Switching Thienopyridines: Hypothetical Versus Real Risks

I enjoyed reading the quality paper by Campo et al. (1) that tried to determine whether platelet response after thienopyridines is drug or class specific in a broad spectrum of post-stent patients. The team should be acknowledged for the effort and for realistic rates for low response after clopidogrel (21%), and ticlopidine (19%). The major take-home message conveyed to the readership is that clopidogrel-treated patients may be switched to ticlopidine if “resistance” is determined by the platelet tests. However, the practical implications of this idea are not obvious, may be dangerous, may not be supported by clinical or epidemiologic evidence, and deserve at least some clarification and/or adjustment.

In fact, low response to clopidogrel as a major risk factor for the worsened vascular outcomes has been suspected but never proven to be a real clinical phenomena, especially considering that no load 75 mg clopidogrel saved 119 lives, and provided an absolute mortality benefit after myocardial infarction in COMMIT and deserves at least some clarification and/or adjustment. Therefore, “clopidogrel resistance” is a laboratory finding, rather than a clinically relevant hazard unless further randomized evidence became available (3).

On the other hand, substituting clopidogrel with ticlopidine definitely increases the bone marrow toxicity risks. Indeed, neutropenia and thrombocytopenia were 2-fold higher in the ticlopidine arm than in patients treated with clopidogrel in CLASSICS (Clopidogrel Aspirin Stent International Cooperative Study) (4). Doubled cytotoxicity rates after ticlopidine were confirmed in a post-stent study (5) and a recent meta-analysis of 11,668 patients (6). Therefore, the suggestion that in case of low platelet response after clopidogrel patients should be switched to ticlopidine is not valid. Unless there is proof that response after clopidogrel is indeed linked to the clinical outcomes, monitoring compliance and potential tailoring of dual antiplatelet regimens with aspirin and clopidogrel will be a safer alternative than switching thienopyridines.

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REFERENCES


Letters to the Editor

Reply

We welcome the thoughtful comments by Dr. Serebruany to our recent publication on clopidogrel poor responsiveness in a broad population undergoing coronary stenting (1). Our major focus was to assess whether clopidogrel poor responders display inadequate platelet inhibition also after ticlopidine administration. We found that the great majority (83%) of patients who were clopidogrel nonresponders became responsive to ticlopidine, reaching a higher level of platelet inhibition (platelet aggregation [PA] 69 ± 15 vs. 44 ± 18; p < 0.01). On the other hand, 23 patients who were responsive to clopidogrel showed resistance to ticlopidine and correspondingly less platelet inhibition with this drug (PA 46 ± 15 vs. 70 ± 15; p < 0.01).

When taken together our findings strongly suggest that poor responsiveness to currently commercially available thienopyridines may frequently be a drug-specific more than a class-effect mechanism. This conclusion holds particularly true in consideration that in the currently recommended regimen ticlopidine at steady state