LETTER TO THE EDITOR

Rapid reversal of coagulopathy in patients on platelet aggregation inhibitors immediately prior to renal transplantation with recombinant factor VIIa?

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Because of the increasing prescriptions of platelet aggregation inhibitors for secondary prophylaxis of arterial thromboembolism, more and more problems arise in the context of nonelective surgical interventions because of an increased risk of bleeding. These inhibition of platelet function desired to date may lead to massive coagulation problems during surgical interventions. There are no sufficient options for antagonization available. On the other side, transplantation's are characterized by a lack of lead time for the withdrawal or switch of the preoperative medication.

The activated coagulation factor VIIa constitutes an available pharmacological option for the short-term stabilization of haemostasis. Recombinant factor VIIa (rFVIIa) (NovoSeven®, Novo Nordisk, Bagsvaerd, Denmark) is authorized for the treatment or prophylaxis of bleeding associated with surgical or other invasive interventions in haemophilia patients [1]. The use in patients with Glanzmann's disease shows the potential of rFVIIa to contribute to the stabilization of coagulation if platelet function is impaired [2].

In the period from October 2004 to December 2004, five patients with end-stage renal disease received treatment with rFVIIa prior to renal transplantation in order to reduce their bleeding risk induced by platelet aggregation inhibitors without major delay. All patients had an impaired platelet function because of a premedication with acetylsalicylic acid and/or clopidogrel. According to our clinical standard protocol, the assessment plasmatic coagulation was performed by the standard clotting tests prothrombin time, activated partial thromboplastin time, thrombin time (TT) and completed by bleeding time (BT) to screen the platelet function. However, taking into consideration the specific methodological limitations and the current controversy in the literature regarding the predictive value of the available platelet function test tests, especially in patients with renal failure, we used the BT as the routine screening tool [4–6]. If the BT exceeds 15 min, further platelet function analysis should be conducted.

The initial increased BT up to 14 min in our patients declined after the administration of rFVIIa markedly till 3 min, showing improved haemostasis. No further complications in the sense of thrombosis or embolism occurred. Unlike previous case reports on the administration of rFVIIa to patients with renal transplantation, this is the first case series on the preoperative administration with the aim of reducing a drug-related increased risk of bleeding during renal transplantations [9–11].

Today, the administration of desmopressin (1-deamino-8-δ-vasopresin) is the commonly used alternative concept for reversal of the platelet aggregation inhibitors effects after acetylsalicyl acid [3,7,12]. Its use in the field of renal transplantation is, however, questionable and is rejected by us and other work teams as the postoperative onset of organ functioning of the graft is delayed [3,14].

In our opinion, the effect of rFVIIa can be explained mainly by a disproportionately increased thrombin formation, which in turn leads to an enhanced inhibition of fibrinolysis via activation of thrombin activatable fibrinolysis inhibitor and also to an activation of platelets [13].

The use of rFVIIa to correct a coagulation disorder induced by previous platelet aggregation, inhibiting treatment has been described only for a small number of patients with renal transplantation. Those cases did not constitute prophylactic administrations but treatment of severe bleeding [15,16]. The use of rFVIIa did not induce any life-threatening thrombotic event in those patients nor in the few cases of application associated with renal transplantation [11,12].

However, the administration of rFVIIa could be a reliable concept in transplant surgery in patients on platelet aggregation inhibitors. The reversal of the specific drug effect is possible without functional impairment of the renal graft, as shown by the lack of impact on diuretic function and the experiences from placebo-controlled studies for use in other indications [8]. The absence of clinically relevant bleeding complications and the rapid postoperative onset of organ functioning suggests the conduct of studies with a bigger population. This appears to be urgent as other therapeutic options seem to be inappropriate for renal transplantation.

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