

The role of cilostazol (Pletal) in the management of intermittent claudication.

Reference: Int J Clin Pract. 2003 ;57(5):405-9.

Intermittent claudication affects 5% of the middle-aged population in developed countries and is associated with a significant reduction in health-related quality of life and cardiovascular morbidity and mortality. The mainstay of treatment is best medical therapy (BMT) comprising smoking cessation, antiplatelet agents, lipid-lowering, advice to exercise, and correction of other modifiable vascular risk factors. Although BMT is highly effective in reducing cardiovascular risk and may also improve walking distance, many patients remain unacceptably symptomatic despite it. Until recently, the only available adjuvant therapies were supervised exercise programmes, angioplasty and surgery. Many patients are unable to comply with the first, and the last two are associated with limited durability and risk. The advent of cilostazol (Pletal) adds evidence-based pharmacotherapy to the vascular specialist's armamentarium for the first time. Here cilostazol and its role in the management of intermittent claudication are discussed.

Effect of cilostazol on vasomotor reactivity in patients with vasospastic angina pectoris.

Reference: Am J Cardiol. 2003 Jul 1;92(1):21-5.

We examined the effects of cilostazol on impaired coronary arterial responses in patients with vasospastic angina (VSA). Thirty patients who were diagnosed with VSA based on an acetylcholine provocation test and 10 subjects with normal coronary arteries were enrolled. The patients were divided into the following 3 groups: no antiplatelet agent treatment group, aspirin treatment, or cilostazol treatment groups. Coronary flow reserve (CFR), coronary flow volume at maximum hyperemia, and epicardial coronary artery diameter after administration of N(G)-

monomethyl-L-arginine (L-NMMA) were examined using a Doppler flow wire before and 6 months after the start of this study. CFR, coronary flow volume at maximum hyperemia, and diameter changes by L-NMMA were significantly increased in the cilostazol treatment group compared with the other 2 groups. In conclusion, cilostazol increased CFR and flow-dependent coronary dilation; these changes were attributable to nitric oxide. Cilostazol may improve coronary vascular endothelial dysfunction and coronary hemodynamics in patients with VSA.

Antiplatelet therapy in peripheral arterial disease. Consensus statement. Peripheral Arterial Diseases Antiplatelet Consensus Group.

Reference: Eur J Vasc Endovasc Surg. 2003;26(1):1-16.

OBJECTIVES: Antiplatelet agents are commonly prescribed to reduce the risk of myocardial infarction, stroke and graft occlusion in patients with peripheral arterial disease (PAD). The objective was to summarise current evidence and provide recommendations on the use of antiplatelet agents in PAD.

METHODS: A consensus group was assembled including 20 specialists from a variety of fields involved in the management of patients with PAD. Data was circulated in a systematic manner prior to a main consensus meeting held in November 2001. The document subsequently produced was circulated within the group to ensure agreement in the interpretation and presentation of its findings.

RESULTS: Consensus recommendations are provided in 7 common or contentious scenarios in PAD. The recommendations are graded to reflect the evidence available and interpretations of the group. Although the document provides recommendations, it is stressed that they must be interpreted in the light of individual patient circumstances.

CONCLUSION: Antiplatelet agents have an important role in the management of patient with PAD. Although this document provides consensus recommendations, the optimum treatment in many scenarios remains unclear due to a lack of focussed clinical trials in PAD.

Platelet activation is increased in peripheral arterial disease.

Reference: *J Vasc Surg.* 2003 Jul;38(1):99-103.

OBJECTIVE: Platelet activation was assessed in patients with peripheral arterial disease compared with healthy control subjects.

METHODS: This prospective comparative study included 100 subjects: 40 consecutive patients with intermittent claudication, 20 consecutive patients with critical ischemia and tissue loss, and 40 healthy control subjects. Whole blood flow cytometric analysis was performed to determine resting and stimulated platelet P-selectin expression and resting and stimulated platelet fibrinogen binding. Results are presented as platelet percentage and also as mean fluorescence intensity.

RESULTS: P-selectin expression was significantly increased in patients with intermittent claudication (median, 0.85%; range, 0.31%-4.77%; $P = .023$) and critical ischemia (median, 1.11%; range, 0.2%-3.26%; $P = .028$) compared with control subjects (median, 0.59%; range, 0.16%-4.58%). The percentage of platelets binding fibrinogen was also significantly higher in patients with intermittent claudication (median, 2.89%; range, 1.08%-9.59%; $P < .001$) compared with control subjects (median, 1.57%; range, 0.17%-10.7%). There was no significant difference in percentage of platelet fibrinogen binding between control subjects and patients with critical ischemia. Fibrinogen binding by stimulated platelets was significantly diminished in patients with critical limb ischemia compared with control subjects (67.2% vs 77.9%; $P = .006$).

CONCLUSIONS: Platelet activation is increased in patients with peripheral arterial disease, suggesting an underlying prothrombotic state. Platelets from patients with critical limb ischemia are less responsive to in vitro stimulation.



Prevalence of peripheral artery disease in urban high-risk Malaysian patients.

Reference: *Int J Clin Pract.* 2003;57(5):369-72.

Atherosclerosis is a progressive, disseminated condition that affects all the vascular beds. Peripheral arterial disease (PAD), a manifestation of atherosclerosis, measured non-invasively in the legs by ankle-brachial index (ABI) is associated with increased cardiovascular morbidity and mortality. Though several studies in the western industrialised countries have shown that PAD is widely prevalent in the general older population at risk, not much data are available in the South East Asian developing countries. We have conducted an epidemiological survey on the prevalence of PAD in high-risk patients at an urban hospital in Malaysia. A total of 301 consecutive patients aged 32-90 years were recruited during their follow-up clinic visits for established cardiovascular disease, ischaemic stroke or diabetes mellitus ≥ 5 years. All participants underwent ABI measurement and were subjected to the Edinburgh claudication questionnaire to assess leg symptoms. The prevalence of PAD in our high-risk population was 23%, of which only 27% were symptomatic with the classical intermittent claudication. All the patients with PAD were diagnosed at the time of the study. PAD was found in 33% of patients with pre-existent cardiovascular disease, 28% in patients with ischaemic stroke and 24% in diabetic patients. PAD was also highly prevalent among the younger patients. Our study has shown that PAD is highly prevalent among high-risk Malaysian patients and is not necessarily a disease of older age. Only 27% of these patients were symptomatic. All the subjects with PAD were diagnosed at the time of the study, which would suggest it is an unrecognised and underdiagnosed condition, even in patients with atherosclerotic risk factors.



<http://www.thai-otsuka.co.th/pxnews/index.html> Opinions and suggestions are welcomed Dr. Shwe Win, shwewin@thai-otsuka.co.th