Single combination pill provides benefit to patients with or at risk of CVD

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In a randomized trial that included about 2,000 patients with or at high risk of cardiovascular disease (CVD), use of a fixed-dose combination medication for blood pressure, cholesterol, and platelet control compared to usual care resulted in significantly improved medication adherence after 15 months and small improvements in systolic blood pressure and low-density lipoprotein cholesterol, according to a study in the September 4 issue of *JAMA*.

"The long-term use of cardiovascular disease preventive therapy is low among people with established disease. This shortfall is greatest in low- and middle-income countries, but even in high-income countries treatment coverage in the community is only about 50 percent in those with coronary disease and 35 percent in those with stroke. People who are at similar risk but have not reached the clinical threshold of experiencing a CVD event are even less likely to be adequately treated. Fixed-dose combination (FDC) therapy may reduce these treatment gaps by reducing cost, complexity, therapeutic inertia, and low adherence," according to background information in the article. "Previous trials of cardiovascular FDCs have assessed short-term effects compared with placebo or no treatment."

Simon Thom, M.B., B.S., M.D., of the International Centre for Circulatory Health, Imperial College London, and colleagues conducted a study to assess whether FDC delivery of aspirin, statin, and 2 blood pressure-lowering agents vs. usual care improves long-term adherence to indicated therapy and 2 major CVD risk factors, systolic blood pressure

(SBP) and low-density lipoprotein cholesterol (LDL-C). The randomized trial included 2,004 participants with established CVD or at risk of CVD enrolled July 2010-July 2011 in India and Europe. The trial follow-up concluded in July 2012. Participants were randomly assigned (1:1) to an FDC-based strategy (n=1,002) containing either (1) 75 mg aspirin, 40 mg simvastatin, 10 mg lisinopril, and 50 mg atenolol or (2) 75 mg aspirin, 40 mg simvastatin, 10 mg lisinopril, and 12.5 mg hydrochlorothiazide or to usual care (n=1,002).

At baseline, average BP was 137/78 mm Hg, LDL-C was 91.5 mg/dL, and 1,233 (61.5 percent) of 2,004 participants reported use of antiplatelet, statin, and 2 or more BP-lowering medications. The median (midpoint) duration of follow-up was 15 months for both groups. At the end of the study, 829 (86.3 percent) of 961 participants in the FDC group were continuing with indicated medications compared with 621 (64.7 percent) of 960 in the usual care group. In absolute terms, this amounted to a 21.6 percent difference in treatment rates. Overall, SBP (-2.6 mm Hg) and LDL-C (-4.2 mg/dL) levels were modest but significantly lower in the FDC group compared with the usual care group at the end of the study.

"Although there was consistency of effects across predefined subgroups, evidence existed of larger benefits in patients with lower adherence at baseline. In this subgroup of 727 participants (36 percent), adherence at the end of study was 77 percent vs. 23 percent, SBP was reduced by 4.9 mm Hg, and LDL-C was reduced by 6.7 mg/dL. There were no significant differences in serious adverse events or cardiovascular events between the groups," the authors write.

"To the best of our knowledge, this was the first randomized trial to assess the long-term use of an FDC containing antiplatelet, statin, and BP-lowering drugs compared with usual care in patients with CVD. The results show that access to FDCs in patients with CVD or similarly high

risk improved adherence, BP, and cholesterol levels. The reductions in BP and cholesterol level were small overall in this comparatively well-treated population but were larger in the subgroup not receiving all recommended treatments at baseline."

In an accompanying editorial, J. Michael Gaziano, M.D., M.P.H., of the VA Boston Healthcare System, Brigham and Women's Hospital and Harvard Medical School, Boston, (and Associate Editor, *JAMA*), comments on the findings of this study.

"Although the potential remains for use of various CVD polypills in certain settings, the precise advantage of this strategy remains largely unproven. Until additional rigorous data are available that demonstrate that the polypill improves clinical CVD outcomes, it may be more important to carefully assess the multiple medications many patients currently are prescribed, often by several physicians. Another way to reduce the number of pills patients are taking is to eliminate those medications for which the benefits are marginal."

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