Assessment of gallopamil (D 600) in patients with chronic stable angina pectoris
Results of a placebo-controlled single-blind study

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The anti-anginal effects of calcium antagonists are due to a reduction of myocardial oxygen uptake and/or an improvement of oxygen supply to the myocardium, depending on the affinity of the drug to specific sites of action and differences in the pathogenesis of the myocardial ischaemia.

D 600 is a new calcium antagonist which differs from verapamil only by the addition of a methoxyl group. As a result of this modification of the molecule, D 600 is five to six times more potent than verapamil (1, 2).

D 600 has been shown to increase the exercise tolerance of patients with stable, exercise-induced angina (3, 4, 5, 6, 7). The anti-anginal effect of D 600 appears to be related to an improvement in the myocardial oxygen balance. However, the mechanisms responsible for the anti-ischaemic effect, and the tolerance in D 600 in patients who had suffered an acute myocardial infarction (AMI) still required investigation.

A multicentre study on exercise-induced angina pectoris was carried out on collaboration with the Cardiology Department of the Policlinico S. Matteo, Pavia (IRCCS) and the Cardiology Departments of the Medical Rehabilitation Centres in Montescano and Veruno (Fondazione Clinica Lavoro di Pavia IRCCS).

Twenty-nine patients, 28 men and one woman, who had had an acute myocardial infarction were recruited for the study. They were between 41 and 65 years of age (on average 54 ± 5.3).

Thirty days after the acute myocardial infarction, the patients underwent an initial symptom-limited exercise test in the sitting position on a bicycle ergometer. The initial work load was 25 watts and this was increased in 25-watt increments every 3 minutes. Part of the study was a wash-out phase for which beta-blockers and verapamil were withdrawn 7 days, and nifedipine and nitrates 24 hours before the first exercise test.

During the exercise tests, all the patients showed an ST-segment depression of at least 1 millimetre. This was associated with pain in 12 patients and was asymptomatic in 17.

A second exercise test was carried out within 2 days, in order to verify the stability of the ischaemia threshold, which was expressed as a variability of not more than maximal ± 20% of the double product at 1-mm ST-segment depression from two exercise tests.

In the cross-over single-blind trial all the patients were to undergo two treatment phases, either with the trial medication (50 mg t.i.d.) or with placebo. Further exercise tests were carried out on the 7th day and 14th day after the administration of D 600 or placebo (Figure 1).
Altogether 4 patients dropped out of the study, 2 because of a skin rash, one because of anginal pain under placebo and the fourth because of 1st degree AV block after gallopamil. During the run-in phase none of the 25 patients who completed the study showed significant changes of heart rate, blood pressure or in the double product, either at rest or during exercise. Nor were there any significant changes in the exercise time, the mean ST-segment depression at the maximum work load or in the double-product ischaemia threshold. Thus, the response to D 600 could be assessed by comparison with the mean values for the parameters measured in the two exercise tests in the run-in phase (Table 1).

In comparison with placebo, treatment with D 600 did not alter the resting heart rate, systolic blood pressure or double product. However, D 600 significantly increased the exercise time (12.6 ± 0.5 vs 10.9 ± 0.7; p<0.01) and the elapsed time before the ischaemia threshold was reached (ST depression = 1 mm), (9.4 ± 1.1 vs 7 ± 1; p<0.01). At the maximum work load, D 600 reduced the maximum ST depression (1.2 ± 0.2 vs 1.7 ± 0.1) without significantly altering the double-product ischaemia threshold (249 ± 20 vs 213 ± 14; ns).

A provisional conclusion from analysing these data is that D 600 increased the exercise tolerance of patients with chronic stable angina pectoris following acute myocardial infarction, probably by reducing myocardial oxygen uptake.

This conclusion appears to be confirmed by the results of another study on the effect of D 600 on blood flow in the coronary sinus during myocardial ischaemia induced by atrial pacing (8).

Ten patients with chronic stable angina pectoris and angiographically proven coronary heart disease (stenosis ≥75%), in all cases involving the proximal portion of the interventricular branch of the left coronary artery, took part in the study.

Blood flow in the coronary sinus was measured by the thermodilution technique using a triple thermistor catheter which was advanced into the sinus from a peripheral vein. Arterial blood pressure was recorded continuously via a Teflon cannula inserted in a brachial artery.