Management of Antiplatelet Agents

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Antiplatelet agents play a crucial role in the prevention or treatment of vascular occlusive events by inhibiting platelet aggregation. These drugs can reduce the risk of cardiovascular events in patients with acute coronary syndromes, angina, stroke, transient ischemic attacks, peripheral arterial disease, and atrial fibrillation.[1] Management of perioperative antiplatelet agents should involve a multidisciplinary team with shared decision-making after a thorough risk/benefit analysis.[2] The decision to continue or discontinue these drugs before a scheduled surgery or procedure depends on the specific drug, indication for its' use, and the bleeding risk of the surgery/procedure. In patients who have undergone recent coronary angioplasty with or without coronary stents, a more important factor to consider rather than discontinuation of antiplatelet therapy is minimum time to delay noncardiac surgery.[2] In urgent or emergent situations where drug washout cannot occur, options are limited as there are no true reversal agents for antiplatelet medications. However, bentracimab (a recombinant monoclonal antibody) has shown promising results for ticagrelor reversal.[3] Platelet transfusion is thought to help manage antiplatelet-associated bleeding; however, the specific antiplatelet agent and timing since last dose will determine actual efficacy.[4,5] Furthermore, there is concern that platelet transfusions may actually lead to harm without any benefit in decreasing re-bleeding in gastrointestinal bleeding patients on antiplatelets (without thrombocytopenia).[6] The PATCH trial also suggested that platelet transfusion compared to the standard of care resulted in worse neurological outcomes in acute intracerebral hemorrhage patients on antiplatelet medications.[7] There may be a role for platelet function testing to help identify patients who can be operated on sooner than the recommended antiplatelet discontinuation times. These tests also identify those that are at higher bleeding risk.[8,9] However, there is wide variability among the available tests with no universal standardization on normal values. While platelet transfusion remains controversial and the role of platelet function tests remain uncertain in urgent bleeding management, the remainder of our discussion will now focus on timing of discontinuation of antiplatelet medications prior to a scheduled surgery or procedure.

Aspirin

In cardiac surgery for coronary artery bypass grafting, the protective effects of aspirin have been well-established for decreasing the incidence of myocardial infarction and thrombotic risk.[8] However, aspirin has been associated with an increased risk of bleeding in cardiac surgery. Therefore, the current STS/SCA/AmSect/SABM guidelines on patient blood management state that it is reasonable to discontinue aspirin in elective cases without acute coronary syndromes with the expectation that transfusion will be reduced (Class IIA; level of evidence A).[9] This is further supported by recent society consensus statements stating that aspirin should be discontinued, in the absence of coronary artery disease or a strong antithrombotic indication, to reduce the risk of bleeding in cardiac surgery.[8] Ultimately, the decision on timing will need to consider the preventative effects versus the risk of bleeding.[8]

In noncardiac surgery, aspirin has also contributed to a greater risk of bleeding events, while simultaneously been credited for prevention of perioperative acute cardiovascular syndromes.[2] The POISE-2 trial found that aspirin did not actually have a beneficial impact on reducing death or myocardial infarction when compared to placebo, but it did lead to increased bleeding.[10] However, when considering only patients with prior coronary stents, aspirin use was superior to placebo in decreasing perioperative myocardial infarctions.[11] Current guidelines for elective noncardiac surgery also recommend continuation of aspirin into the perioperative period rather than aspirin interruption; however, if the proposed surgery carries an elevated bleeding risk, then aspirin can be discontinued less than or equal to 7 days prior to the procedure.[12]

Table 1. Timing of P2Y12 antiplatelet therapy effect

Antiplatelet Drug	Minimum Time from Drug Discontinuation to Recovery of Platelet Function
Clopidogrel	5 – 7 days
Ticagrelor	3 – 5 days
Prasugrel	7 – 10 days

Adapted from Reference #2.

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Clopidogrel

The current recommendations for the discontinuation of P2Y12 inhibitors varies depending on the time to restoration of platelet function after drug interruption (Table 1).[2] In both elective cardiac and noncardiac surgery, clopidogrel discontinuation for 5 days is recommended according to both the STS/SCA/AmSECT/SABM and Chest guidelines.[9,12] While it was once suggested that 3 days may be sufficient time for withdrawal of the drug, more recent studies suggest that clopidogrel discontinuation less than 5 days leads to increased bleeding.[13] As with any decision regarding antiplatelet agent interruption, certain high-risk patients may warrant clopidogrel continuation such as in surgeries for peripheral arterial disease or carotid disease. Current data suggests that clopidogrel continuation for carotid endarterectomy surgery does not result in an increased risk of postoperative complications, including bleeding.[14]

Ticagrelor

The withdrawal time for ticagrelor prior to elective cardiac and noncardiac surgery is a minimum of 3 days, although some guidelines suggest 3 to 5 days.[8,9,12] Unlike clopidogrel and prasugrel, ticagrelor is a reversible antiplatelet that does not require activation from a prodrug form, and therefore, it exhibits more reliable inhibition of platelet function.[9] Studies have demonstrated an increased risk of bleeding if patients undergo surgery within 72 hours of ticagrelor exposure. As mentioned above, in emergent situations where drug washout was not possible, bentracimab may become a specific ticagrelor reversal agent; however, FDA approval is still pending.[3]

Prasugrel

Like aspirin and clopidogrel, prasugrel is an irreversible antiplatelet agent. However, it does result in more consistent platelet inhibition due to less of an impact from genetic polymorphisms.[9] Discontinuation prior to elective procedures was once based on expert consensus opinion; however, current evidence from trial data suggest that 7 days of drug interruption is needed.[8,9,12] This recommendation is similar for both cardiac and noncardiac surgery.

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