Anti-Platelet Therapy in the Cardiac Surgical Patient

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Introduction

Patients with cardiovascular disease are frequently prescribed anti-platelet medication due to an accelerated risk of thrombosis which has been linked to platelet hyperactivity. Patients undergoing coronary intervention who present for urgent cardiac surgery are almost universally on a regimen of anti-platelet agents that renders them susceptible to excessive bleeding during and after surgery. Pharmacologic and strategic management of these patients is discussed.

Mechanisms of Action of Anti-Platelet Agents

Aspirin is still the most commonly used anti-platelet agent. Aspirin exerts its effect by inhibition of cyclo-oxygenase which inhibits formation of thromboxane A2 (TXA2), a potent platelet agonist. Calcium entry and the resultant aggregation are prevented from occurring, however, platelets can still respond to exogenous thromboxane analogs or an aggregatory stimulus that utilizes another pathway. The glycoprotein IIbIIIa (GPIIbIIIa) receptor is responsible for mediating platelet-platelet aggregation via fibrinogen bridging. Drugs that inhibit this receptor in a reversible or an irreversible fashion are potent inhibitors of platelet aggregation and include abciximab, eptifibatide, and tirofiban. They are frequently infused to prevent thrombus formation in patients who have undergone a high risk coronary interventional procedure. Large-scale multicenter studies have shown that re-thrombosis and infarction rates after percutaneous angioplasty and after stent procedures have been reduced with the use of these drugs.1 Reductions in mortality and re-infarction rates have been shown in such patient groups as diabetics and patients with prior cardiac surgery, respectively.2,3
The thienopyridine derivatives ticlopidine and clopidogrel (Plavix®, Sanofi) act by non-competitive antagonism at one of the platelet ADP receptors, the P2Y12 receptor. Stimulation of this receptor by ADP or its analogues causes an inhibition of the production of adenyl cyclase which potentiates platelet aggregation. Blockade of this receptor by ticlopidine or clopidogrel causes increased levels of adenyl cyclase, elevated cAMP levels, and hence a profound a rapid disaggregation.4 (Figure 1) The duration of anti-platelet activity is the life-span of the platelet because the P2Y12 receptor is permanently altered. The effects of clopidogrel plus aspirin are not just additive, they are synergistic and this may explain why cardiac surgical patients having received this combination of drugs seem to have excessive postoperative bleeding.5

Patients on these medications who then present for cardiac surgery are at increased risk for bleeding complications and have a documented increase in transfusions and reoperations for bleeding.6,7 For this reason, specific platelet function monitoring could guide platelet transfusion therapy so that indiscriminate platelet transfusions are not given.8 Specific monitoring of the platelet defect induced by these anti-thrombotic drugs would be advantageous for a number of reasons. For therapeutic efficacy, the degree to which patients are protected from thrombotic events is related to the degree of platelet inhibition.9 In cardiac surgery, the use of one of these platelet function monitoring devices can be incorporated into a transfusion algorithm to reduce transfusion therapy. In addition to monitoring, the use of high-dose aprotinin therapy has been shown to reduce bleeding and transfusions in cardiac surgical patients having recently taken clopidogrel. Even when clopidogrel therapy is continued until the
day of surgery, the addition of aprotinin resulted in less blood transfused, less bleeding, and faster recovery indices. The removal of aprotinin from our clinical armamentarium makes this therapy and it is unclear if the synthetic antifibrinolytic agents offer the same degree of protection from hemorrhagic complications. Incorporation of an antifibrinolytic agent into the perioperative plan would seem prudent, assuming there is no contraindication.

The use of anti-platelet therapy in cardiovascular medicine is pervasive and will not disappear from clinical practice. The ACC/AHA Guidelines for patients with percutaneous interventions are that anti-platelet therapy with clopidogrel should be continued for a minimum of 12 months, if there is no risk for bleeding. Imminent cardiac surgery does pose a risk for bleeding. The optimal time for discontinuation of these drugs prior to cardiac surgery has not yet been elucidated. Our role as practitioners should be to learn to monitor these drugs, titrate them to effect, and to rationally treat the adverse sequelae of their administration.

References:


