Predicting response to recombinant factor VIIa in non-haemophiliac patients with severe haemorrhage

Editor—With the exception of cases of blunt trauma, there is no evidence from randomized controlled trials to support the use of recombinant factor VIIa (rFVIIa) as rescue treatment for severe haemorrhage in non-haemophiliacs. Uncertainty remains regarding what dose of rFVIIa to give, when to give it, how often, and how to optimize its efficacy. Furthermore, a crucial question is: who do you give rFVIIa to and who do you not give it to? A scoring system that could accurately predict which patients are least likely to achieve haemostasis and least likely to survive would help to minimize futile administration of an extremely expensive drug. Before the study by Bowles and colleagues,1 Biss and Hanley2 described a scoring system developed after studying 36 patients who had received rFVIIa for a wide range of pathology. It incorporated clinical and laboratory variables into a simple score and demonstrated 82% mortality among those patients deemed high risk. It has yet to be validated.

The relationship between organ dysfunction, illness severity, and outcome after rFVIIa rescue therapy is interesting. A significant proportion of patients who die after treatment with rFVIIa succumb to multiple organ failure rather than directly to haemorrhage.1–3 Bowles and colleagues3 demonstrated that the Sequential Organ Failure Assessment (SOFA) scores of 18 non-haemophiliac patients treated with rFVIIa for haemorrhage were significantly higher among non-survivors than survivors and that presence of organ failure was associated with non-survival.

That SOFA scores were higher in non-survivors of critical illness is perhaps unsurprising. However, among ICU patients as a whole, all organ system failures do not have equal influence on mortality.4 In the context of severe haemorrhage, the equal weighting that the SOFA score gives to failure of each organ is a limitation; in their study, for example, patients with liver failure had 100% mortality. In addition, the influence of coagulopathy on response to rFVIIa and survival is attenuated. Previous studies have shown an association between coagulopathy and failure to respond to rFVIIa and mortality.2 5 Among patients with traumatic haemorrhage, a PT of greater than 17.6 s at the time of administration of rFVIIa independently predicted failure to respond.6

Acidosis may also prove to be an important predictor of outcome after rFVIIa administration. In vitro studies suggest that the efficacy of rFVIIa is greatly diminished by acidosis.7 Two studies of trauma patients have demonstrated that acidosis is associated with failure of rFVIIa to arrest haemorrhagic shock.6 8 A larger study of 315 non-haemophiliac patients found that pH < 7.2 was an independent predictor of failure of bleeding cessation after rFVIIa administration.9 Significant acidaemia probably represents another marker of illness severity but is also associated directly with impaired coagulation.7

Despite the fact that Bowles and colleagues were unable to quantify a predictive value for the SOFA score because of the study size, it is notable that patients with a SOFA score >10 at the time of administration of rFVIIa had an in-hospital mortality of 88%. Further work is needed to establish and validate an accurate scoring system able to predict those most and least likely to survive after rFVIIa rescue therapy; however, measures of organ dysfunction and illness severity are likely to play an important role.

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Editor—We are grateful to Drs Pugh and Wenstone for their interest in our paper.1 We agree with them that it is important to identify who not to give the drug to and who would benefit from it. Not only is it an expensive drug, it may also increase the risk of thrombotic events. A scoring system that identifies who might benefit and who might be harmed would be useful. Using measures of organ dysfunction and illness severity is needed to assess the likely response to rFVIIa in critically ill patients. Most of the studies referred to in their reply have, like us, identified various factors that can predict whether rFVIIa will work or not. However, none of these has been validated properly. We would also agree that this area warrants urgent prospective study of these factors. Indeed, we highlight in our paper that scoring systems seem an appropriate area for further evaluation. We must move beyond the present indiscriminate uncontrolled use of rFVIIa in critically ill patients to a more targeted and considered approach. We welcome further debate on this important issue.

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sevoflurane and analgesia

editor—we were interested to read the papers by yeo and colleagues on the use of sevoflurane as an analgesic in labour. the anaesthetic properties of sevoflurane have been well documented since its introduction into clinical practice and, like all other modern inhalation agents, it has not demonstrated any significant analgesia. its use, therefore, in general anaesthesia is usually associated with the use of analgesic adjuvant. yeo and colleagues have suggested that sevoflurane acts as a significant analgesic in obstetric patients; the observation, originally made by toscano and colleagues, being supported by patient-completed visual analogue scores. we believe that it is still unclear that what has been measured is a direct analgesic effect of sevoflurane and may represent a small change in conscious level or even an alteration in uterine contractility due to the known tocolytic effect of the drug.

in the mid-1980s, there was significant correspondence related to whether unconscious patients feel pain and if analgesics were really required. it has been argued that analgesia is a matter of self-report. thus, the immobile patient with no memory of intraoperative events cannot reveal the presence or absence of analgesia. however, modern teaching has supplanted these views reinforced by understanding of the neuroendocrine response to painful stimulus, and thus analgesia is normally routinely used as a part of balanced anaesthesia technique.

a paper published by tomi and colleagues in 1993 showed that sevoflurane or isoflurane at 0.2 mac has no effect on the perception of pain in volunteers. the bnf states that ‘early post operative pain relief may be required with sevoflurane because emergence and recovery are particularly rapid’, a suggestion that is not in keeping with the hypothesis that a sub-anaesthetic concentration of sevoflurane may have an analgesic effect.

although we recognize the importance of these interesting findings in obstetrics, we are concerned that the repercussions of suggesting significant analgesic effects of sevoflurane may lead to practice that avoids the use of concomitant analgesia with sevoflurane anaesthesia. we believe that this could lead to a detrimental effect on patient care.

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