

Antihypertensive agents affect serum lipid levels

Kasike BL, Ma JZ, Kabil RS, Louis TA. Effects of antihypertensive therapy on serum lipids. *Ann Intern Med.* 1995 Jan 15;122:133-41.

Objective

To determine the effects of antihypertensive agents on serum lipid levels.

Data Sources

MEDLINE was searched (1966 to 1993) using the terms hypertension, therapy, human, cholesterol, and lipids, and bibliographies of review articles and pharmaceutical company-supplied bibliographies were reviewed.

Study Selection

Selected studies examined the effects of antihypertensive agents on blood pressure and levels of fasting total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, or very-low-density lipoprotein. Studies reported the mean lipid levels or absolute change before and after treatment or mean lipid levels at baseline and mean percentage change. 474 trials comprising 65 000 patients were identified.

Commentary

The meta-analysis by Kasike and colleagues provides a useful summary of the effects of antihypertensive drugs on lipids in various populations. This is important because the goal of therapy is to lower not only blood pressure but also the total cardiovascular risk (1). This study confirmed the association of diuretics and increased total and LDL cholesterol and triglyceride levels but did not resolve the controversy about the implications of these effects. A dose-response effect also was shown for doses of hydrochlorothiazide > 50 mg/d. The authors did not comment on a possible dose-response effect of low-dose diuretics (hydrochlorothiazide at < 25 mg/d). Unlike some studies that showed a reduction of cholesterol levels over time

Data Extraction

Effects of different antihypertensive agents, classes of agents (diuretics, β -blockers, α -blockers, sympatholytic agents, angiotensin-converting enzyme [ACE] inhibitors, calcium antagonists, and vasodilators) on lipid levels and blood pressure. Dosage, treatment duration, patient characteristics, and study design quality were entered in a multiple linear regression model.

Main Results

Total cholesterol levels were increased by diuretics (0.13 mmol/L; 95% CI, 0.09 to 0.18) and decreased by α -blockers (-0.23 mmol/L; CI, -0.28 to -0.18), sympatholytic agents (-0.21 mmol/L; CI, -0.31 to -0.12), and vasodilators (-0.22 mmol/L; CI, -0.30 to -0.14). LDL cholesterol levels were increased by high-dose diuretics (0.19 mmol/L; CI, 0.10 to 0.29) and decreased by α -blockers (-0.20 mmol/L; CI, -0.25 to -0.15) and vasodilators (-0.20 mmol/L; CI, -0.29 to -0.11). Only β -blockers with intrinsic sympathomimetic activity (ISA) were associated with a decrease in total and LDL cholesterol levels. HDL cholesterol levels were increased by α -block-

ers (0.02 mmol/L; CI, 0.01 to 0.04) and vasodilators (0.06 mmol/L; CI, 0.02 to 0.09) and decreased by β -blockers (-0.10 mmol/L; CI, -0.12 to -0.08) and sympatholytic agents (-0.05 mmol/L; CI, -0.10 to -0.01). β -blockers with ISA increased HDL cholesterol levels (0.16 mmol/L; CI, 0.09 to 0.23). Calcium antagonists and ACE inhibitors did not affect cholesterol levels. Triglyceride levels were increased by diuretics (0.10 mmol/L; CI, 0.03 to 0.18) and β -blockers (0.35 mmol/L; CI, 0.31 to 0.39) and decreased by α -blockers (-0.07 mmol/L; CI, -0.11 to -0.03) and ACE inhibitors (-0.07 mmol/L; CI, -0.12 to -0.02). Patient characteristics influenced the treatment effect of some agents.

Conclusion

With the exception of calcium antagonists, antihypertensive agents affected serum lipid levels.

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(2), the effect of diuretics in this meta-analysis was independent of study duration. The correlation between the changes in cholesterol and glucose levels showed the subtle metabolic abnormalities associated with diuretic use.

Should these findings influence the use of drugs in the routine treatment of hypertension? For individual patients, the changes in lipid levels induced by drugs are small, but the results may have larger implications in the treatment of populations. If diuretics are used, they should be used in low doses. Various populations differed in their response to medications. For example, in patients with diabetes, ACE inhibitors lowered blood pressure and lipids, whereas diuretics did not. Other than these

special cases, the most appropriate drug for the treatment of routine hypertension is sure to remain debatable.

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