Venous thromboembolism chemoprophylaxis in traumatic brain injury: is a conservative approach justified?

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Intensive care medicine demands the near constant management of risk, which in any given clinical scenario is frequently limited by a paucity of evidence. In such circumstances, clinicians commonly rely on anecdote, legacy, plausibility, expert consensus, and key stakeholder opinion, which promote conformity and potentially limit recrimination. However, this may also suppress critical thinking and impede practice change. Although countless different scenarios exist, the timing of venous thromboembolism (VTE) chemoprophylaxis following traumatic brain injury (TBI) is a commonly encountered and intensely debated example.

Current international recommendations provide little guidance, with the latest Brain Trauma Foundation guidelines stating: "There is insufficient evidence to support recommendations regarding the preferred agent, dose, or timing of pharmacologic prophylaxis for deep vein thrombosis".[1] Indeed, the validity of this statement is supported by a recent systematic review[2] that included 17 studies, only one of which was a randomised controlled trial. In combination with the perceived risk of intracranial haematoma expansion, it is understandable why some clinicians may be anxious about commencing VTE chemoprophylaxis early in this setting.

In Australia and New Zealand, this certainly appears to be the case. In the multicentre, multinational Erythropoietin in Traumatic Brain Injury (EPO-TBI) trial, all participants received protocolised screening for deep vein thrombosis via twice weekly bilateral lower limb compression ultrasonography.[3] Moreover, the study protocol provided guidelines on pulmonary embolism diagnosis and management.[4] In 603 patients with moderate to severe TBI, 119 (20%) developed VTE.[5] The median time to diagnosis from ICU admission was 6 days (interquartile range, 2–12 days), with almost one-third (n = 35) occurring within the first 3 days. VTE chemoprophylaxis was provided to only 30% (n = 181) of patients by day 3, and to only 57% (n = 343) by day 7.[5] Crude VTE rates were almost twice as high in Australia and New Zealand compared with other study regions (25% *v* 14%), but initiation of VTE chemoprophylaxis was delayed in Australia and New Zealand compared with TBI centres in other countries (median, 5 *v* 4 days).[5] Development of VTE was associated with significantly longer intensive care unit (ICU) and hospital lengths of stay, although VTE itself was seen in older, more severely injured patients and was not independently associated with increased mortality.

Data from Park and colleagues,[6] published in this issue of *Critical Care and Resuscitation*, further explore this area of practice. In a single centre, retrospective observational study, the authors provide insights into the development of VTE, use of chemoprophylaxis, and occurrence of secondary intracranial haematoma in 100 mechanically ventilated adult patients with TBI who remained in ICU for at least 7 days.[6] VTE occurred in 12% of patients — primarily pulmonary embolism and most frequently after day 6. Only 13% of patients had commenced VTE chemoprophylaxis by day 3 (most commonly 40 mg enoxaparin subcutaneous daily), and the median time to initiation was 6.5 days.[6] Moreover, greater illness severity (higher Acute Physiology and Chronic Health Evaluation [APACHE] II scores) and the use of invasive neuromonitoring were associated with delayed initiation.

In contrast, secondary intracranial haematoma occurred in 43% of patients, with a median onset on day 1.[6] Overall, 82% of secondary intracranial haematoma events had occurred by day 3, the majority were defined radiologically as mild, and many were associated with separate neurosurgical intervention — insertion of intracranial monitoring or cerebrospinal fluid drainage devices or other invasive neurosurgical procedures. Of note, crude in-hospital mortality was substantially higher in this group (26%), particularly in comparison to those who developed VTE (8%),[6] although this observation is highly confounded by such factors as age and duration of follow-up.

While the external validity of these data must be viewed very cautiously, they should prompt closer examination of local practice. The observation that the majority of secondary intracranial haematoma events were mild, occurred early, and in the absence of notable coagulopathy is consistent with clinical observation. Indeed, expansion of an existing intracranial haematoma or development

of additional areas of intraparenchymal haemorrhage most often represents the expected evolution of a severe underlying brain injury. Moreover, recent data suggest that 40 mg enoxaparin subcutaneous daily as VTE chemoprophylaxis is unlikely to significantly alter plasma anti-Xa activity in many trauma patients.[7]

The article by Park et al[6] also almost certainly under-reports the incidence of VTE in critically ill patients with TBI. Moreover, while most of the VTE events were documented after day 6, this reflects a diagnostic approach reliant on clinical suspicion, as opposed to systematic screening. Finally, the attributable morbidity and mortality due to VTE remains uncertain because, although VTE is associated with a longer ICU and hospital length of stay, this is clearly confounded by illness severity.

Despite these limitations, Park and colleagues[6] provide some local data on which to inform practice. Based on their findings, and that of others,[8] in the setting of stable intracranial imaging, patients with TBI should ideally be commenced on VTE chemoprophylaxis by day 3 and certainly no later than day 6. Utilisation of invasive neuromonitoring, including extraventricular drainage, should not be considered a contraindication. Where possible, surveillance ultrasonography should also be used in high risk patients, particularly in patients for whom prophylaxis is delayed. The optimal dose and frequency of VTE chemoprophylaxis requires further research, although a fixed daily schedule may be insufficient for many patients. Critically, the consideration of such data allows for additional well reasoned decision making, which has benefits for patients and clinicians.

Competing interests

No relevant disclosures.

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