitations. First, those members of the Australasian Society of Thrombosis and Haemostasis and the Hematology Society of Australia and New Zealand who have previously experienced complications of bone marrow biopsy may have been less likely to respond to our survey. Secondly, haematologists may avoid performing a bone marrow examination or trephine biopsy in thrombocytopenic or anticoagulated patients. This information was not captured in the survey.

Preventing adverse events after bone marrow biopsy is important for individual patients as well as public health. Extrapolating the UK data, it is likely that hundreds of thousands of bone marrow biopsies are performed worldwide each year. Assuming a complication rate of 0.1% (probably an underestimate because adverse events are often under-reported), hundreds of adverse events occur worldwide each year. Accurate data on the incidence of complications following bone marrow biopsy in thrombocytopenia and anticoagulated patients are required so that appropriate management guidelines can be developed.

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John W. Eikelboom

Department of Medicine, McMaster University, Hamilton, Canada.
E-mail: eikelb@mcmaster.ca

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