Race and ethnicity in trials of antihypertensive therapy to prevent cardiovascular outcomes: a systematic review  
Park I U, Taylor A L

CRD summary
The authors’ conclusion appears to be that in cardiovascular disease prevention trials of antihypertensive therapies, treatment efficacy was similar for white and ethnic minorities for the primary outcomes. However, owing to the methodology used in the review, these results should be considered as exploratory rather than conclusive.

Authors’ objectives
To assess racial and ethnic differences in the efficacy of hypertensive therapies for the prevention of cardiovascular outcomes.

Searching
MEDLINE, EMBASE, African Index Medicus, LILACS and the Cochrane CENTRAL Register were searched from inception to December 2005 (MEDLINE was searched to 2006); the search terms were reported. The search was not restricted by language. Additional studies were sought by handsearching systematic reviews and national practice guidelines, and by contacting experts.

Study selection
Studies that evaluated participants with hypertension from different population groups (i.e. including Asians, black African/African Americans, Hispanics and Native Americans/First Nations) were eligible for inclusion. None of the included studies evaluated Native Americans. The majority of studies evaluated participants older than 50 years of age.

Studies evaluating antihypertensive therapy, including diuretics, β-blockers, α-blockers, calcium-channel blockers, angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers, were eligible for inclusion. Studies that assessed single-drug therapy or single-drug-based combinations versus placebo, or single-drug-based combinations versus other combinations of drugs, were eligible for inclusion. A variety of drugs were evaluated in the included studies, but the dosages were not specified.

To be included, studies had to report on outcomes related to cardiovascular morbidity and mortality, including fatal or nonfatal myocardial infarction, fatal or nonfatal stroke, cardiovascular death, revascularisation, or a combination of these outcomes. Studies with primary outcomes other than cardiovascular disease (CVD) were excluded, as were studies that excluded hypertensive participants and studies that examined surrogate end points for CVD (e.g. blood-pressure). To be included, studies had to present outcomes by different population groups.

Double-blind, randomised controlled trials (RCTs), or prospective, randomised, open-label, blinded end point studies, with a follow-up of at least 1 year, were eligible for inclusion. Follow-up of the included studies ranged from 2.7 to 5.0 years.

Two reviewers selected studies for inclusion, and any disagreements were resolved through discussion.

Assessment of study quality
Each study was allocated a score from 0 (lowest) to 5 (highest) using the Jadad scale. The criteria were adequacy of randomisation, allocation concealment, blinding, and descriptions of withdrawals and losses to follow-up. It was also noted if the studies used intention-to-treat analysis.

Two authors independently assessed studies for quality.

Data extraction
Outcome data for various population groups were extracted from each study, and study authors were contacted where such data were unavailable.

Two reviewers performed the data extraction.

**Methods of synthesis**

The studies were combined in a narrative. Relative risks (RRs) and 95% confidence intervals (CIs) were also presented in forest plots for each study, but not pooled.

**Results of the review**

Eight studies, with a total of 107,364 participants, were included in the review.

The Jadad scores ranged from 3 to 5; all but one study used intention-to-treat analysis.

Four studies evaluated outcomes in Asians. In one study, felodipine with hydrochlorothiazide prevented more strokes than hydrochlorothiazide alone (RR 0.73, 95% CI: 0.60, 0.95, p=0.002). One study that included Asians and non-Asians found that ACE inhibitors compared with placebo were equally effective for preventing stroke in both population groups: Asians (RR 0.61, 95% CI: 0.48, 0.78) and Westerners (RR 0.78, 95% CI: 0.65, 0.95). The other two studies, conducted exclusively in Japanese participants, did not demonstrate significant differences in composite cardiovascular events when nifedipine was compared with an ACE inhibitor, or when nicardipine was compared with trichlormethiazide.

Two studies evaluated outcomes in black African/African Americans. One study reported that chlorthalidone significantly reduced stroke compared with lisinopril in blacks (RR 1.40, 95% CI: 1.17, 1.68, p<0.001), but not in non-blacks; this difference between population groups was significant (p=0.01). There was also a significant improvement in combined CVD with chlorthalidone in blacks (RR 1.19, 95% CI: 1.09, 1.30, p<0.001), but not in non-blacks; this difference between population groups was also significant (p=0.04). No significant differences between chlorthalidone versus lisinopril or chlorthalidone versus amlodipine were observed for fatal or nonfatal coronary heart disease. The second study reported that atenolol significantly improved fatal CVD compared with losartan in blacks (RR 1.66, 95% CI: 1.04, 2.66, p=0.03), but not in non-blacks; the difference between population groups was not significant.

Two studies evaluated outcomes in multiple ethnic groups. One study compared lisinopril with an atenolol-based strategy, but found no significance differences in mortality and nonfatal cerebrovascular accident or myocardial infarction between interventions for any population group. The second study compared valsartan with amlodipine and also found no significant differences in composite cardiac events between interventions for any population group.

**Authors' conclusions**

The authors' conclusion appears to be that in CVD prevention trials of antihypertensive therapies, treatment efficacy was similar for white and ethnic minorities for the primary outcomes. There may be evidence that the efficacy of angiotensin-receptor blockers in black patients is questionable, though the authors expressed that this should be interpreted with caution. It was not possible to determine whether calcium-channel blockers are cardioprotective in Asians, apart from lowering blood-pressure.

**CRD commentary**

The study inclusion criteria were stated clearly. A number of databases were searched without language restrictions. Although unpublished studies do not appear to have been sought, authors were contacted as part of the search strategy. However, only published trials were analysed and this might have introduced publication bias. Validity was assessed using published criteria. Whilst it appears that two reviewers were involved in the review process, it is unclear if the data extraction and quality assessment were conducted by one reviewer and checked by another. The studies were appropriately summarised in a narrative synthesis. However, as some data from some studies were analysed in subgroups (i.e. by population group), the randomisation process of the original studies might have been lost. As such, the results and conclusions should be interpreted with caution and should be considered exploratory.
Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that future studies should increase participation of different population groups to determine optimal prevention therapies, particularly in outcome-driven trials comparing multi-drug antihypertensive treatment regimens.

Funding
Health Resources and Services Administration, faculty development grant 1DHP05168-01-00.

Bibliographic details

PubMedID
17893387

DOI
10.1370/afm.708

Original Paper URL
http://www.annfammed.org/cgi/content/full/5/5/444

Indexing Status
Subject indexing assigned by NLM

MeSH
African Americans /statistics & numerical data; Antihypertensive Agents /therapeutic use; Asian Continental Ancestry Group statistics & numerical data; Cardiovascular Diseases /ethnology /prevention & control; Continental Population Groups; Ethnic Groups; European Continental Ancestry Group /statistics & numerical data; Global Health; Hispanic Americans /statistics & numerical data; Humans; Hypertension /drug therapy /ethnology; Randomized Controlled Trials as Topic /statistics & numerical data; Research Subjects; Treatment Outcome

AccessionNumber
12007003464

Date bibliographic record published
09/08/2008

Date abstract record published
01/12/2008

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.