

LETTER

# Renal function and thromboprophylaxis in critically ill patients

Gareth M Scholey, Anton G Saayman, Christopher D Hingston and Matt P Wise

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Robinson and colleagues [1] recently examined the effective dose of enoxaparin for thromboprophylaxis in critically ill patients recorded over 24 hours. The study concluded that the standard dose of 40 mg led to sub-therapeutic anti-factor Xa activity (aFXa) and 60 mg daily was optimal. The high rate of thromboembolic disease observed in critically ill patients could thus be explained by inadequate aFXa with the standard 40 mg dose.

Low molecular weight heparins (LMWHs) are renally excreted and Robinson and colleagues excluded patients receiving renal replacement therapy as this may have influenced aFXa [1]. Douketis and colleagues [2] documented that excessive anticoagulation did not occur with prophylactic doses of dalteparin in critically ill patients with severe renal impairment. However, in a study of two different prophylactic LMWHs in elderly patients with impaired renal function, enoxaparin but

not tinzaparin accumulated over 8 days [3]. The pharmacokinetics of different LMWHs varies [3,4], and excessive anticoagulation over time might occur with a 60 mg daily dose of enoxaparin, especially if renal function is impaired.

Perturbations of renal function may also explain why standard dose enoxaparin is subtherapeutic in many critically ill patients [1]. Fuster-Lluch and colleagues [5] reported that 30% of patients show augmented renal clearance during the first week of critical illness. Typically, those with supranormal creatinine clearance were post-operative patients or had sepsis or trauma. This patient group is hypercoagulable and at high risk of thromboembolic disease; however, augmented renal clearance would reduce the effectiveness of LMWHs. The optimal prophylactic dose of LMWHs in critical illness is probably, therefore, best determined by monitoring of aFXa.

## Authors' response

Sian Robinson, Palle Toft and Thomas Strøm

We thank Dr Scholey and colleagues for the careful reading of our paper, and agree that the problem of prophylactic anticoagulation in this patient population is a complex one. Whilst our study seems to support the theory of inadequate dosage being a possible mechanism for the higher failure rate of enoxaparin in ICU patients, we acknowledge that there may be other possible mechanisms at play. Scholey and colleagues point to augmented renal function in particular, while still other researchers have implicated the presence of multiple organ dysfunction syndrome, obesity, and the use of vasopressors as likely culprits [6].

Conversely, Dr Scholey and colleagues note that renal impairment may lead to the bioaccumulation of a 60 mg dose of enoxaparin. In fact, renal impairment may lead to enoxaparin accumulation at standard doses [7], and most authorities advocate avoidance of LMWHs in this patient population [8]. Such patients were thus excluded from our study. However, patients with renal impairment do account for a sizeable portion of ICU clientele, and it is incongruous to attempt the establishment of guidelines for the use of LMWH prophylaxis in ICU patients, whilst continuing to exclude this important subgroup.

aFXa is only a surrogate parameter, one that has never been conclusively shown to be directly related to clinical outcome [9,10]. We are currently at the design phase in a study intended to determine whether the improved aFXa levels associated with 60 mg enoxaparin will translate into fewer venous thromboembolic events without the concomitant risk of increased bleeding episodes.

\*Correspondence: [mattwise@doctors.org.uk](mailto:mattwise@doctors.org.uk)  
Adult Critical Care, University Hospital of Wales, Cardiff, UK

#### Abbreviations

aFXa = anti-factor Xa activity; LMWH = low molecular weight heparin.

#### Competing interests

The authors declare that they have no competing interests.

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