Insight ... impact of reticulated platelets on antiplatelet response to thienopyridines is independent of platelet turnover

Young platelets out-of-control

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Reticulated platelets are newly formed cells that are large, highly granular, and contain detectable RNA, which is lost as platelets age. Reticulated platelets are often monitored to assess platelet turnover. In addition, investigators have found that reticulated platelets are more active than mature platelets (1). These observations are of clinical importance since reticulated platelets are associated with myocardial infarction (MI) and death from MI. Recent evidence suggests that decreased responsiveness to the thienopyridines clopidogrel and prasugrel contribute to the risk of MI associated with reticulated platelets (2, 3). Impaired responsiveness of reticulated platelets to thienopyridines has been attributed to the fact that reticulated platelets are associated with increased platelet turnover. Investigators have argued that, given the short half-life of the active metabolites of thienopyridines, in patients with high platelet turnover, more platelets will be produced during the period when thienopyridine levels are subtherapeutic.

Stratz et al. now provide evidence for an alternative explanation, showing that reticulated platelets are intrinsically resistant to thienopyridines (4). The authors studied 199 patients following a loading dose of clopidogrel or prasugrel. They assessed platelet reactivity by measuring ADP-induced platelet aggregation at several time points including 120 minutes after exposure (peak thienopyridine level) and one day after exposure (trough level). They subsequently divided the patients into tertiles based on their reticulated platelet count and evaluated the relationship between platelet reactivity and reticulated platelets. Particularly for the clopidogrel group, there was a significant correlation between reticulated platelet count and platelet reactivity, even when clopidogrel levels would be expected to be at peak levels. This correlation did not change significantly over time. The authors also found that reticulated platelets showed higher expression of P-selectin and enhanced αIIbβ3 activation in response to ADP both before and after clopidogrel exposure.

These studies indicate that platelet turnover is not the primary reason why patients with elevated reticulated platelet counts have decreased responsiveness to thienopyridines. Rather intrinsic properties of the reticulated platelets themselves account for these differences. This insight raises the basic question of what mechanisms of reticulated platelets account for this relative resistance to thienopyridines and the clinical question of whether modifying P2Y12 targeted therapy based on reticulated platelet count could improve outcome in coronary artery disease.

Conflicts of interest
None declared.

References

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