

Management of peripheral arterial disease.

Reference: Am Fam Physician 2004;69(3):525-32.

Peripheral arterial disease is common, but the diagnosis frequently is overlooked because of subtle physical findings and lack of classic symptoms. Screening based on the ankle brachial index using Doppler ultrasonography may be more useful than physical examination alone. Noninvasive modalities to locate lesions include magnetic resonance angiography, duplex scanning, and hemodynamic localization. Major risk factors for peripheral arterial disease are cigarette smoking, diabetes mellitus, older age (older than 40 years), hypertension, hyperlipidemia, and hyperhomocystinemia. Nonsurgical therapy for intermittent claudication involves risk-factor modification, exercise, and pharmacologic therapy. Based on available evidence, a supervised exercise program is the most effective treatment. All patients with peripheral arterial disease should undergo aggressive control of blood pressure, sugar intake, and lipid levels. All available strategies to help patients quit smoking, such as counseling and nicotine replacement, should be used. Effective drug therapies for peripheral arterial disease include aspirin (with or without dipyridamole), clopidogrel, cilostazol, and pentoxifylline.

Remnant Lipoprotein Particles Induce Apoptosis in Endothelial Cells by NAD(P)H Oxidase-Mediated Production of Superoxide and Cytokines via Lectin-Like Oxidized Low-Density Lipoprotein Receptor-1 Activation. Prevention by Cilostazol.

Reference: Circulation 2004 Feb 16;

BACKGROUND: Remnant lipoprotein particles (RLPs), products of lipolytic degradation of triglyceride-rich lipoprotein derived from VLDL, exert atherogenesis. In this study, we observed how RLPs induced cytotoxicity in human umbilical vein endothelial cells (HUVECs) and cilostazol prevented cell death. METHODS AND RESULTS: RLPs were isolated from the plasma of hyperlipidemic patients by use of an immunoaffinity gel mixture of anti-apolipoprotein A-1 and anti-apolipoprotein B-100 monoclonal antibodies. RLPs (50

micro g/mL) significantly increased superoxide formation in HUVECs associated with elevated gp91phox mRNA and protein expression and Rac1 translocation, accompanied by increased production of tumor necrosis factor (TNF)-alpha and interleukin-1beta, DNA fragmentation, and cell death. Cilostazol (1 to 100 micro mol/L) significantly suppressed not only NAD(P)H oxidase-dependent superoxide production but also TNF-alpha and interleukin-1beta release and restored viability. RLPs activated a lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1), which was not inhibited by cilostazol. Treatment of HUVECs with monoclonal antibody for LOX-1 attenuated RLP-mediated production of superoxide, TNF-alpha, and interleukin-1beta and DNA fragmentation. CONCLUSIONS: RLPs stimulated NAD(P)H oxidase-dependent superoxide formation and induction of cytokines in HUVECs via activation of LOX-1, consequently leading to reduction in cell viability with DNA fragmentation, and cilostazol exerts a cell-protective effect by suppressing these variables.

Prostanoids for intermittent claudication.

Reference: Cochrane Database Syst Rev. 2004;1:CD000986

BACKGROUND: Peripheral arterial occlusive disease (PAOD) is a common cause of morbidity in the general population. While numerous studies have established the efficacy of prostanoids in PAOD stages III and IV the question of the role of prostanoids as an alternative or additive treatment in patients suffering from claudication intermittens (PAOD II) has not yet been clearly answered. OBJECTIVES: The aim of this review was to evaluate effects of prostanoids in patients with intermittent claudication. SEARCH STRATEGY: Computerised searches of the Cochrane Peripheral Vascular Diseases Specialised Register (last searched April 2003), The Cochrane Central Register of Controlled Trials (CENTRAL) (last searched Issue 1, 2003), MEDLINE and EMBASE were undertaken. In addition relevant journals were hand-searched. SELECTION CRITERIA: Randomized clinical trials describing the effects of prostanoids in the treatment of patients suffering from intermittent claudication have been considered for inclusion. DATA COLLECTION AND ANALYSIS: All reviewers assessed the quality of studies and extracted data unblinded. Statistical analysis including tests for heterogeneity and overall effect were performed by using MetaView of Review Manager 4.2. All numeric values are expressed as mean +/- Standard deviation (SD). MAIN RESULTS: Eighteen studies were included for analysis. A significant heterogeneity between the included studies

