PREVENTION

Polypills reduce CVD risk factors

Two separate trials have shown significant reductions in blood pressure (BP) and LDL-cholesterol (LDL-C) levels in individuals taking a 'polypill'. The investigators predict that these risk-factor modifications will reduce the incidence of cardiovascular events in the long term.

David Wald *et al.* from London, UK tested a polypill containing half-standard doses of three BP-lowering agents (2.5 mg amlodipine, 12.5 mg hydrochlorothiazide, and 25 mg losartan), and a standard 40 mg dose of simvastatin. In total, 84 individuals with no history of cardiovascular disease (CVD), who were candidates for primary prevention purely on the basis of their age (≥ 50 years), completed the trial. The double-blind study had a crossover design to maximize statistical power. Participants

took the polypill for 12 weeks and a placebo for 12 weeks in a random sequence. On the polypill, systolic and diastolic BPs and LDL-C levels were reduced by 17.9 mmHg, (12%), 9.8 mmHg (11%), and 1.4 mmol/l (54 mg/dl; 39%), respectively. The drug was well tolerated, and no participant had a serious adverse event. The researchers predict that risk-factor reductions on this scale would decrease the incidence of ischemic heart disease events and stroke by 72% and 64%, respectively.

In The Second Indian Polycap Study (TIPS-2), the polypill contained three BP-lowering drugs (50 mg atenolol, 12.5 mg hydrochlorothiazide, and 5 mg ramipril), 20 mg simvastatin, and also 100 mg aspirin, whose use in primary prevention is controversial. In total, 518 individuals eligible for secondary prevention were randomly allocated to receive either a single polypill, or two capsules of the polypill plus K^+ supplementation for 8 weeks. Compared with the single dose, the double ('full') dose reduced systolic and diastolic BPs and LDL-C levels by an additional 2.8 mmHg,

© Duskbabe | Dreamstime.com

1.7 mmHg, and 6.6 mg/dl, respectively. Both doses were similarly well tolerated. The investigators anticipate that the full-dose regimen would reduce the risk of coronary heart disease by 75%, and of stroke by 65%.

The TIPS-3 investigators now plan to assess hard clinical end points over 5 years in a primary-prevention population of $>5,000$ individuals at moderate or high risk of, but without documented, CVD. In the $2 \times 2 \times 2$ factorial trial, the polypill will be tested without aspirin, with aspirin, and with vitamin D. The measured outcomes will be CVD, CVD or cancer, and CVD or fractures in each trial arm, respectively.

Gregory B. Lim

Original articles Wald, D. S. *et al.* Randomized polypill crossover trial in people aged 50 and over. *PLoS ONE* 7, e41297 (2012) | Yusuf, S. *et al.* Comparison of risk factor reduction and tolerability of a full-dose polypill (with potassium) versus low-dose polypill (polycap) in individuals at high risk of cardiovascular diseases. The Second Indian Polycap Study (TIPS-2) investigators. *Circ. Cardiovasc. Qual. Outcomes* doi:10.1161/CIRCOUTCOMES.111.963637