Blood-Pressure and Cholesterol Lowering in Persons without Cardiovascular Disease

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Abstract

BACKGROUND

Elevated blood pressure and elevated low-density lipoprotein (LDL) cholesterol increase the risk of cardiovascular disease. Lowering both should reduce the risk of cardiovascular events substantially.

METHODS

In a trial with 2-by-2 factorial design, we randomly assigned 12,705 participants at intermediate risk who did not have cardiovascular disease to rosuvastatin (10 mg per day) or placebo and to candesartan (16 mg per day) plus hydrochlorothiazide (12.5 mg per day) or placebo. In the analyses reported here, we compared the 3180 participants assigned to combined therapy (with rosuvastatin and the two antihypertensive agents) with the 3168 participants assigned to dual placebo. The first coprimary outcome was the composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke, and the second coprimary outcome additionally included heart failure, cardiac arrest, or revascularization. The median follow-up was 5.6 years.

RESULTS

The decrease in the LDL cholesterol level was 33.7 mg per deciliter (0.87 mmol per liter) greater in the combined-therapy group than in the dual-placebo group, and the decrease in systolic blood pressure was 6.2 mm Hg greater with combined therapy than with dual placebo. The first coprimary outcome occurred in 113 participants (3.6%) in the combined-therapy group and in 157 (5.0%) in the dual-placebo group (hazard ratio, 0.71; 95% confidence interval [CI], 0.56 to 0.90; P=0.005). The second coprimary outcome occurred in 136 participants (4.3%) and 187 participants (5.9%), respectively (hazard ratio, 0.72; 95% CI, 0.57 to 0.89; P=0.003). Muscle weakness and dizziness were more common in the combined-therapy group than in the dual-placebo group, but the overall rate of discontinuation of the trial regimen was similar in the two groups.

CONCLUSIONS

The combination of rosuvastatin (10 mg per day), candesartan (16 mg per day), and hydrochlorothiazide (12.5 mg per day) was associated with a significantly lower rate of cardiovascular events than dual placebo among persons at intermediate risk who did not have cardiovascular disease. (Funded by the Canadian Institutes of Health Research and AstraZeneca; ClinicalTrials.gov number, NCT00468923.)

Keywords

KeyWords Plus: RISK-FACTORS; TRIAL; PREVENTION; MORTALITY; METAANALYSIS; INTERHEART; COUNTRIES; STRATEGY; STROKE; ADULTS

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Blood-pressure and cholesterol lowering in persons without cardiovascular disease (Article)

Yusuf, S.[a,b], Lonn, E.[a,b], Pais, P.[g], Bosch, J.[a,c], López-Jaramillo, P.[i], Zhu, J.[k], Xavier, D.[g,h], Avezum, A.[i], Leiter, L.A.[j], Piegas, L.S.[m], Parkhomenko, A.[n], Keltai, M.[o], Keltai, K.[o], Sliwa, K.[p], Chazova, I.[q], Peters, R.J.G.[r], Held, C.[s], Yusoff, K.[tu], Lewis, B.S.[v], Jansky, P.[ao], Khunti, K.[x], Toff, W.D.[yz], Reid, C.M.[aaab], Varigos, J.[ab], Accini, J.L.[ac], McKelvie, R.[ab], Pogue, J.[w], Jung, H.[a], Liu, L.[k], Díaz, R.[ad], Dans, A.[ae], Dagenais, G.[f]

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Abstract

BACKGROUND Elevated **blood pressure** and elevated low-density lipoprotein (LDL) **cholesterol** increase the risk of **cardiovascular disease**. **Lowering** both should reduce the risk of **cardiovascular** events substantially. METHODS **In** a trial with 2-by-2 factorial design, we randomly assigned 12,705 participants at intermediate risk who did not have **cardiovascular disease** to rosuvastatin (10 mg per day) or placebo and to candesartan (16 mg per day) plus hydrochlorothiazide (12.5 mg per day) or placebo. **In** the analyses reported here, we compared the 3180 participants assigned to combined therapy (with rosuvastatin and the two antihypertensive agents) with the 3168 participants assigned to dual placebo. The first coprimary outcome was the composite of death from **cardiovascular** causes, nonfatal myocardial infarction, or nonfatal stroke, and the second coprimary outcome additionally included heart failure, cardiac arrest, or revascularization. The median follow-up was 5.6 years. RESULTS The decrease **in** the LDL **cholesterol** level was 33.7 mg per deciliter (0.87 mmol per liter) greater **in** the combined-therapy group than **in** the dual-placebo group, and the decrease **in** systolic **blood pressure** was 6.2 mm Hg greater with combined therapy than with dual placebo. The first coprimary outcome occurred **in** 113 participants (3.6%) **in** the combined-therapy group and **in** 157 (5.0%) **in** the dual-placebo group (hazard ratio, 0.71; 95% confidence interval [CI], 0.56 to 0.90; P = 0.005). The second coprimary outcome occurred **in** 136 participants (4.3%) and 187 participants (5.9%), respectively (hazard ratio, 0.72; 95% CI, 0.57 to 0.89; P = 0.003). Muscle weakness and dizziness were more common **in** the combined-therapy group than **in** the dual-placebo group, but the overall rate of discontinuation of the trial regimen was similar **in** the two groups. CONCLUSIONS The combination of rosuvastatin (10 mg per day), candesartan (16 mg per day), and hydrochlorothiazide (12.5 mg per day) was associated with a significantly lower rate of **cardiovascular** events than dual placebo among **persons** at intermediate risk who did not have **cardiovascular disease**. Copyright © 2016 Massachusetts Medical Society. All rights reserved.

Indexed keywords

EMTREE drug terms: antihypertensive agent; candesartan; hydrochlorothiazide; low density lipoprotein **cholesterol**; placebo; rosuvastatin; antihypertensive agent; benzimidazole derivative; candesartan; hydrochlorothiazide; hydroxymethylglutaryl coenzyme A reductase inhibitor; low density lipoprotein **cholesterol**; rosuvastatin; tetrazole derivative

EMTREE medical terms: adult; Article; **blood pressure** measurement; **cardiovascular disease**; **cardiovascular** risk; cerebrovascular accident; **cholesterol blood** level; controlled study; dizziness; double blind procedure; factorial design; female; heart arrest; heart failure; heart infarction; human; hypotension; major clinical study; middle aged; multicenter study; muscle weakness; myalgia; priority journal; randomized controlled trial; revascularization; risk factor; risk reduction; aged; **blood**; **Cardiovascular** Diseases; clinical trial; combination drug therapy; comparative study; hypertension; male; medication compliance

MeSH: Aged; Antihypertensive Agents; Benzimidazoles; **Cardiovascular** Diseases; **Cholesterol**, LDL; Double-Blind Method; Drug Therapy, Combination; Female; Humans; Hydrochlorothiazide; Hydroxymethylglutaryl-CoA Reductase Inhibitors; Hypertension; Male; Medication Adherence; Middle Aged; Risk Factors; Rosuvastatin Calcium; Tetrazoles

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