was detected in most of the subgroup analysis. Five studies compared the effects of prostaglandin E1 (PGE1) versus placebo, and reported in their individual results significant increases in walking distances after the administration of PGE1. The attained increase in walking distances appears to be not merely a short-term effect because several studies reported that walking capacity remained increased even after termination of treatment. On the other hand, oral or intravenous prostacyclin did not increase the walking distances significantly. At least one adverse reaction was reported from 23.6% of the patients treated with prostacyclin (PGI2), and its analogues and from 13.7% of the patients treated with PGE1. REVIEWER'S CONCLUSIONS: Because of the heterogeneity between most of the included studies, we did not pool relevant parts of the data by meta-analysis. Based on the individual results of the published literature, patients with intermittent claudication seem to benefit from administration (intravenous or intra-arterial) of PGE1 by a significant improvement of their walking capacity. Further well-conducted randomized, double blinded trials, with a sufficient number of patients to provide statistical powerful information, should be performed to confirm the results of this review.

Relationship between intermittent claudication, inflammation, thrombosis, and recurrent cardiac events among survivors of myocardial infarction.

Reference: Arch Intern Med. 2004 Feb 23;164(4):440-6.

BACKGROUND: Among coronary disease patients, concomitant peripheral arterial disease is a potent risk factor for future cardiac events and mortality. We sought to determine clinical and biochemical markers that might better elucidate the relationship between coronary and peripheral arterial disease. METHODS: Two months after an index myocardial infarction, 1045 patients provided detailed medical histories and underwent blood testing for selected hemostatic, lipid, and inflammatory markers. Patients were then followed up prospectively for a mean of 26 months. RESULTS: Compared with individuals without intermittent claudication (n = 966), those with claudication (n = 78) (information was unavailable for 1 individual) were significantly older and demonstrated an increased frequency of diabetes mellitus, tobacco use, prior cardiac and cerebrovascular events, and depressed left ventricular function. Individuals with claudication were less likely to receive beta-blocker therapy after the index infarction. Individuals with claudication had evidence of enhanced procoagulant and proinflammatory states manifested by relative elevations in plasma fibrinogen, D-dimer, C-reactive

protein, and serum amyloid A concentrations. During follow-up, the presence of claudication was associated with an independent 2-fold increase in the combined end point of death or nonfatal cardiac event (38.5% vs 17.8%, P = .001) and a 5-fold increase in cardiac mortality (19.2% vs 3.6%, P = .001). Patients with intermittent claudication who were not treated with beta-blockers had a significant 3-fold mortality excess relative to those receiving beta-blockers.

CONCLUSIONS: Following myocardial infarction, the added presence of intermittent claudication is associated with heightened procoagulant and proinflammatory states and an underuse of beta-blocker therapy and is a strong independent predictor of recurrent cardiovascular events.

Outcome of conservative therapy of patients with severe intermittent claudication.

Reference: Eur J Vasc Endovasc Surg. 2004 Mar;27(3):254-8.

Background. Intermittent claudication due to peripheral artery disease (PAD) can be treated conservatively, or by revascularization. Objectives. To assess the short-term outcome of conservatively-treated claudicants, and determine predictors for clinical improvement. Design. A retrospective cohort study. Methods. We evaluated Fontaine stage, walking distance and ankle brachial index (ABI) at baseline and after median 9 months (interquartile range (IQR) 6-24) in 181 patients with severe claudication. Results. We found clinical improvement by at least one Fontaine stage in 38 patients (21%) with an increased walking distance from baseline median 100 m (IQR 50-150) to follow-up median 650 m (IQR 300 to unlimited; p<0.001), but without changes in ABI (median 0.57, IQR 0.48-0.73 vs. median 0.54, IQR 0.45-0.81; p=0.10). One hundred and thirty-eight patients (76%) remained clinically and hemodynamically stable. A worsening of the clinical stage but without amputation was recorded in five patients (3%). Female gender (hazard ratio (HR) 0.51, p=0.052), diabetes (HR 0.35, p=0.020), and baseline ABI below 0.44 (HR 0.31, p=0.019) were associated with a reduced probability of clinical improvement. Conclusion. Certain patients with intermittent claudication show substantial clinical improvement with conservative medical therapy, despite any lack of hemodynamic improvement. Given the low number of patients with clinical deterioration in the short term, primarily conservative therapy should be the preferred initial option for most claudicants.

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