TOP Journal Club

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Effects of cilostazol in patients with Raynaud's syndrome.

Reference: Am J Cardiol. 2003 Dec 1;92(11):1310-5.

Raynaud's syndrome (RS), which is characterized by recurrent episodes of vasospasm with exposure to cold, may occur alone (primary RS) or in association with connective tissue diseases or other underlying conditions (secondary RS). We investigated the effect of cilostazol on vessel wall responses in RS. Patients were diagnosed (primary or secondary RS associated with connective tissue diseases) and randomized to placebo or cilostazol 100 mg twice daily for 6 weeks in a double-blind manner. Brachial artery vasoreactivity, laser Doppler fluxmetry, and cold pressor testing (CPT) were performed at study initiation and completion. Symptoms were assessed using standardized questionnaires. Forty subjects completed the study (19 with primary RS and 21 with secondary RS). Cilostazol significantly increased the mean brachial artery diameter at 6 weeks (primary RS, p = 0.006; secondary RS, p = 0.06). There was no change in median flow-mediated dilation (FMD) with cilostazol in primary RS (25th, 75th percentiles) (4.06% [2.5, 6.1] to -0.77% [-2.4, 3.4] or secondary RS (2.2% [0.05, 6.3] to 2.95% [1.7, 7.4]). There were no changes in nitroglycerin-mediated dilation or microvascular flow indexes in either cohort. In patients with primary RS, cilostazol treatment yielded a positive change in the slope of brachial responsiveness to CPT (increase of 0.32 mm/min; p = 0.002 vs placebo). Cilostazol treatment remained significantly associated with increased brachial artery diameter when controlling for baseline values (p = 0.018). Cilostazol increased conduit vessel diameter in patients with primary and secondary RS, with a favorable impact on conduit vessel responsiveness to cold in patients with primary RS without affecting microvascular flow or symptoms.

Limited influence of P-glycoprotein on small-intestinal absorption of cilostazol, a high absorptive permeability drug.

Reference: J Pharm Sci. 2003 Nov;92(11):2249-59.

Intestinal transport of the type III phosphodiesterase inhibitor cilostazol was characterized to evaluate the influence of secretory transporter. Intestinal absorption of cilostazol measured by the in situ closed loop method, showed regional differences, with high permeability in the upper part of the small intestine. Intestinal secretory transport of cilostazol at the ileum was tended to be decreased by the increase of tested concentration of cilostazol from 10 to 20 microM when evaluated by means of a Ussing-type chamber method with mounted rat intestinal tissues. Transcellular transport of cilostazol in the basolateral-to-apical direction in LLC-GA5-COL150 cells, which overexpress P-glycoprotein, was higher than that in parental LLC-PK1 cells. In addition, cilostazol reduced the basolateral-to-apical transport and increased the accumulation of [(3)H]daunomycin in LLC-GA5-COL150 cells. Accordingly, cilostazol was demonstrated to be transported by P-glycoprotein, while cilostazol is not likely to cause induction of the expression level of P-glycoprotein by the same manner with rifampin. Apical-to-basolateral transport of cilostazol in Caco-2 cells was increased in a low concentration range, followed by a decrease with further increase of the concentration, while the permeability coefficient of cilostazol was above 1 x 10(-6) cm/s at any concentration. Initial uptake of [(14)C]cilostazol by Caco-2 cells was temperature dependent and was reduced in the presence of unlabeled cilostazol, suggesting that apical uptake is also mediated by a transporter(s). In conclusion, intestinal absorption of cilostazol, which has a high absorptive permeability, may not be significantly hampered by efflux transporters, such as P-glycoprotein.

Influence of anti-ulcer drugs used in Japan on the result of (13)C-urea breath test for the diagnosis of Helicobacter pylori infection.

Reference: J Gastroenterol. 2003;38(10):937-41.

BACKGROUNDMETHODS. The subjects of the study were 64 adult volunteers who tested positive for H. pylori infection by the serum antibody method. Eight classes of anti-ulcer drugs used in Japan were administered at their usual doses to these subjects: lansoprazole, a proton pump inhibitor (PPI); nizatidine, an H(2)-receptor antagonist (H(2)RA); and polaprezinc, ecabet sodium, rebamipide, teprenone, cetraxate hydrochloride, and sucralfate, all mucoprotective agents. The study drugs were randomized for administration to the subjects, and each of the drugs was administered for 14 consecutive days. The UBT was performed on days 0, 14, and 21. RESULTS. The mean Delta(13)C per thousand in the lansoprazole group was significantly decreased on day 14, to below 10 per thousand, in 4 of 16 subjects, and in 1 of the 4 subjects, the test result was negative, with the Delta(13)C per thousand falling to 1.7 per thousand.

