

TOP Journal Club

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Cilostazol treatment of claudication in diabetic patients.

Reference: Curr Med Res Opin 2002;18(8):479-87.

OBJECTIVE: To compare the efficacy and safety of cilostazol in diabetic and non-diabetic patients from eight (six placebo- and two active-controlled) randomised, double-blind phase II trials.

DESIGN: We only included patients from the trial data set receiving cilostazol 100 mg twice daily (216 diabetic/599 non-diabetic) or placebo (220/616). Efficacy was measured by absolute claudication distance (ACD), using standard treadmill exercise protocols.

RESULTS: Among diabetic and non-diabetic patients, cilostazol was superior to placebo (estimated treatment effect 1.15, 95% confidence interval, 1.05-1.25, $p = 0.001$; and 1.24, 1.18-1.31, $p < 0.0001$, respectively). There was no statistical difference in response between diabetic and non-diabetic subjects. In the efficacy analysis, cilostazol-treated diabetic subjects with the lowest baseline ACD (but not those with greater baseline ACD) walked approximately 34% farther than at baseline, whereas their non-diabetic counterparts walked 23% farther. There was no significant difference in the adverse event profile of the diabetic and non-diabetic patients on cilostazol. No excess haemorrhagic events occurred in cilostazol-treated diabetic patients. Trial duration varied from 12 to 24 weeks.

CONCLUSIONS: Diabetic and non-diabetic patients with intermittent claudication respond favourably to cilostazol, with no significant difference in their overall response. Diabetic individuals with the most severe claudication respond better than those less affected, but the response of non-diabetic patients increases as baseline ACD increases. Adverse event incidence was comparable in the two populations, although diabetic patients might be expected to experience greater morbidity. Cilostazol is a safe and effective treatment for claudication in diabetic and non-diabetic populations.

Hepatic amino-acid metabolism in liver cirrhosis and in the long-term course after liver transplantation.

Reference: Transpl Int 2003 Jan;16(1):1-8

The aim of this study was to investigate the impact of orthotopic liver transplantation (OLT) on plasma levels and splanchnic turnover of key amino acids for muscular (branched-chain amino acids: BCAAs) and hepatic metabolism (aromatic amino acids (AAAs) and methionine) in 48 patients with cirrhosis, 14 patients after OLT, and 46 controls. Also, hepatic amino-acid supply and resting energy expenditure were measured. BCAA levels (no hepatic uptake) decreased in cirrhosis ($P < 0.001$) and were improved, although not normalized, after OLT ($P < 0.001$). AAA and methionine levels were raised in cirrhosis ($P < 0.001$) and normalized after OLT ($P < 0.001$). Hepatic supply of these amino acids increased in patients graded Child B and C and decreased significantly after OLT. Splanchnic uptake of AAAs and methionine increased significantly in Child-B and decreased in Child-C patients. After OLT, splanchnic extraction of AAAs and methionine was as in Child A. Circulating AAAs and methionine correlated with indocyanine-green half-life ($r = 0.71$, $P < 0.001$) and resting energy expenditure ($r = 0.50$, $P < 0.001$), indicating that levels of circulating AAAs and methionine in cirrhosis are determined by hepatic and extra-hepatic metabolic factors. This study demonstrates persistent changes in muscular metabolism of BCAAs after OLT, while the hepatic amino-acid metabolism is normalized due to (1) a significant reduction in the rate of peripheral proteolysis, and (2) improved liver function compared with that in patients with cirrhosis.

Endovascular stents for intermittent claudication (Cochrane Review).

Reference: Cochrane Database Syst Rev 2003;(1):CD003228

BACKGROUND: Endovascular stents have been suggested as a means to improve the patency of arteries after angioplasty in patients with intermittent claudication.

OBJECTIVES: The null hypothesis to be tested by this review is that for individuals with claudication, the use of an endovascular stent in addition to percutaneous transluminal angioplasty, does not improve symptoms of

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life-style limiting claudication, when compared to percutaneous angioplasty alone.

