Atorvastatin–Clopidogrel Interaction

To the Editor:

We read with some fascination the paper by Lau et al.1 exploring the possibility of an interaction between atorvastatin and clopidogrel. Unfortunately, the authors do not make clear whether the patients in the first study received aspirin, which would be the normal standard of care in patients undergoing percutaneous coronary interventions. The two subsequent studies did not use aspirin, a fact that the authors could have elaborated on in their discussion. Given the well-characterized effects of aspirin on platelet aggregation and its widespread clinical use, we feel this omission limits the clinical concerns raised by this study.

Was aspirin used in the first study?

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Response

We reported that atorvastatin, but not pravastatin, inhibited the “platelet antiaggregatory effect of clopidogrel in a dose-dependent manner.”1 We offered no data on how the atorvastatin-clopidogrel drug-drug interaction might influence clinical outcomes. This subject requires additional evaluation.

In the first part of our study, the numbers of patients on aspirin therapy before and after percutaneous coronary intervention (PCI) were as follows: (1) In the clopidogrel group, 14 of 16 (87%) patients were receiving aspirin therapy prior to PCI, and 100% were receiving aspirin (325 mg) after PCI for life; (2) in the clopidogrel + pravastatin group, 9 of 9 (100%) patients were receiving aspirin therapy prior to PCI and 100% after PCI for life; and (3) in the clopidogrel + atorvastatin group, 18 of 19 (95%) patients were receiving aspirin therapy prior to PCI and 100% after PCI for life. Blood samples for the second platelet aggregation test were all obtained after aspirin administration. The data suggest that the observed interference of the platelet antiaggregatory effect of clopidogrel by atorvastatin was independent of aspirin therapy.

In the two subsequent studies, stringent exclusion criteria, including ingestion of other antiplatelet agents, were applied to healthy volunteer subjects to alleviate potential confounding variables in the assessment of the antiaggregatory effect of clopidogrel.

Finally, aspirin exerts its effect primarily by interfering with the biosynthesis of thromboxane A2,2 whereas clopidogrel inhibits the GTP inhibitory (Gi) protein-coupled P2Y12 ADP receptor.3 We did not specifically test for the platelet inhibitory effect of aspirin; we tested for the platelet antiaggregatory effect of clopidogrel by using 20 μmol/L ADP as the agonist.

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