ALTERNATIVE VIEWPOINTS

Antiplatelet Drug Resistance: Almost Ready for Prime Time

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The article on antiplatelet drug resistance by Drs. Burns, Mooss, and Hilleman[1] was an excellent, yet cautionary, review that had several points that we feel deserve comment. First, the authors included a point-of-care measure of platelet function that could be more completely explained—the VerifyNow instrument (Accumetrics, San Diego, CA). This assay is for three types of platelet inhibition: aspirin mediated inhibition, $P2Y_{12}$ (thienopyridine) receptor inhibition, and glycoprotein IIb/IIIa receptor inhibition. Resistance to drugs that act through these pathways is measured through three different cartridges that can all be used in the VerifyNow device and are approved by the United States Food and Drug Administration.[2]

The aspirin assay uses an arachidonic acid agonist to activate platelets. Through light transmittance, the device then measures the amount of platelet aggregation that occurs and reports the result as an aspirin responsive unit (ARU). The interpretation of the result is based on an assigned cutoff (< 550 units indicates platelet inhibition consistent with aspirin is present, ≥ 550 units indicates platelet inhibition consistent with aspirin is not present). In contrast to the information provided in the article by Dr. Burns and his colleagues,[1] this device has been compared with optical aggregometry. The correlation coefficient for the VerifyNow aspirin cartridge was excellent when compared with epinephrine-induced platelet aggregation measured by the Chrono-Log optical Aggregometer (Chrono-Log Corp., Havertown, PA) (r=0.902).[3] Furthermore, the P2Y12 (thienopyridine) assay is made to have a greater specificity for the $P2Y_{12}$ rather than $P2Y_1$ receptor. It accomplishes this by using prostaglandin E_1 added to adenosine 5′-diphosphate. This assay incorporates baseline platelet function and the $P2Y_{12}$ reaction units to provide a percentage of platelet inhibition consistent with thienopyridines such as clopidogrel.

Since clinical trials have clearly correlated antiplatelet resistance to adverse outcomes, we feel that this information could be valuable in practitioners' hands in patient-specific scenarios. For example, in a patient with aspirin resistance, alternate pharmacologic antiplatelet strategies such as thienopyridines or higher doses of aspirin[4] may be considered. In addition, it may be helpful to measure the effectiveness of clopidogrel in patients concomitantly receiving a cytochrome P450 3A4 inhibitor.[5–7] Recent guidelines have also incorporated a recommendation to increase the dose of clopidogrel to 150 mg/day if less than 50% inhibition of platelet aggregation is demonstrated after high-risk percutaneous coronary intervention.[8]

Although these clinical management strategies have yet to be clinically validated, the potential adverse outcome of platelet resistance to antiplatelet therapy is concerning. As a profession that thrives on therapeutic drug monitoring, pharmacists should embrace technology that allows us to further manage our patient's drug

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regimens. Of course this will require investing in the resources to validate the utility of the assay in order to determine the clinically meaningful scenarios in which antiplatelet drug therapy should be adjusted.

References

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Authors' Reply

The authors appreciate the insightful comments of Drs. Dorsch and Dunn and offer no further comments.