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Wright JM, Musini VM, Gill R

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[Intervention Review]

First-line drugs for hypertension

James M Wright[1], Vijaya M Musini[1], Rupam Gill[2]

[1]Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, Canada. [2]Department of Pharmacology, Manipal University, Manipal, India

Contact address: James M Wright, Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, 2176 Health Sciences Mall, Vancouver, BC, V6T 1Z3, Canada. jim.wright@ti.ubc.ca.

A B S T R A C T

Background

This is the first update of a review published in 2009. Sustained moderate to severe elevations in resting blood pressure leads to a critically important clinical question: What class of drug to use first-line? This review attempted to answer that question.

Objectives

To quantify the mortality and morbidity effects from different first-line antihypertensive drug classes: thiazides (low-dose and high-dose), beta-blockers, calcium channel blockers, ACE inhibitors, angiotensin II receptor blockers (ARB), and alpha-blockers, compared to placebo or no treatment.

Secondary objectives: when different antihypertensive drug classes are used as the first-line drug, to quantify the blood pressure lowering effect and the rate of withdrawal due to adverse drug effects, compared to placebo or no treatment.

Search methods

The Cochrane Hypertension Information Specialist searched the following databases for randomized controlled trials up to November 2017: the Cochrane Hypertension Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (from 1946), Embase (from 1974), the World Health Organization International Clinical Trials Registry Platform, and ClinicalTrials.gov. We contacted authors of relevant papers regarding further published and unpublished work.

Selection criteria

Randomized trials (RCT) of at least one year duration, comparing one of six major drug classes with a placebo or no treatment, in adult patients with blood pressure over 140/90 mmHg at baseline. The majority (over 70%) of the patients in the treatment group were taking the drug class of interest after one year. We included trials with both hypertensive and normotensive patients in this review if the majority (over 70%) of patients had elevated blood pressure, or the trial separately reported outcome data on patients with elevated blood pressure.

Data collection and analysis

The outcomes assessed were mortality, stroke, coronary heart disease (CHD), total cardiovascular events (CVS), decrease in systolic and diastolic blood pressure, and withdrawals due to adverse drug effects. We used a fixed-effect model to to combine dichotomous outcomes across trials and calculate risk ratio (RR) with 95% confidence interval (CI). We presented blood pressure data as mean difference (MD) with 99% CI.

Main results

The 2017 updated search failed to identify any new trials. The original review identified 24 trials with 28 active treatment arms, including 58,040 patients. We found no RCTs for ARBs or alpha-blockers. These results are mostly applicable to adult patients with moderate to severe primary hypertension. The mean age of participants was 56 years, and mean duration of follow-up was three to five years.

High-quality evidence showed that first-line low-dose thiazides reduced mortality (11.0% with control versus 9.8% with treatment; RR 0.89, 95% CI 0.82 to 0.97); total CVS (12.9% with control versus 9.0% with treatment; RR 0.70, 95% CI 0.64 to 0.76), stroke (6.2% with control versus 4.2% with treatment; RR 0.68, 95% CI 0.60 to 0.77), and coronary heart disease (3.9% with control versus 2.8% with treatment; RR 0.72, 95% CI 0.61 to 0.84).

Low- to moderate-quality evidence showed that first-line high-dose thiazides reduced stroke (1.9% with control versus 0.9% with treatment; RR 0.47, 95% CI 0.37 to 0.61) and total CVS (5.1% with control versus 3.7% with treatment; RR 0.72, 95% CI 0.63 to 0.82), but did not reduce mortality (3.1% with control versus 2.8% with treatment; RR 0.90, 95% CI 0.76 to 1.05), or coronary heart disease (2.7% with control versus 2.7% with treatment; RR 1.01, 95% CI 0.85 to 1.20).