The value returned to baseline 1 week after the discontinuation of lansoprazole. The other drugs administered had no significant effect on the result of the UBT, except that the mean Delta(13)C per thousand showed a tendency to decrease after the administration of ecabet sodium and rebamipide. CONCLUSIONS. Administration of a PPI may produce a false-negative UBT result, while other anti-ulcer drugs, for the most part, have little effect on the result of the UBT when used alone.The (13)C-urea breath test (UBT) is a simple test for the diagnosis of Helicobacter pylori infection, but several factors have been reported to affect the results of this test. In this study, the effects of the anti-ulcer drugs used in Japan on the results of the UBT were determined.

Tissue (muscle) oxygen saturation (StO2): a new measure of symptomatic lower-extremity arterial disease.

Reference: J Vasc Surg. 2003 Oct;38(4):724-9.

OBJECTIVES: Near-infrared spectroscopy provides a noninvasive method of measuring tissue oxygen saturation and has been used to monitor extremity compartment syndrome. Tissue O(2) saturation (StO(2)) is potentially useful in assessing patients with peripheral arterial disease (PAD). The purposes of this feasibility study are to (1) explore the diagnostic sensitivity of StO(2) in subjects with PAD and symptoms of intermittent claudication (IC) compared with normal subjects, and (2) correlate the change in StO(2) during and after exercise with the ankle brachial index (ABI) in patients with IC.Material and methods Forty-nine subjects, 35 normal and 14 PAD, from two centers were evaluated in a prospective cross-sectional analysis comparing StO(2) by using the InSpectra tissue spectrometer and ABI at rest (baseline) and after treadmill exercise. Measurements were obtained at baseline and peak exercise (normal subjects) and at baseline, initial claudication distance (ICD) and absolute claudication distance (ACD) in PAD subjects. Endpoint values were the mean of 15 data points. Times to 50% of StO(2) recovery to baseline (T(50)) and complete recovery to baseline (T(100)) were measured. Receiver-operator characteristic curves were constructed to assess the sensitivity/specificity values associated with various StO(2) cut-points. RESULTS: The PAD patients were older (P =.0002) and 57% were male, compared with 37% males in the normal group. The ABI was 0.68 +/- 0.14 in PAD patients versus 1.14 +/- 0.08 in normal subjects (P <.0001). The baseline StO(2) was 65% in both groups. The peak exercise StO(2) was significantly lower and the absolute change in StO(2) and the percent change in StO(2) were significantly greater in PAD patients (P < 0.45). The T(50) and T(100) were longer in the PAD patients compared to normal subjects (P =.0001 and.002, respectively). A T(50) of >70 seconds yielded a sensitivity of 89% and a specificity of 85% for PAD. CONCLUSIONS: StO(2) is a new and potentially useful technique to evaluate patients with PAD. Resting StO(2) was similar in PAD-IC subjects and normals. There was a significantly greater drop in StO(2) and longer recovery times in PAD-IC subjects. Interestingly, StO(2) at the ICD and ACD was similar. StO(2) offers a different and perhaps more appropriate end point for diagnosis and monitoring of the management of patients with PAD, and may offer additional insight into the pathophysiology of exercise-induced muscle ischemia and its recovery.

Are National Cardiac Guidelines being Applied by Vascular Surgeons?

Reference: Eur J Vasc Endovasc Surg. 2003 Dec;26(6):623-8.

Introduction. National cardiac guidelines recommend that patients with intermittent claudication should be managed in the same way as those with established coronary heart disease. This survey aimed to determine the attitudes of vascular consultants to risk factor management in new patients attending their out-patient clinic. Methods. An anonymous postal questionnaire was sent to all 394 members of the Vascular Surgical Society in June 2002. Questions were asked about the following measures: serum cholesterol levels, the presence of diabetes, antiplatelet therapy, exercise regimens, blood pressure, thrombophilia, smoking and the availability of local guidelines and expertise. Results. A response rate of 65% was obtained. Most (85%) consultants would measure a random cholesterol, but 34% would only treat claudicants if the cholesterol was greater than 5.5 mmol/l. Furthermore, 23% would inappropriately use diet alone as initial cholesterol lowering therapy. Over a quarter of consultants would not screen for diabetes or measure blood pressure. Nearly all (99%) would recommend aspirin and 66% would recommend nicotine replacement therapy. Only 55% had access to a smoking cessation clinic, and 34% to a formal exercise program. The majority (56%) did not have local risk factor management guidelines, only 16% had access to a vascular physician, and 65% would prefer to have this expertise available for difficult cases. Discussion. Management of major risk factors was found to be sub-optimal. Thus guidelines for the prevention of coronary disease in clinical practice are not being applied to claudicants.

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