Long Term Efficacy of a Controlled-Release Formulation of Isosorbide 5-Mononitrate (Imdur®) in Angina Patients Receiving β-Blockers

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Summary

In a multicentre double-blind crossover study the clinical efficacy and tolerability of a controlled-release formulation, Durules®, of isosorbide 5-mononitrate (Imdur®) 60mg once daily was compared with placebo over 2 weeks in 70 patients with stable exercise-induced angina pectoris who were receiving concomitant long term β-blockade. Isosorbide 5-mononitrate significantly improved exercise capacity and signs of myocardial ischaemia, while reducing the number of anginal attacks and consumption of short-acting glyceryl trinitrate tablets compared with β-blocker therapy alone. During an open follow-up period of 1 year, there was no attenuation of the antianginal efficacy of isosorbide 5-mononitrate. The drug was well tolerated during both phases of the study, and the only significant adverse effect was headache, which rapidly disappeared during continued treatment.

The medical treatment of angina pectoris is aimed at improving the balance of myocardial oxygen supply and demand. Three groups of drugs are normally used for prophylactic antianginal treatment: β-blockers, calcium antagonists and long-acting nitrates. All these drugs have a well-documented effect in angina pectoris. Because of the positive effect of β-blockers on ischaemic heart disease and after myocardial infarction, β-blockers are often considered as first-line agents in the treatment of angina pectoris in Scandinavia (Beta-Blocker Heart Attack Trial Research Group 1982; Hjalmarson et al. 1981; Olsson et al. 1985; The Norwegian Multicenter Study Group 1981).

In an earlier study by our research group (Uusitalo et al. 1986), some additional benefit was found when the calcium antagonist nifedipine was added to the β-blocker metoprolol. The aim of the present study was to determine the possible additional antianginal effect and tolerability of a Durules® formulation of isosorbide 5-mononitrate (Imdur®) when given to patients receiving concomitant β-blockade.

1. Patients and Methods

Seven centres in Finland, Norway and Sweden participated in this multicentre study. Special attention was paid during the design of the study to standardisation of exercise testing, treatment and reporting of results. All the patients had stable exercise-induced angina of at least 6 months’ duration, with a history of at least 5 attacks per week, and were receiving treatment with β-blockers, which were maintained unchanged and stable in

Fig. 1. Mean (+ SD) exercise loads at baseline (□) and after 2 weeks' therapy with placebo (◮) and isosorbide 5-mononitrate (Imdur®) (△) in angina patients receiving β-blockers.

Fig. 2. Change in mean exercise loads versus baseline after 2 weeks' therapy with placebo (◮) and isosorbide 5-mononitrate (Imdur®) (△) in angina patients receiving β-blockers.

Fig. 3. Consumption of short-acting glyceryl trinitrate tablets (mean + SD) at baseline (□) and after 2 weeks' therapy with placebo (◮) and isosorbide 5-mononitrate (Imdur®) (△) in angina patients receiving β-blockers.