

TOP Journal Club

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Effect of Cilostazol, a Phosphodiesterase Inhibitor, on Carotid IMT in Japanese Type 2 Diabetic Patients.

Reference: *Endocrine Journal* 2004;51:545

The aim of this study was to investigate the effect of cilostazol, a cAMP phosphodiesterase inhibitor, on carotid artery intima-media thickness (IMT) and on the incidence of cardiovascular events in Japanese subjects with type 2 diabetes. A total of 62 type 2 diabetic subjects were allocated equally to the cilostazol treatment group (n = 31) and the control group (n = 31). Carotid IMT was evaluated before and after treatment using B-mode ultrasonography. After the study period (mean +/- SD: 2.6 +/- 0.17 years), carotid IMT showed a significantly greater increase in the control group than in the cilostazol group (0.12 +/- 0.14 mm vs. 0.04 +/- 0.02 mm, p<0.05). In the control group, 1 out of 31 patients suffered from symptomatic cerebral infarction and 1 had angina pectoris during the observation period. On the other hand, no subject in the cilostazol group developed cardiovascular events during the study period. At baseline, the diabetic patients given cilostazol had a significantly lower HbA(1c) level than the control subjects, but the other atherosclerotic risk factors (BMI, blood pressure, and serum lipids) and the duration of diabetes did not differ between the two groups. These results indicate that cilostazol therapy can attenuate the increase of carotid artery IMT in Japanese subjects with type 2 diabetes.

Cilostazol, clopidogrel or ticlopidine to prevent sub-acute stent thrombosis: a meta-analysis of randomized trials.

Reference: *Am Heart J.* 2004 Dec;148(6):990-7

BACKGROUND: Sub-acute thrombosis is a serious complication of coronary artery stenting. Clopidogrel plus aspirin is the accepted prophylactic regimen, but has yet to be proven superior to ticlopidine plus aspirin, and a new regimen combining cilostazol and aspirin has been introduced. **METHODS:** We conducted a meta-analysis of all trials that compared >or=2 oral anti-thrombotic strategies in patients undergoing coronary stent placement to determine which treatment optimally prevents adverse cardiac events in the 30 days following stent insertion. We used meta-regression to compare all strategies to a shared control strategy:

ticlopidine plus aspirin. We also compared randomized trials to historically controlled and other non-randomized trials. We conducted sensitivity analysis and subgroup analysis to assess for possible heterogeneity. **RESULTS:** In comparison to ticlopidine plus aspirin the odds-ratios for cardiac events, with 95% confidence intervals were: aspirin alone, 4.29 (3.09-5.97), coumadin plus aspirin, 2.65 (2.18-3.21), clopidogrel plus aspirin, 1.06 (0.86-1.31), cilostazol plus aspirin, 0.73 (0.47-1.14). Among trials that compared clopidogrel plus aspirin to ticlopidine plus aspirin, historically controlled trials were statistically distinct from randomized trials. The analysis of cilostazol was sensitive to the small size of the included studies. **CONCLUSIONS:** Neither clopidogrel plus aspirin nor cilostazol plus aspirin can be statistically distinguished from ticlopidine plus aspirin for the prevention of adverse cardiac events in the 30 days after stenting. A randomized trial including cilostazol is warranted.

The phosphodiesterase 3 inhibitor cilostazol dilates large cerebral arteries in humans without affecting regional cerebral blood flow.

Reference: *J Cereb Blood Flow Metab.* 2004 Dec;24(12):1352-8.

Cilostazol, an inhibitor of phosphodiesterase (PDE) type 3, is used clinically in peripheral artery disease. PDE3 inhibitors may be clinically useful in the treatment of delayed cerebral vasospasm after subarachnoid hemorrhage. The authors present the first results on the effect of cilostazol on cerebral hemodynamics in normal participants. In this double-blind, randomized, crossover study, 200 mg cilostazol or placebo was administered orally to 12 healthy participants. Cerebral blood flow was measured using ¹³³Xe inhalation and single photon emission computerized tomography. Mean flow velocity in the middle cerebral arteries (VMCA) was measured with transcranial Doppler, and the superficial temporal and radial arteries diameters were measured with ultrasonography. During the 4-hour observation period, there was no effect on systolic blood pressure (P = 0.28), but diastolic blood pressure decreased slightly compared with placebo (P = 0.04). VMCA decreased 21.5 +/- 5.7% after cilostazol and 5.5 +/- 12.2% after placebo (P = 0.02, vs. placebo), without any change in global or regional cerebral blood flow. The superficial temporal artery diameter increased 17.6 +/- 12.3% (P < 0.001 vs. baseline) and radial artery diameter increased 12.6 +/- 8.6% (P < 0.001 vs. baseline). Adverse events, especially headache, were common. The findings suggest that cilostazol is an interesting candidate for future clinical trials of delayed cerebral vasospasm.

