

Conclusion

Antiplatelet Therapy and Platelet Function Testing

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Conclusion

The use of combination antiplatelet therapy with aspirin (ASA) and a thienopyridine has resulted in improved clinical outcomes in patients with acute coronary syndromes (ACS) and in those who undergo percutaneous coronary interventions (PCI). The most appropriate dose of thienopyridine therapy and its optimal duration of pretreatment and administration post-PCI remain unknown. It appears that platelet inhibitors are currently being used more aggressively in patients at higher risk for further ischemic events, such as patients with elevated troponin levels, or in those who urgently undergo PCI. However, the ongoing shift in platelet inhibition strategies in PCI toward the use of higher clopidogrel loading doses, an increased time interval for preprocedural loading, and an extended duration of postprocedural clopidogrel treatment is symptomatic of a current clinical situation where multiple unmet clinical needs remain; most notably the problem of interindividual variability and hyporesponse to platelet inhibition. Indeed, it appears that one dosing strategy does not fit all patients as it pertains to the use of platelet inhibitors.

Platelet function testing is an evolving tool that may eventually become a practical method by which clinicians can identify patients who are at increased risk for thrombotic events. However, before these assays can be routinely incorporated into clinical pathways, clinically meaningful definitions of hyporesponse to antiplatelet therapy need to be devised; also, there is a definite need for well-controlled trials that support improved clinical effectiveness as a direct result of therapeutic alteration based on laboratory values. Novel platelet inhibitors in development possess altered pharmacokinetic and pharmacodynamic profiles compared

with currently available thienopyridines. It has been hypothesized that the use of platelet inhibitors with higher and less variable inhibition of platelet aggregation will improve clinicians' ability to prevent ischemic events following PCI. This hypothesis was substantiated in a large Phase III trial to assess improvement in therapeutic outcomes by optimizing platelet inhibition with prasugrel-thrombolysis in myocardial infarction (TRITON-TIMI 38). This trial assessed the effectiveness of the novel thienopyridine, prasugrel, which provided greater blockade of the platelet P2Y₁₂ receptor than clopidogrel in 13,608 patients with ACS scheduled to undergo PCI. A 19% highly significant reduction of the composite clinical endpoint (death, myocardial infarction, and stroke) was observed, albeit at the cost of more serious bleeding. Other newer compounds may potentially address some of the shortcomings of currently available thienopyridines by providing a more rapid onset of platelet inhibition and more predictable and durable antiplatelet responses. It is hoped that results from randomized controlled clinical trials with these investigational agents will advance the field by addressing the aforementioned clinically unmet needs. Lastly, there remains a need to improve patient adherence to prescribed antiplatelet strategies after ACS and PCI, and also to prevent unnecessary and potentially catastrophic early discontinuation of platelet inhibitors in patients who have received drug-eluting stents.

Reference

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