Low- to moderate-quality evidence showed that first-line beta-blockers did not reduce mortality (6.2% with control versus 6.0% with treatment; RR 0.96, 95% CI 0.86 to 1.07) or coronary heart disease (4.4% with control versus 3.9% with treatment; RR 0.90, 95% CI 0.78 to 1.03), but reduced stroke (3.4% with control versus 2.8% with treatment; RR 0.83, 95% CI 0.72 to 0.97) and total CVS (7.6% with control versus 6.8% with treatment; RR 0.89, 95% CI 0.81 to 0.98).

Low- to moderate-quality evidence showed that first-line ACE inhibitors reduced mortality (13.6% with control versus 11.3% with treatment; RR 0.83, 95% CI 0.72 to 0.95), stroke (6.0% with control versus 3.9% with treatment; RR 0.65, 95% CI 0.52 to 0.82), coronary heart disease (13.5% with control versus 11.0% with treatment; RR 0.81, 95% CI 0.70 to 0.94), and total CVS (20.1% with control versus 15.3% with treatment; RR 0.76, 95% CI 0.67 to 0.85).

Low-quality evidence showed that first-line calcium channel blockers reduced stroke (3.4% with control versus 1.9% with treatment; RR 0.58, 95% CI 0.41 to 0.84) and total CVS (8.0% with control versus 5.7% with treatment; RR 0.71, 95% CI 0.57 to 0.87), but not coronary heart disease (3.1% with control versus 2.4% with treatment; RR 0.77, 95% CI 0.55 to 1.09), or mortality (6.0% with control versus 5.1% with treatment; RR 0.86, 95% CI 0.68 to 1.09).

There was low-quality evidence that withdrawals due to adverse effects were increased with first-line low-dose thiazides (5.0% with control versus 11.3% with treatment; RR 2.38, 95% CI 2.06 to 2.75), high-dose thiazides (2.2% with control versus 9.8% with treatment; RR 4.48, 95% CI 3.83 to 5.24), and beta-blockers (3.1% with control versus 14.4% with treatment; RR 4.59, 95% CI 4.11 to 5.13). No data for these outcomes were available for first-line ACE inhibitors or calcium channel blockers. The blood pressure data were not used to assess the effect of the different classes of drugs as the data were heterogeneous, and the number of drugs used in the trials differed.

Authors' conclusions

First-line low-dose thiazides reduced all morbidity and mortality outcomes in adult patients with moderate to severe primary hypertension. First-line ACE inhibitors and calcium channel blockers may be similarly effective, but the evidence was of lower quality. First-line high-dose thiazides and first-line beta-blockers were inferior to first-line low-dose thiazides.

P L A I N   L A N G U A G E   S U M M A R Y

Thiazides best first choice for hypertension

Review Question(s)

In this first update of a review published in 2009, we wanted to determine which drug class was the best first-line choice in treating adult patients with raised blood pressure.

We searched the available medical literature to find all the trials that compared the drugs to placebo or no treatment to assess this question. The data included in this review are up to date as of November 2017.

Background

High blood pressure or hypertension can increase the risk of heart attacks and stroke. One of the most important decisions in treating people with elevated blood pressure is what drug class to use first. This decision has important consequences in terms of health outcomes and cost.

Study characteristics

We found no new trials in this updated search. In the original review, we found 24 studies that randomly assigned 58,040 adult people (mean age 62 years) with high blood pressure, to four different drug classes or placebo. Duration of these studies ranged from three to five years. Drug classes studied included thiazide diuretics, beta-blockers, ACE inhibitors, and calcium channel blockers.

Key Results

We concluded that most of the evidence demonstrated that first-line low-dose thiazides reduced mortality, stroke, and heart attack. No other drug class improved health outcomes better than low-dose thiazides. Beta-blockers and high-dose thiazides were inferior.

Conclusions

High-quality evidence supported that low-dose thiazides should be used first for most patients with elevated blood pressure. Fortunately, thiazides are also very inexpensive.

Quality of evidence

The evidence for first-line low dose thiazides was high quality. For the other classes, we judged the evidence to be moderate or low quality.