

Antiplatelet Drugs in Acute Coronary Syndromes

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Over 1.5 million patients in the United States each year are admitted to the hospital with acute coronary syndromes (ACS). The most common underlying mechanism is the rupture or erosion of atherosclerotic plaque in the coronary artery, leading to the formation of an obstructive thrombus. During this process, platelet adhesion and activation are initiated. Platelet aggregation occurs when fibrinogen molecules bind to the activated platelet receptors, and subsequently forming cross-linking activated platelets.

For this reason, patients with an ACS are treated with targeted antiplatelet therapies. Antiplatelet therapy has been shown to significantly reduce cardiovascular events, especially in high-risk patients, in a collaborative meta-analysis that included multiple trials. Moreover, across the spectrum of ACS and in those undergoing percutaneous coronary interventions (PCI) with stenting, dual antiplatelet therapy with aspirin and a thienopyridine inhibitor of the platelet P2Y₁₂ adenosine diphosphate (ADP) receptor is standard of care. Currently, the most commonly prescribed thienopyridine is clopidogrel; however, the pharmacodynamic response to clopidogrel displays substantial inter-patient variability, and patients with coronary disease with lesser degrees of platelet inhibition in response to clopidogrel appear to be at increased risk of cardiovascular events. Environmental, drug-drug, and pharmacogenetic factors explain in part the variable response to clopidogrel.

Newer antiplatelet agents are currently available, such as prasugrel, a 3rd-generation thienopyridine that achieves greater platelet inhibition than does clopidogrel with less variability. The TRITON-TIMI 38 trial demonstrated that treatment with prasugrel, compared with clopidogrel, resulted in a significantly lower rate of ischemic events but more bleeding among patients presenting with ACS with planned PCI. Ticagrelor is another P2Y₁₂ inhibitor with a rapid onset of action and a high degree of platelet inhibition. The PLATO study found that ticagrelor versus clopidogrel in post-ACS patients was associated with a reduction in cardiovascular death and ischemic events, with an increase in non-CABG PLATO major or minor bleeding but no increase in CABG major or minor bleeding. Ticagrelor is not currently approved by the FDA. Expanding the number of antiplatelet treatment options will allow physicians to tailor therapies for each patient. However, over the next few years, selecting the optimal strategy for each person following ACS may be challenging.