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Primary prevention of cardiovascular disease

Statins and hypotensive drugs: not for everyone

● **In a large-scale placebo-controlled trial in which about 13 000 patients at risk of a first cardiovascular event were followed for approximately six years, low-dose *rosuvastatin* and the combination of *candesartan* + *hydrochlorothiazide* did not reduce total mortality or cardiovascular mortality.**

Apart from dietary or lifestyle changes, some treatments have proven efficacy in certain groups of patients in reducing the risk of a first cardiovascular event, i.e. for primary prevention (1,2). These include blood pressure-lowering drugs used in hypertensive patients.

A large-scale, randomised, double-blind trial, the HOPE-3 trial, has evaluated two treatments in comparison to placebo for the prevention of a first cardiovascular event (3,4,5).

This trial included 12 705 patients: men aged 55 years or older and women aged 65 years or older who had at least one cardiovascular risk factor, and women aged 60 years or older who had at least two cardiovascular risk factors. Patients were included irrespective of their blood pressure and LDL-cholesterol levels. The main risk factors were smoking, family history of cardiovascular disease, and more controversial factors such as a low HDL-cholesterol level and central obesity (**a**)(3,4,5). On average, participants were 66 years of age, with a body mass index of 27 kg/m^2, blood pressure of 138/82 mmHg, and a serum LDL-cholesterol level of 1.28 g/l (3.3 mmol/l). At enrolment, 38% were hypertensive (5).

After randomisation, the patients were assigned to one of four groups: *rosuvastatin* (10 mg per day) plus a fixed-dose combination of *candesartan* (16 mg per day) + *hydrochlorothiazide* (12.5 mg per day), versus *rosuvastatin* plus placebo, versus *candesartan* + *hydrochlorothiazide* plus placebo, versus double placebo. The trial protocol did not mandate a target value for blood pressure or cholesterol levels.

After a median follow-up of 5.6 years, total mortality (5%) was similar in the four groups, as was cardiovascular mortality (2.5%) (5).

In comparison to placebo, *rosuvastatin* reduced the incidence of a composite outcome consisting of nonfatal myocardial infarction, nonfatal stroke and death from cardiovascular causes (3.7% versus 4.8%, p = 0.002). There was no difference between the *candesartan* + *hydrochlorothiazide* combination and placebo in the incidence of this outcome (3,4,5).

In comparison to the placebo group, there was an increase in muscle disorders in the *rosuvastatin* group (5.8% versus 4.7%, p = 0.005); and symptomatic hypotension, dizziness and light-headedness, leading to treatment discontinuation in the *candesartan* + *hydrochlorothiazide* group (3.4% versus 2%, p < 0.001) (3,4).

In practice The addition of *candesartan* + *hydrochlorothiazide*, without taking blood pressure into account, was not effective in primary cardiovascular prevention for patients with several cardiovascular risk factors. In this trial, the addition of *rosuvastatin*, irrespective of LDL-cholesterol levels, prevented one vascular event for every 91 patients treated for nearly 6 years, without reducing either cardiovascular mortality or total mortality. These findings do not justify routinely exposing all patients at cardiovascular risk due to tobacco use or family history to the adverse effects of these drugs.

▶ Translated from *Rev Prescrire* **October 2017**
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***a-** For inclusion, patients needed to have at least one or two of the following cardiovascular risk factors: waist-to-hip ratio greater than or equal to 0.85 for women and 0.90 for men; low HDL-cholesterol (less than 0.50 g/l (1.3 mmol/l) in women and 0.39 g/l (1.0 mmol/l) in men); regular tobacco use within the previous 5 years; abnormal blood glucose levels or diabetes treated with diet only; family history of premature coronary disease; microalbuminuria or moderate renal insufficiency without hypertension, with glomerular filtration rate between 45 ml/min and 60 ml/min (ref 5).*

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