TOP Journal Club
Vol: 7 No: 10 October 2004

Antithrombotic Therapy in Peripheral Arterial Occlusive Disease: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy.

Reference: Chest. 2004 Sep;126(3 S):609S-26S.

This chapter about antithrombotic therapy for peripheral arterial occlusive disease is part of the seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence Based Guidelines. Grade 1 recommendations are strong and indicate that the benefits do, or do not, outweigh risks, burden, and costs, and Grade 2 suggests that individual patients' values may lead to different choices (for a full understanding of the grading see Guyatt et al, CHEST 2004;126:179S-187S). Among the key recommendations in this chapter are the following: For patients with chronic limb ischemia, we recommend lifelong aspirin therapy in comparison to no antiplatelet therapy in patients with clinically manifest coronary or cerebrovascular disease (Grade 1A) and in those without clinically manifest coronary or cerebrovascular disease (Grade 1C+). We recommend clopidogrel over no antiplatelet therapy (Grade 1C+) but suggest that aspirin be used instead of clopidogrel (Grade 2A). For patients with disabling intermittent claudication who do not respond to conservative measures and who are not candidates for surgical or catheter-based intervention, we suggest cilostazol (Grade 2A). We suggest that clinicians not use cilostazol in patients with less-disabling claudication (Grade 2A). In these patients, we recommend against the use of pentoxifylline (Grade 1B). We suggest clinicians not use prostaglandins (Grade 2B). In patients with intermittent claudication, we recommend against the use of anticoagulants (Grade 1A). In patients with acute arterial emboli or thrombosis, we recommend treatment with immediate systemic anticoagulation with unfractionated heparin (UFH) [Grade 1C]. We also recommend systemic anticoagulation with UFH followed by long-term vitamin K antagonist (VKA) in patients with embolsim [Grade 1C]). For patients undergoing major vascular reconstructive procedures, we recommend UFH at the time of application of vascular cross-clamps (Grade 1A). In patients undergoing prosthetic infrainguinal bypass, we recommend aspirin (Grade 1A). In patients undergoing infrainguinal femoropopliteal or distal vein bypass, we suggest that clinicians do not routinely use a VKA (Grade 2A). For routine patients undergoing infrainguinal bypass without special risk factors for occlusion, we recommend against VKA plus aspirin (Grade 1A). For those at high risk of bypass occlusion and limb loss, we suggest VKA plus aspirin (Grade 2B). In patients undergoing carotid endarterectomy, we recommend aspirin preoperatively and continued indefinitely (Grade 1A). In nonoperative patients with asymptomatic or recurrent carotid stenosis, we recommend lifelong aspirin (Grade 1C+). For all patients undergoing extremity balloon angioplasty, we recommend long-term aspirin (Grade 1C+).

Cilostazol inhibits platelet-leukocyte interaction by suppression of platelet activation.

Reference: Platelets. 2004;15(5):293-301.

The influence of three anti-platelet drugs, cilostazol, aspirin, and tirofiban, was investigated on platelet-leukocyte interaction by flow cytometry. When platelets and leukocytes were pre-incubated with anti-platelet drugs and stimulated by thrombin or collagen,

cilostazol was found to inhibit platelet adhesion to monocytes and polymorphonuclear cells (PMNs). Similar effects were observed with anti-CD62P antibody, while aspirin and tirofiban did not appear to interfere with interaction between platelets and leukocytes. In the platelets pre-incubated with anti-platelet drugs, cilostazol significantly reduced CD62P expression and GPIIb/IIIa activation on platelet surface stimulated by thrombin or collagen. Aspirin inhibited CD62P expression and GPIIb/IIIa activation induced by collagen, but not thrombin. Tirofiban significantly blocked GPIIb/IIIa activation induced with both, and weakly inhibited CD62P expression induced by collagen. When added after stimulation of platelets, cilostazol again significantly inhibited CD62P expression and GPIIb/IIIa activation, although to a lesser extent than in the pre-incubation study. Aspirin hardly inhibited CD62P expression or GPIIb/IIIa activation, while tirofiban strongly blocked GPIIb/IIIa activation induced by thrombin or collagen, but had little effects on CD62P expression. In conclusion, our results suggest that cilostazol inhibits platelet-leukocyte interaction by reducing CD62P expression on the platelet surface.

Balloon angioplasty plus cilostazol administration versus primary stenting of small coronary artery disease: Final results of COMPASS.

Reference: Catheter Cardiovasc Interv. 2004 Sep;63(1):44-51

Efficacy of primary stenting in small coronary artery disease is still controversial. Cilostazol has been reported to control restenosis after balloon angioplasty (BA). The aim was to compare primary stenting with BA plus cilostazol administration in small coronary artery disease. Of 106 lesions located in small coronary artery (reference < 3.0 mm), 50 lesions were randomly assigned to the stenting and 56 lesions to the BA-cilostazol group. Multilink stent was implanted in the stenting group. In the BA-cilostazol group, cilostazol (200 mg/day) without aspirin was administered for 6 months after BA. Ticlopidine was given for 1 month when bailout stent was implanted. Serial quantitative angiography was performed at the procedure and 6 months. The primary endpoint was 6-month angiographic restenosis. Clinical event rates at 1 year were also assessed. Baseline characteristics were similar. All procedures were successful. Bailout stenting was performed in three lesions in the BA-cilostazol group. No side effects of cilostazol were observed. Postprocedural lumen diameter was significantly larger (2.69 vs. 2.03 mm; $P < 0.0001$) in the stenting group. However, the follow-up lumen diameter was not different (1.76 vs. 1.85 mm, stenting vs. BA-cilostazol). Although the difference was not statistically significant, restenosis rate was lower in the BA-cilostazol group (13.2% vs. 24.5%; $P = 0.11$). Subacute thrombosis occurred in one patient and target revascularization rate was higher in the stenting group (22.0% vs. 10.7%; $P = 0.10$). BA plus cilostazol administration seems to be a favorable strategy for small coronary artery disease.

Analysis of the effects of phosphodiesterase type 3 and 4 inhibitors in cerebral arteries.

Reference: Eur J Pharmacol. 2004;489(1-2):93.

Inhibitors of phosphodiesterases 3 and 4, the main cyclic AMP (cAMP) degrading enzymes in arteries, may have therapeutic potential in cerebrovascular disorders. This study suggests that phosphodiesterase 3 inhibitors are still effective under conditions with possible dysfunctional nitric oxide-cGMP pathway, such as in ischemic stroke or cerebral vasospasm.