Brugada Syndrome. Report of the Second Consensus Conference. Endorsed by the Heart Rhythm Society and the European Heart Rhythm Association

Reference: *Circulation* 2005;111:

Since its introduction as a clinical entity in 1992, the Brugada syndrome has progressed from being a rare disease to one that is second only to automobile accidents as a cause of death among young adults in some countries. Electrocardiographically characterized by a distinct ST-segment elevation in the right precordial leads, the syndrome is associated with a high risk for sudden cardiac death in young and otherwise healthy adults, and less frequently in infants and children. Patients with a spontaneously appearing Brugada ECG have a high risk for sudden arrhythmic death secondary to ventricular tachycardia/fibrillation. The ECG manifestations of Brugada syndrome are often dynamic or concealed and may be unmasked or modulated by sodium channel blockers, a febrile state, vagotonic agents, -adrenergic agonists, -adrenergic blockers, tricyclic or tetracyclic antidepressants, a combination of glucose and insulin, hypo- and hyperkalemia, hypercalcemia, and alcohol and cocaine toxicity. In recent years, an exponential rise in the number of reported cases and a striking proliferation of articles defining the clinical, genetic, cellular, ionic, and molecular aspects of the disease have occurred. The report of the first consensus conference, published in 2002, focused on diagnostic criteria. The present report, which emanated from the second consensus conference held in September 2003, elaborates further on the diagnostic criteria and examines risk stratification schemes and device and pharmacological approaches to therapy on the basis of the available clinical and basic science data.

Hypokalemia has been implicated as a contributing cause of the prevalence of SUNDS in northeastern Thailand, where potassium deficiency is endemic. Serum potassium in this northeastern population is significantly lower than that of the population in Bangkok, which lies in the central part of Thailand, where potassium is abundant in food.

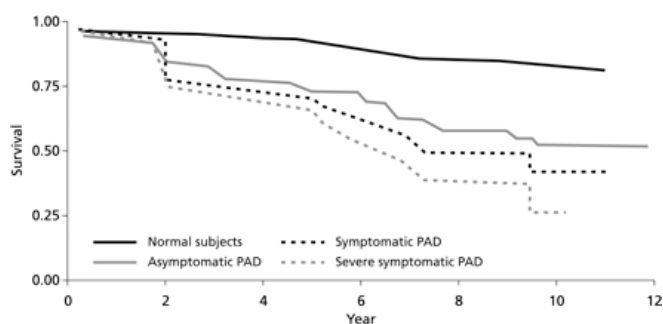
The 1990 report of the Thai Ministry of Public Health found an association between a large meal of glutinous ("sticky") rice or carbohydrates ingested on the night of death in patients with SUNDS. Consistent with this observation, a recent study by Nogami et al found that glucose and insulin could unmask the Brugada ECG.

The most recent addition to the pharmacological armamentarium is a phosphodiesterase III inhibitor, cilostazol, which normalizes the ST segment most likely by augmenting the calcium current (I_{Ca}), as well as by reducing I_{to} secondary to an increase in heart rate.

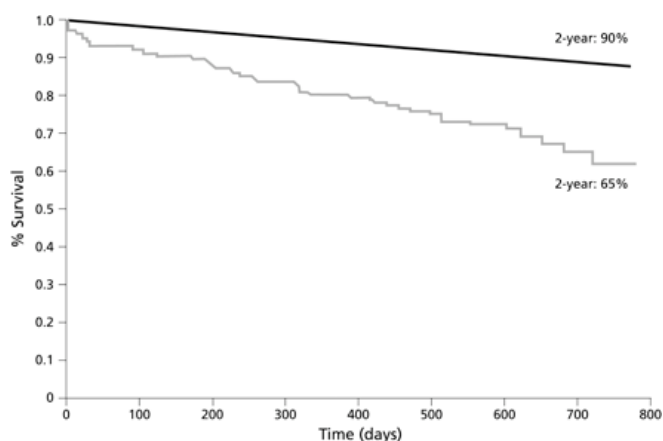
What does the future hold for the patient with peripheral arterial disease?

Eur. Heart J. Suppl., Jul 2004; 6: 43 - 48.

PAD SURVIVAL RATES



Cumulative survival following peripheral bypass for critical lower limb ischaemia.



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