Letter to Editor

Low dose aprotinin increases mortality and morbidity in coronary artery bypass surgery

I read with interest the article of Dr Sabzi and colleagues entitled "Low dose aprotinin increases mortality and morbidity in coronary artery bypass surgery" in this journal.[1] In this clinical trial study the authors have enrolled about 650 patients undergoing coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass (CPB). Low dose aprotinin (2 million kallikrein inactivation units (KIU) during initiation of CPB) had been given to 273 patients in aprotinin group. The authors have found decreased rate of blood product transfusions but increased rate of morbidity in this group.

Two major points should be mentioned about this study. First, management of early peri-operative bleeding, attenuating post bypass coagulopathy and decreasing blood product utilization is a real challenge in cardiac surgery specifically with CPB. Second, it has been shown that antifibrinolytics including aprotinin, tranexamic acid and epsilon-aminocaproic acid (EACA) may decrease hemostatic activation and associated bleeding complications during cardiac surgical procedures. Indeed, aprotinin may decrease perioperative blood product use and diminish biomarkers of inflammation.[2] However, past studies had worried about probable adverse events of aprotinin. According to one study entitled the Blood Conservation Using Antifibrinolytic in a Randomized Trial (BART) published in 2008, it was reported that aprotinin had initial adverse events including renal and vascular complications and higher relative risk for 30 day mortality on patients.[3]Therefore it was a reason for early terminating the BART study and removal of aprotinin from routine clinical use. Thereafter lysine analogues including tranexamic acid and EACA have been used as primary anti-fibrinolytic agents in the setting of cardiac surgery. However, it seems that these agents might in turn contribute to an increase in adverse events when used with high doses.[4]

In the BART study, patient receiving aprotinin had higher risks of comorbidities which may have influence on post-operative morbidity and mortality. Moreover, in that study the relative risk of blood product utilization was not assessed in the context of perioperative cardiac surgery. On the other hand, in many studies removal of aprotinin has not resulted in a decrease in post-operative morbidities such as incidence of renal failure.[5]

Meanwhile, in this post-aprotinin era, the relative risk for refined blood products utilization has increased significantly.[5] Actually, in one study increased use of recombinant activated factor VIIa (rFVIIa) has been accompanied by an increase in the risk of arterial thrombotic events.[6]

Thus, management of postoperative bleeding and fibrinolysis remain contemporary problems in the field of cardiac surgery. Considering the fact that increased use of blood products imposes potential risks and costs, more studies re-evaluating the safety of antifibrinolytic agents and associated adverse effects are required to be designed and conducted.

Keywords: Coronary Artery Bypass Graft (CABG) Surgery, Antifibrinolytic Agents, Aprotinin

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