Randomized double-blinded clinical investigation of roxithromycin versus placebo as secondary and tertiary prevention in patients with peripheral atherosclerosis

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ABSTRACT

Much focus has been on whether infections could be involved in the development of atherosclerosis. The bacterium which has attracted most attention in this research is *C. pneumoniae*. In search for improved treatment of atherosclerosis, focusing has also much been on finding potential predictors of future cardiovascular events. The acute phase reactant CRP has attracted much attention. The main purpose of this study was to investigate the effect of roxithromycin treatment as prevention of future cardiovascular events in peripheral arterial disease patients. The project had two secondary purposes; 1) Investigation of CRP as a potential marker for development of future cardiovascular events in patients with peripheral arterial disease, 2) Validation of Doppler ultrasound technique compared to strain gauge technique to measure ankle blood pressure.

Fivehundred-seven patients were included; all patients had an established diagnosis of peripheral arterial disease. Their mean age was 66 years (36-85). Patients were randomized to Roxithromycin 300 mg daily for 28 days. Primary events were defined as death, peripheral revascularisation and major lower limb amputation. Secondary events were thrombosis, stroke, transient cerebral ischaemic attack and myocardial infarction. Change in ankle brachial blood pressure index was also investigated. Data were analyzed mainly by Cox regression and linear regression. Mean follow-up was 2.1 years (range 0.06-5.1 years). The hazard ratio of death was 1.13 (95% CI: 0.68; 1.90), and of primary events 0.92 (95% CI: 0.67; 1.26). Also on secondary events and ankle brachial blood pressure index changes, no significant differences were found.

Four-hundred-and-twenty patients of the initial 507 had a baseline CRP measurement. Among these 420 patients there were 40 (9.5%) deaths and a total of 125 (29.8%) primary events. For those with CRP>100 mg/l the hazard ratio of death was 3.2 (95% CI: 0.8; 12.4), thus the mortality was almost significantly increased (P = 0.086). Furthermore, for those with CRP >100 mg/l, the hazard ratio of thrombosis at 29 (95% CI: 2.26; 373) was significantly increased.

Our study provides evidence that in patients with peripheral arterial disease, baseline levels of CRP is almost significantly associated to future death, and strongly associated to future thrombotic events. However, we found that roxithromycin is ineffective in preventing death, amputation, peripheral revascularization, myocardial infarction, stroke, transient cerebral ischaemic attack, thrombosis and decline in ankle brachial blood pressure index.