Choosing a first-line antihypertensive

In their systematic review of antihypertensive therapies, James M. Wright and colleagues conclude that "low-dose thiazide therapy can be prescribed as the first-line treatment of hypertension with confidence that the risk of death, coronary artery disease and stroke will be reduced. The same cannot be said for high-dose thiazide therapy, β-blockers, calcium-channel blockers or ACE [angiotensin-converting-enzyme] inhibitors."[1] Although there may be good reasons for selecting thiazide therapy, such as low cost and low rate of withdrawal for adverse effects, the efficacy data in Table 4 do not support the authors' conclusions that only low-dose thiazide therapy will prevent death and cardiovascular morbidity in patients with hypertension.

Table 4 shows that there was essentially no difference among low-dose thiazide, high-dose thiazide, and calcium-channel blocker therapy with respect to mortality (relative risks 0.89, 0.90 and 0.86 respectively) or total cardiovascular events (relative risks 0.68, 0.72 and 0.71 respectively). For total cardiovascular events, a Mantel–Haenszel analysis[2] finds no evidence of heterogeneity between these medications ($\chi 2$ = 3.6 on 2 degrees of freedom, p = 0.16). There was lower risk reduction for β-blockers than for the other medications, but there was no significant difference between the β-blockers and low-dose thiazide therapy for mortality (relative risk 1.01 and 0.89 respectively). For the β-blockers, the risk reduction for total cardiovascular events just failed to reach significance at the 5% level (relative risk 0.89, 95% confidence interval 0.78–1.02). There were no trials of ACE inhibitors against placebo, but the one trial comparing ACE inhibitors with calcium-channel blockers (Table 2) suggested that the ACE inhibitor was at least as good as the calcium-channel blockers in reducing mortality and cardiovascular events.

I conclude that the data presented by Wright and colleagues show that low- and high-dose thiazide therapy, calcium-channel blockers and ACE inhibitors are similarly efficacious in reducing mortality and cardiovascular events in patients with hypertension.

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References

1. Wright JM, Lee C-H, Chambers GK. Systematic review of antihypertensive therapies: Does the evidence assist in choosing a first-line drug? *CMAJ* 1999;161(1):25-32.
2. Rothman KJ, Greenland S. *Modern epidemiology*. 2nd ed. Baltimore: Lippincott Williams & Wilkins; 1998.

[The authors respond:]

We appreciate Murray Finkelstein's comments about our systematic review; however, we disagree with his conclusion. We carefully chose the wording of our 2 concluding statements. Our first statement, that "low-dose thiazide therapy can be prescribed as the first-line treatment of hypertension with confidence that the risk of death, coronary artery disease and stroke will be reduced," is substantiated by the statistical significance (95% confidence intervals) of the reduction of total mortality, coronary artery disease and stroke with low-dose thiazides, as presented in Table 4. Our second statement was that "the same cannot be said for high-dose thiazide therapy, β-blockers, calcium-channel blockers or ACE inhibitors." A statistically significant reduction in all 3 measures has not been shown for high-dose thiazides, β-blockers or calcium-channel blockers (in Table 4 the confidence intervals include 1.00). Nor has it been shown for ACE inhibitors or any other class of drugs, as they have not been studied in trials meeting the criteria of this review.

We therefore cannot prescribe these other classes as first-line agents with confidence that they will reduce each of these 3 adverse outcomes. We did not conclude, as suggested by Finkelstein, that only low-dose thiazides will prevent death and cardiovascular morbidity. Nor did we conclude, as Finkelstein has, anything about the relative effectiveness of low-dose thiazides and the other classes of drugs; the available head-to-head evidence is insufficient to comment on the relative effectiveness of the different classes of antihypertensive drugs.

We did demonstrate in this review that using thiazides as first-line therapy was associated with a greater reduction in systolic blood pressure and a lower rate of withdrawal for adverse drug effects than that associated with some of the other classes of antihypertensive drugs. We did not comment on the cost advantage of thiazides but are pleased that Finkelstein has made this point.

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White-coat hypertension

In his recent *CMAJ* editorial on white-coat hypertension,[1] David Spence reviews the question of 24-hour ambulatory monitoring of blood pressure, which often demonstrates a lower blood pressure reading than that done in a medical centre. I agree with this phenomenon.

The patients I refer to a cardiologist for ambulatory monitoring are those whose blood pressure is uncontrolled by combinations of antihypertensive drugs. The cardiologist often measures a normal ambulatory reading, leaving me looking like a fool.

When these patients return to me, do I proceed to ignore the readings over 150/100 mm Hg in my office because their ambulatory numbers were normal? No, I treat on the basis of the higher readings I see in my office. If I am charged with overtreatment, Spence will back me up, as he correctly states