Is There a Surgical Role for Topical Aprotinin?

To the Editor:—Two classes of intravenous drugs are commonly used in the perioperative setting to mitigate bleeding after cardiac surgery: lysine analogs (e.g., aminocaproic acid, tranexamic acid) and serine protease inhibitors (e.g., aprotinin). In contrast to the lysine analogs, intravenous aprotinin administration has been shown in several non-randomized studies to be associated with worsened postoperative outcomes, and on November 5, 2007, the US Food and Drug Administration requested that Bayer Pharmaceuticals Corporation suspend marketing of aprotinin (Trasylol; Bayer Schering Pharma, Berlin, Germany) pending a detailed review of the preliminary results from the BART (Blood conservation using antifibrinolytics: A randomized trial in a cardiac surgery population) study, which suggested that aprotinin administration increases the risk of death. However, the safety of topical aprotinin administration remains largely unaddressed.

Although the use of topical aprotinin to reduce perioperative bleeding was first described in the 1990s, it was not until recently that randomized, double-blind, prospective data supporting topical antifibrinolytic administration were available. In this study, the effects of topical aprotinin (1 million units), tranexamic acid (2.5 g), and placebo administration before sternal closure were compared in 300 adults undergoing cardiac surgery. Although both topical aprotinin and tranexamic acid significantly reduced postoperative bleeding compared with placebo, this study was not sufficiently powered to look at potential adverse perioperative outcomes associated with topical antifibrinolytic administration. Bovine aprotinin is also a component of a human thrombin and fibrinogen topical sealant (Tisseel; Baxter Healthcare, Deerfield, IL) commonly used to achieve surgical hemostasis. In this instance, aprotinin (3,000 KIU/ml) is added to prevent premature degradation of fibrin formed by mixing of the thrombin and fibrinogen. Although administered topically and in relatively low doses, some aprotinin is absorbed systemically (half life of 30–60 min) and is eliminated by the kidneys. Although there have been reports of aprotinin-associated anaphylaxis with Tisseel administration, there are currently no prospective, randomized data suggesting other adverse perioperative outcomes. Moreover, the third generation of a fibrinogen-coated, aprotinin-free collagen patch known as the surgical patch (SP-3) was recently shown in preclinical trials to reduce bleeding, suggesting that aprotinin may not be necessary for the therapeutic efficacy of topical fibrin sealants.

In sum, topical aprotinin reduces postoperative bleeding and is a component of several commercially available topical hemostatic sealants. However, further randomized, double-blind prospective data are needed to determine the safety profile of topical aprotinin and whether aprotinin is more efficacious than other topically administered antifibrinolytics.

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