ACE hypertension treatment

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Abundant evidence from randomised controlled trials has documented that antihypertensive drug treatment is of benefit in reducing cardiovascular (CV) events in people with hypertension.

Hypertension is an important treatable contributor to death and disease globally. Most patients with hypertension, however, have other CV risk factors which increase the absolute risk of hypertension. Which group of drugs best reduces the risk of hypertension or offers the best protection?

In this article, we explore the role of angiotensin converting enzyme inhibitors (ACE-I) in the management of hypertension.

RISK REDUCTION

In 1993/4, evidence presented on blood pressure lowering in more than 47,000 patients using mainly diuretics and beta-blockers showed a reduction of 38% of stroke and 16% of coronary heart disease.

> Overwhelming data exists as to the effectiveness of ACE-I to not only reduce blood pressure but also to reduce CV events and to protect against the consequences of hypertension.

A number of large hypertension trials with ACE-I e.g. the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack have shown that ACE-I reduced mortality in patients with heart failure (HF) and acute myocardial infarction.

The first meta-analysis of the Blood Pressure Lowering Treatment Trialists' Collaboration in 2000, evaluated four trials of ACE-Inhibitors in hypertension in 12 124 people. It showed a relative risk reduction (RRR) in stroke of 30% and RRR of coronary heart disease (CHD) of 20% as compared to placebo. In 2003 the same group reported a second meta-analysis which demonstrated ACE-I had a RRR stroke 28%, CHD 20%, HF 18%, CV death 20% and total mortality 12%.

A third meta-analysis by the Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC), evaluating different drugs in patients with and without diabetes, showed that in patients with and without diabetes mellitus, all the major drug regimens, including ACE-I had broadly the same benefit over the short- and medium-term.

A summary of another two meta-analyses showed the effect of ACE-I as compared to placebo: RRR stroke 16%, coronary artery disease 21%, HF 18%, CV mortality 20% and total mortality 12%.

The BPLTTC, in another meta-analysis, evaluating the effect of treatment of patients of different ages, showed that ACE-I reduced CV events in age above 65 years with RRR 17% and in those younger than 65 years with 24%.

In the very large meta-analysis of Law *et al* (147 trials involving 958 000 people), ACE-I were associated with RRR of 17% for coronary heart disease and 22% in stroke risk. The incidence of new-onset diabetes mellitus is also significantly reduced by ACE-I by 20% in a recent meta-analysis.

Another meta-analysis showed that the use of ACE-I was associated with a lower risk to develop HF in hypertension: RRR risk 29%. In a meta-analysis of 324 168 patients, ACE-I did not increase the risk of cancer: RRR 2.03 (95%CI: Increase of 9% to reduction of 8%).

COMBINATION ACE-I

ACE-I plus a diuretic is one of the most successful approaches to contemporary combination therapy. There is additive blood pressure reduction and the combination blunts the hypokalemia response of the diuretic. ACE-I also combine well with calcium channel blockers (CCBs).

ADVERSE EVENTS

- Symptomatic hypotension, with a greater risk in those patients who are sodium and volume depleted.
- Hyperkalemia.
- Renal function decline, especially those with too low blood pressure and low perfusion pressure and in those with renal artery stenosis.
- Cough (0.5% to 20% prevalence).
- Angioneurotic oedema (0.1% to 1.2%) and especially Black patients are more predisposed and have a relative risk three to four times higher than White patients.

CONCLUSIONS

- No attempt was made to compare the efficacy of ACE-I to any other class of antihypertensive therapy.
- Overwhelming data exists as to the effectiveness of ACE-I to not only reduce blood pressure but also to reduce CV events and to protect against the consequences of hypertension.
- ACE-I combine well with diuretics and CCBs.
- Two large trials suggested the superiority of ACE-I and dehidropyridine CCBs as possibly the most effective combination.

References available on request. SF