SEARCH STRATEGY: We searched the Specialised Register of the Cochrane Peripheral Vascular Disease Group, (last searched October 2002), and the Cochrane Central Register of Controlled Trials (CENTRAL), (last searched Issue 3, 2002). We also searched MEDLINE and EMBASE (up to and including January 2001); bibliographies of published data, and hand searched the Journal of Vascular Interventional Radiology (1990-2001). Enquiries were made to stent manufacturers for unpublished trial data.

SELECTION CRITERIA: Randomised trials comparing angioplasty alone, versus angioplasty with endovascular stents, in subjects with intermittent claudication.

DATA COLLECTION AND ANALYSIS: Both reviewers independently assessed trial quality and extracted the data. Only published trial data were used. Effectiveness was measured by pre-defined primary outcome measures: restenosis / reocclusion rates and maximum walking distance.

MAIN RESULTS: Two trials were included with a total sample size of 104 subjects. Both trials included only individuals with femoro-popliteal disease and compared angioplasty and stenting with the Palmaz stent against angioplasty alone. Although one study showed a slight statistical advantage in arterial patency after angioplasty alone, this was not found when the two studies were combined. No differences in the secondary outcomes in either study were detected.

REVIEWER'S CONCLUSIONS: The small number of relevant trials identified, together with the small sample sizes and methodological weaknesses, severely limit the usefulness of this review in guiding practice. Larger multicentre trials are needed.

Efficacy of Rebamipide as Adjunctive Therapy in the Treatment of Recurrent Oral Aphthous Ulcers in Patients with Behcet's Disease: A Randomised, Double-Blind, Placebo-Controlled Study.

Reference: Drugs R D 2003;4(1):19-28.

BACKGROUND: Behcet's disease (BD) is a recurrent inflammatory disease involving chronic recurrent oral aphthous ulcers (aphthae), uveitis, skin lesions and genital ulcers. We prospectively investigated the efficacy

of rebamipide, a gastroprotective drug, against oral aphthous ulcers in BD patients.

METHODS: In a multicentre, double-blind, placebo-controlled study, 35 patients with BD, having as the main symptom oral aphthosis, were randomised to receive rebamipide 300 mg/day or placebo for 12 to 24 weeks between August 1994 and December 1996. Oral aphthosis must have occurred within 4 weeks prior to enrolment and must have been visible for at least 7 days during that time. Oral aphthae count and pain scores were recorded daily in a diary by the patients themselves. Monthly aphthae count and pain scores were defined as the sum of aphthae count and pain scores for a month, respectively. Investigators rated the global improvement in aphthae count and pain using a 6-point scale. The rate of change in monthly aphthae count and pain scores in the first 3 and last 3 months of treatment were assessed in patients with more severe symptoms whose aphthae count and pain score were >28 at baseline (trial entry).

RESULTS: The rate of moderate or marked improvement in aphthae count and pain was 36% (5 of 14 subjects) in the placebo group and 65% (11 of 17 subjects) in the rebamipide group. During months 2 to 6 of treatment, aphthae count tended to increase and reached a peak at month 4 in the placebo group but decreased in the rebamipide group. Pain score decreased to the same extent in both groups for the first 3 months of treatment; however, in the fourth to sixth months of treatment, the pain score tended to increase in the placebo group but decreased in the rebamipide group. In patients with a monthly aphthae pain score >28 at baseline, pain and count scores decreased throughout the 6 months of rebamipide treatment but increased during the last 3 months of treatment in the placebo group ($p < 0.01$ for the between-group comparisons).

CONCLUSIONS: Rebamipide is well tolerated and improves the aphthae count and pain score in BD patients. It may therefore be useful in the treatment and prevention of frequently recurrent oral aphthous ulcers (not restricted to BD). Administration of rebamipide is not cumbersome, and it does not cause any discomfort, which corticosteroid ointments for example may do; furthermore, there are no specific adverse drug reactions. Rebamipide is therefore recommended as a long-term treatment for recurrent oral aphthous ulcers.

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