Effects of antihypertensive therapy on serum lipids

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Authors' objectives
To compare and contrast the effects of antihypertensive agents on serum lipids and blood-pressure in different patient populations.

Searching
MEDLINE was searched from 1966 to 1993. References of comprehensive reviews and bibliographies from major pharmaceutical companies were also examined.

Study selection
Study designs of evaluations included in the review
Controlled trials: randomised controlled trials (RCTs), non-randomised controlled trials, and trials using a historical control in which the means of lipid values before and after treatment or the change was recorded. All languages were included.

Specific interventions included in the review
Antihypertensive therapy using the following: diuretics, alpha-blockers, sympatholytic agents, angiotensin-converting enzyme (ACE) inhibitors, calcium antagonists, beta-blockers, vasodilators, low-salt diet and low-fat diet.

Participants included in the review
Hypertensive patients.

Outcomes assessed in the review
Changes in serum triglyceride, total cholesterol, and low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol levels.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The studies were assigned weights for quality including factors such as randomisation, inclusion/exclusion criteria, study participants, placebo-control, multi-agent comparison, crossover design, blinding and drop-outs. The authors do not state how the papers were assessed for quality, or how many of the authors performed the quality assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
Multiple linear regression was used to estimate the effects of different agents, classes of agents, treatment durations, patient characteristics, and study design on serum lipids in controlled and uncontrolled studies.

How were differences between studies investigated?
Effects of different antihypertensive agents, treatment duration, patient characteristics, and study quality were
examined using multiple linear regression. Sensitivity analysis was used to examine the results by different weighting methods.

**Results of the review**
There were 474 studies with 945 experimental or control groups investigating 85 antihypertensive agents, and involving more than 65,000 patients. Fifty-six RCTs compared the effects of monotherapy with those of a placebo.

Cholesterol level increased when patients were treated with diuretics (regression coefficient, \( r \) 0.13 mmol/L, 95% confidence interval, CI: 0.09, 0.18). Beta-blockers increased triglyceride levels (\( r \) 0.35 mmol/L, 95% CI: 0.31, 0.39), except agents with intrinsic sympathomimetic activity. Alpha-blockers reduced total cholesterol (\( r \) -0.23 mmol/L, 95% CI: -0.28, -0.18), LDL-cholesterol (\( r \) -0.20 mmol/L, 95% CI: -0.25, -0.15), triglycerides (\( r \) -0.07 mmol/L, 95% CI: -0.11, -0.03), and in younger persons, increased HDL-cholesterol (\( r \) 0.02 mmol/L, 95% CI: 0.01, 0.04).

ACE inhibitors reduced triglycerides (\( r \) -0.07 mmol/L, 95% CI: -0.12, -0.02), and in diabetic patients, total cholesterol levels (\( r \) -0.22 mmol/L, 95% CI: -0.34, -0.10). Vasodilators reduced total (\( r \) -0.22 mmol/L, 95% CI: -0.30, -0.10) and LDL-cholesterol (\( r \) -0.22 mmol/L, 95% CI: -0.29, -0.11) and increased HDL-cholesterol (\( r \) 0.06 mmol/L, 95% CI: 0.02, 0.09). The results were robust to different weighting methods, and were similar to those pooling only RCTs comparing a single agent with a placebo.

**Authors’ conclusions**
With the exception of calcium antagonists, nearly all antihypertensive agents affect serum lipids. These effects differ among patients populations.

**CRD commentary**
A complex statistical method is used. The individual trials were not listed in the paper, though they are available on request. The authors did not report how the primary studies were assessed or how the data were extracted. The quality control of the study assessment and data extraction may be crucial when considering the large number of primary studies included (474).

**Implications of the review for practice and research**
The effects of antihypertensive agents on lipid levels may influence the benefit of blood-pressure reduction therapy. Future trials should take this, and the differential effects found in different patient populations, into account.

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