

# Effect of high-dose allopurinol on exercise in patients with chronic stable angina: a randomised, placebo controlled crossover trial.

## BACKGROUND:

Experimental evidence suggests that xanthine oxidase inhibitors can reduce myocardial oxygen consumption for a particular stroke volume. If such an effect also occurs in man, this class of inhibitors could become a new treatment for ischaemia in patients with angina pectoris. We ascertained whether high-dose allopurinol prolongs exercise capability in patients with chronic stable angina.

## METHODS:

65 patients (aged 18-85 years) with angiographically documented coronary artery disease, a positive exercise tolerance test, and stable chronic angina pectoris (for at least 2 months) were recruited into a double-blind, randomised, placebo-controlled, crossover study in a hospital and two infirmaries in the UK. We used computer-generated randomisation to assign patients to allopurinol (600 mg per day) or placebo for 6 weeks before crossover. Our primary endpoint was the time to ST depression, and the secondary endpoints were total exercise time and time to chest pain. We did a completed case analysis. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN 82040078.

## FINDINGS:

In the first treatment period, 31 patients were allocated to allopurinol and 28 were analysed, and 34 were allocated to placebo and 32 were analysed. In the second period, all 60 patients were analysed. Allopurinol increased the median time to ST depression to 298 s (IQR 211-408) from a baseline of 232 s (182-380), and placebo increased it to 249 s (200-375;  $p=0.0002$ ). The point estimate (absolute difference between allopurinol and placebo) was 43 s (95% CI 31-58). Allopurinol increased median total exercise time to 393 s (IQR 280-519) from a baseline of 301 s (251-447), and placebo increased it to 307 s (232-430;  $p=0.0003$ ); the point estimate was 58 s (95% CI 45-77). Allopurinol increased the time to chest pain from a baseline of 234 s (IQR 189-382) to 304 s (222-421), and placebo increased it to 272 s (200-380;  $p=0.001$ ); the point estimate was 38 s (95% CI 17-55). No adverse effects of treatment were reported.

## INTERPRETATION:

Allopurinol seems to be a useful, inexpensive, well tolerated, and safe anti-ischaemic drug for patients with angina.