Management of heparin resistance in an emergency cardiac surgical patient

Sir,

Heparin resistance (HR) is defined as activated clotting time (ACT) <400 s after full-dose heparinization for open heart surgery.[1] Although it is a rare event, in some series, it may be encountered in up to 22% of the patients undergoing cardiac surgery.[2-4] There are some predictors for HR in the patients undergoing coronary artery bypass grafting, such as antithrombin III (AT III) ≤60%, pre-operative subcutaneous or intravenous heparin therapy, platelet count ≥300,000 cells/mm^3 and age ≥65 years.[5] However, management of this problem could be more troublesome in emergent patients due to newly emerging risk factors.

A 59-year-old male with a clinical history of acute anterior myocardial infarction (MI) was administered tissue plasminogen activator in another medical centre. As his general condition worsened, a new precordial pansystolic murmur was detected on physical examination. Therefore, he was referred to our hospital with a diagnosis of suspicious for post-MI ventricular septal defect (VSD). In his physical examination, his blood pressure was 90/55 mmHg and he was tachycardic with a pulse rate of 115/min. On auscultation, he had a grade 4 pansystolic murmur and fine crackles. Chest X-ray showed diffuse pulmonary oedema. Echocardiography revealed an anteroapical VSD. Pre-operative laboratory findings were in the normal range. Intraaortic balloon pump (IABP) was introduced and then heparinization with 1000 IU/h was started.

The patient underwent emergent surgery. The baseline ACT was measured as 189 s. After administration of heparin 300 IU/kg, control ACT of 269 s was not satisfactory. Therefore, 300 mL fresh frozen plasma (FFP) and additional 5000 IU of heparin were added. But, satisfactory ACT was not achieved. FFP transfusion was limited because of clinical and radiological findings of pulmonary oedema pre-operatively. Administration of the next serial doses of heparin and FFP is shown in Table 1. Finally, ACT reached 415 s and cardiopulmonary bypass (CPB) was instituted. The patient was suspected to be AT III deficient. Before AT III infusion, a sample of blood was delivered to the laboratory to detect the plasma AT III level. As plasma AT III level was detected to be 54% (normal range: 75–125%), 2400 IU AT III was administered and, finally, the ACT dramatically increased to 809 s. During CPB, no additional heparin dose was required. VSD was

Table 1: Management protocol of heparin resistance

	Heparin dose (IU)	FFP (mL)	AT III (IU)	ACT (s)
Basal level				189
Step 1	25,000	0	0	269
Step 2	5000	0	0	290
Step 3	5000	300	0	385
Step 4*	5000	0	0	415
Step 5	10,000**	0	2400***	809
During CPB (control)				697‡
After protamine				135

FFP: Fresh frozen plasma; ACT: Activated clotting time; AT: Antithrombin; CPB: cardiopulmonary bypass; *Heparin was administered via peripheral access; **In priming solution; ***Required units=body weight (kg) × (100 - actual antithrombin activity %) × 2/3 (considering the drug prospectus); ‡Lowest ACT of all control samples

repaired with the infarction exclusion technique through ventriculotomy. Total CPB and cross-clamp times were 106 and 69 min, respectively. Control AT III level was 96%. The patient was discharged on post-operative day 26 with good clinical condition.

Consumption of AT III by pre-operative heparin administration may present a risk for HR in patients undergoing cardiac surgery, as in our case. When the first ACT was not satisfactory, we considered HR because of the predisposing risk factors. An additional dose of heparin and then FFP were administrated. Even the intravenous access for heparin administration was changed to peripheral because of plausible misallocation of central catheter; target ACT of 400 s was not achieved.

The increased volume load associated with FFP administration is a safety concern for at-risk patient populations, including those with congestive heart failure.[6] In this patient, pulmonary oedema was a handicap to administer large amounts of FFP, particularly as a first-step treatment, which might raise a risk for developing serious respiratory complications.

When the plasma AT III level was detected as 54%, we calculated the need for AT III and administered 2400 IU of AT III and achieved a rapid increase of ACT to 809 s, with uncomplicated CPB. Approximately 10 units of FFP need to be administrated to equate this amount of AT III. But, we transfused only 300 mL of FFP. Therefore, risks associated with FFP transfusion, particularly volume overload and transfusion-related acute lung injury,[7] were avoided. In this case, we believe that AT III has advantages compared with FFP transfusion.

However, HR may be a predictable event by determining risk factors; physicians should consider HR for emergent cases. Although FFP infusion with additional heparin doses may usually be enough to supply appropriate ACT levels in most of the cases, AT III might be better choice, especially in those with heart failure. This may also be beneficial to avoid transfusion-related complications.

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