LETTER TO THE EDITOR

Warfarin and heterotopic ossification: good, bad or ugly?

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In their interesting systematic review of treatments for heterotopic ossification (HO) after spinal cord injury, Teasell *et al.*¹ considered warfarin treatment as a potential prophylactic measure for inhibiting HO. They report a favourable effect of warfarin on HO, referring to a single retrospective study,² which reported a significant association between warfarin administration and lack of HO.

Specifically, in 227 spinal cord injury patients, 34 patients treated with warfarin for about 5 weeks for deep vein thrombosis did not develop HO, while none of the 34 patients who developed HO was treated with warfarin. According to this study, the positive effect of warfarin should depend on its inhibition of bone matrix formation.

We would like to point out that no other studies after 1992 have suggested a protective role of warfarin in extraskeletal calcification. In contrast, many studies have demonstrated that warfarin can induce cardiovascular calcifications.³ Besides blocking carboxylation of coagulation factors through vitamin K inhibition, warfarin acts on other extrahepatic gamma-carboxyglutamic (Gla) proteins, whose activity is also regulated by vitamin K-dependent carboxylation. These proteins include matrix Gla protein (MGP) and osteocalcin, or bone Gla protein (BGP). Impairment of the function of MGP and BGP results in an increased risk for developing vascular calcification and osteoporosis, respectively, which are the possible side effects of warfarin treatment and have been demonstrated in animal experiments and in clinical practice.³ One way of interpreting the results of the study by Buschbacher *et al.*² is that in the short

term warfarin treatment could be protective by blocking osteocalcin in the presence of pro-inflammatory factors or in the event of a reduction of calcification inhibitors that would favour the ossification process. However, although the results of the study by Buschbacher *et al.*² are intriguing, stronger evidence should be provided for considering warfarin as a potential inhibitor of ossification. In the meantime, it should be kept in mind that long-term warfarin treatment poses high risks of cardiovascular calcification and osteoporosis, besides the well-known risk of bleeding.

Conflict of interest

The authors declare no conflict of interest.

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