

Pharmacological management of claudication

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Available evidence suggests supervised exercise program is the most effective therapy for claudication. All patients with peripheral arterial disease (PAD) should undergo effective management to control their risk factors. In addition to risk factor control, the pharmacological management of PAD includes aspirin (with or without dipyridamole), clopidogrel, cilostazol, and pentoxifylline. Since the antiplatelet therapies were discussed in my previous communication, here we will restrict our discussion to cilostazol and pentoxifylline. Patients with mild to moderate symptoms are best treated by conservative measures such as exercise programs. Pharmacotherapy for claudication can be added on to the exercise regimen, no agent has been shown to have sufficient efficacy to gain wide spread acceptance. While studies have shown to improve treadmill walking distance, lack of robust clinical impact has limited their widespread use [1].

Pentoxifylline: Pentoxifylline is a methylxanthine derivative, approved in 1984 for claudication, increases the deformability of RBC's and WBC's, lowers fibrinogen levels and has antiplatelet effects [2]. A meta-analysis of pentoxifylline studies had found an increase of 44 m in maximal treadmill distance (95 percent confidence interval, 14 to 74) [3]. Two meta-analysis and two more systematic review published on pentoxifylline came to a conclusion that the drug might have a small benefit but lacks conclusive evidence to support wide spread use.

Cilostazol: Approved in 1999 by the FDA, this is a phosphodiesterase type 3 inhibitor (PDE-3), which inhibits platelet aggregation, formation of arterial thrombi, vascular smooth muscle proliferation and causes vasodilatation. However, since vasodilators and antiplatelet agents fail to improve claudication, the mechanism of action of this agent is unknown. It is extensively metabolized by cytochrome P450 enzyme system (CYP 3A4 isoform) in the liver enabling the drugs which inhibit

this enzyme to increase its concentration. In four randomized placebo control trials, cilostazol has been shown to be superior to placebo in improving the pain free and maximal treadmill walking distance [4-7]. The predominant side effect of cilostazol is headache, which affects 34 percent of patients taking 100 mg twice daily, as compared with 14 percent of patients taking placebo. The other side effects are transient diarrhea, palpitations and dizziness. Since cilostazol is a PDE-3 inhibitor like milrinone which has been shown to increase mortality in chronic heart failure, this comes with a black box warning not to use in patients with claudication and heart failure.

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