8th Seah Cheng Siang Memorial Lecture: New Antithrombotic Agents

M Verstraete,*MD, PhD

Abstract

For the long-term prevention of thromboembolic events in patients with atherosclerotic vascular disease, aspirin is the preferred antiplatelet drug. Only clopidogrel was shown to be more effective and at least as safe than medium-dose aspirin in direct comparative large-scale trials. Aspirin inhibits the cyclooxygenase dependent pathway of platelet aggregation while ticlopidine and clopidogrel selectively bind to adenosine diphosphate (ADP) receptors on the platelet surface. Compounds which inhibit the synthesis of thromboxane synthase, block the thromboxane receptor or have the dual activity were effective in experimental thrombosis models in animals but not predictive of results in humans.

Activation of the platelet glycoprotein (GPIIb/IIIa) receptor on the platelet surface is the final pathway of platelet aggregation, regardless of the initiating stimulus. Inhibitors of GPIIb/IIIa receptors include monoclonal antibodies (abciximab) against this receptor and peptidic as well as non-peptidic synthetic specific receptor blockers. Abciximab exchanges between and binds to platelets for as long as two weeks whereas synthetic GPIIb/IIIa inhibitors inhibit* **ex vivo** ***platelet aggregation for only a few hours after the end of infusion but have the advantage of being also orally active.

In the secondary prevention of atherothrombosis, large scale trials were successfully conducted with aspirin, dipyridamole and clopidogrel. In the first large-scale trials with GPIIb/IIIa inhibitors with abciximab was investigated. In aggregate, this class of platelet inhibitors, combined with aspirin and heparin, was shown to reduce ischaemic events in patients with high- and low-risk coronary intervention, stents, unstable angina and non-Q-wave infarction with long-term preservation of the initial benefit. With synthetic GPIIb/IIIa inhibitors there is no suppression of clinical evident restenosis 6 months after the end of treatment. With the doses presently used, bleeding occurs more often with the synthetic GPIIb/IIIa inhibitors (used for 3 days) than with abciximab (used for 12 hours) but there are no direct comparisons between these drugs.

Ann Acad Med Singapore **1999; 28:347-62**

Key words: Aspirin, Clopidogrel, Glycoprotein IIb/IIIa inhibition, Thromboxane synthase and receptor blockers, Ticlopidine, Specific thrombin inhibitors

* *Professor of Medicine*
Center for Molecular and Vascular Biology
University of Leuven, Belgium
Address for Reprints: Dr Marc Verstraete, Center for Molecular and Vascular Biology, University of Leuven, Campus Gasthuisberg, 0 & N, Herestraat 49, B-3000 Leuven, Belgium. E-mail: marc.verstraete@med.kuleuven.ac.be