

Abstract

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Effects of a polypill (Polycap) on risk factors in middle-aged individuals without cardiovascular disease (TIPS): a phase II, double-blind, randomised trial.

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BACKGROUND: The combination of three blood-pressure-lowering drugs at low doses, with a statin, aspirin, and folic acid (the polypill), could reduce cardiovascular events by more than 80% in healthy individuals. We examined the effect of the Polycap on blood pressure, lipids, heart rate, and urinary thromboxane B2, and assessed its tolerability.

METHODS: In a double-blind trial in 50 centres in India, 2053 individuals without cardiovascular disease, aged 45-80 years, and with one risk factor were randomly assigned, by a central secure website, to the Polycap (n=412) consisting of low doses of thiazide (12.5 mg), atenolol (50 mg), ramipril (5 mg), simvastatin (20 mg), and aspirin (100 mg) per day, or to eight other groups, each with about 200 individuals, of aspirin alone, simvastatin alone, hydrochlorothiazide alone, three combinations of the two blood-pressure-lowering drugs, three blood-pressure-lowering drugs alone, or three blood-pressure-lowering drugs plus aspirin. The primary outcomes were LDL for the effect of lipids, blood pressure for antihypertensive drugs, heart rate for the effects of atenolol, urinary 11-dehydrothromboxane B2 for the antiplatelet effects of aspirin, and rates of discontinuation of drugs for safety. Analysis was by intention to treat. This study is registered with ClinicalTrials.gov, number NCT00443794.

FINDINGS: Compared with groups not receiving blood-pressure-lowering drugs, the Polycap reduced systolic blood pressure by 7.4 mm Hg (95% CI 6.1-8.1) and diastolic blood pressure by 5.6 mm Hg (4.7-6.4), which was similar when three blood-pressure-lowering drugs were used, with or without aspirin. Reductions in blood pressure increased with the number of drugs used (2.2/1.3 mm Hg with one drug, 4.7/3.6 mm Hg with two drugs, and 6.3/4.5 mm Hg with three drugs). Polycap reduced LDL cholesterol by 0.70 mmol/L (95% CI 0.62-0.78), which was less than that with simvastatin alone (0.83 mmol/L, 0.72-0.93; p=0.04); both reductions were greater than for groups without simvastatin (p<0.0001). The reductions in heart rate with Polycap and other groups using atenolol were similar (7.0 beats per min), and both were significantly greater than that in groups without atenolol (p<0.0001). The reductions in 11-dehydrothromboxane B2 were similar with the Polycap (283.1 ng/mmol creatinine, 95% CI 229.1-337.0) compared with the three blood-pressure-lowering drugs plus aspirin (350.0 ng/mmol creatinine, 294.6-404.0), and aspirin alone (348.8 ng/mmol creatinine, 277.6-419.9) compared with groups without aspirin. Tolerability of the Polycap was similar to that of other treatments, with no evidence of increasing intolerability with increasing number of active components in one pill.

INTERPRETATION: This Polycap formulation could be conveniently used to reduce multiple risk factors and cardiovascular risk.

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