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Prevention and management of bleeding

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INTRODUCTION

Major components of the hemostasis include the vasculature, platelets, and coagulation proteins. Any deficiencies or abnormality in any of these integral components will lead to pathologic bleeding and postoperative coagulopathy. Multiple aspects of cardiac surgery, either on or off pump procedures can produce bleeding. This discussion will review concepts in the prevention and management of coagulopathies primarily in cardiac surgical patients.

HEMOSTASIS

The hemostatic system is a complex cellular and humoral inflammatory system that can be activated by multiple pathways during cardiac surgery with or without cardiopulmonary bypass (CPB). Activation of the coagulation, fibrinolytic, and inflammatory pathways all contribute to postoperative bleeding and other potential complications in both cardiac and non-cardiac surgical patients. Multiple factors can produce bleeding including interaction of blood with non-endothelial surfaces of extracorporeal circulation, but also activation of hemostasis secondary to surgical tissue trauma, release of tissue factor, and generation of factor VIIa is now recognized to also be an important cause of hemostatic activation. Multiple pharmacologic approaches to attenuating hemostatic system activation and decreasing the need for transfusion of allogeneic blood products have been used and are under evaluation. Pharmacologic approaches to reduce bleeding and transfusion requirements in cardiac surgical patients are based on either preventing or reversing the defects associated with the CPB induced coagulopathy. Further, the use of newer anticoagulants and platelet inhibitors (clopidogrel, Plavix) also may potentiate bleeding.

APROTININ

In cardiac surgery, multiple randomized, placebo-controlled trials on aprotinin safety and efficacy have confirmed that high dose aprotinin therapy reduces bleeding (i.e., mediastinal and chest tube drainage) by 31-81%, and the need for allogeneic transfusion 35-97%, and the proportion of patients requiring transfusion of allogeneic blood by 40-88%. Aprotinin's mechanism of action is complex and may also involve reduction of the inflammatory response. Multiple mechanisms are responsible for aprotinin's ability to reduce bleeding after cardiopulmonary bypass. Aprotinin is also the most potent antifibrinolytic agent. Aprotinin has also been studied in clinical trials in vascular, liver transplantation surgery, and orthopedic surgery. Aprotinin also safely and effectively decreases blood transfusion in these settings.

OTHER AGENTS

Lysine analogs (epsilon aminocaproic acid, tranexamic acid) are widely used in cardiac surgery, but more data supporting their safety and efficacy are needed.

PROHEMOSTATIC AGENTS/RECOMBINANT PROTEINS

Coagulation products used to manage bleeding in patients with hemophilia, von Willebrand's disease (vWD), or acquired inhibitors to antihemophilic factor include AHF concentrates, factor IX concentrates, factor VIIa concentrate, factor IX complexes, anti-inhibitor coagulant complexes, and desmopressin acetate. Recombinant activated factor VIIa (rFVIIa; NovoSeven, Novo Nordisk) has been used as a novel and effective treatment for patients with hemophilia with inhibitors for the treatment of bleeding, and to secure hemostasis in complex clinical situations refractory to standard therapy. Recombinant factor VIIa appears to have multiple mechanisms for its efficacy. Multiple publications are appearing reporting the application of rFactorVIIa in surgical patients. Although 90 μg/kg is usually the initial starting dose in patients with hemophilia, lower doses of 30-45 μg/kg have been reported in surgical patients to be effective. Additional

studies are needed to further evaluate dosing, safety and efficacy in perioperative use of rFVIIa.

THE FUTURE

The potential for bleeding after cardiac surgery and non-cardiac surgery represents an ongoing problem for clinicians, and creates a need for multiple pharmacologic approaches. Current and future pharmacologic approaches to attenuating hemostatic system activation will need to be designed to decrease coagulopathy and the potential need for allogeneic blood administration, but also provide a mechanism to specifically produce hemostatic activation in the bleeding patient. Novel anti-inflammatory strategies are under investigation in cardiac surgery, targeting multiple pathways (ie, kallikrein, complement, reperfusion injury) to reduce the bleeding. The increasing use of clopidogrel and newer anticoagulants will continue to pose new paradigms and potential problems in managing cardiac surgical patients. Newer therapies including recombinant factor VIIa as a therapy for refractory bleeding need to be considered as potential therapies.

SELECTED WEB SITE: BleedingWeb.com

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