Tip 4 (July 2009)

Sensible Combination Therapy

Most individuals with hypertension will require more than one drug (only 30% of those with stage 1 hypertension get to target on 1 drug), and those presenting with stage 2 hypertension (according the JNC-7 Guidelines[1]) should be started on 2 drugs simultaneously. It is important therefore to use combinations of drugs that work well together and have a cumulative antihypertensive effect. This was alluded to in Tip 1 (may 2009) Resistant Hypertension.

What are the best combinations?

ACE-inhibitors (or ARB's in those intolerant of ACE-inhibitors), thiazide diuretics, and calcium channel blockers are the three most important classes of antihypertensives and (in the absence of other compelling indications, or drug intolerances) should be the initial three drugs you use in your patients. They can be added to one another consecutively, or you may start a combination of 2 simultaneously and then add a third.

The general current approach is to start a patient < 60 years on an ACE-inhibitor and > 60 years on a thiazide diuretic. If a second drug is required in the < 60 year old add either a thiazide or CCB and then if a third drug is required add in one from the remaining class. For the > 60 year old, the second drug should (probably) be an ACE-inhibitor and the third a CCB. These rules are not written in stone though and a good deal of flexibility is allowed. In older individuals who are intolerant of thiazides, CCB's are an excellent alternative first choice. Similarly, in older individuals, although thiazides and CCB's share some characteristucs in common (natriuresis, direct vasodilatation) these two classes can be effectively combined in the absence of an ACE-inhibitor or ARB.

Historically, the most tried and tested 2-drug combination is the ACE-inhibitor/ thiazide combination and it is extremely effective across the age and ethnic spectrum. Recently though the ACCOMPLISH[2] trial has shown better cardiovascular outcomes with an ACE-inhibitor/CCB combination than with an ACE-inhibitor/ thiazide combination (for the same degree of BP-lowering). This is only one study, and we await further information in this area, but for the time being I think we should regard both combinations as safe and effective.

Drugs combinations which do not result in much additional BP-lowering effect include (1) adding an ACE-inhibitor (or ARB) to a beta blocker (or vice versa) (2) adding an ARB to an ACE-inhibitor (or vice versa).

1.JNC-7 Guidelines www.nnlbi.nih.gov/guidelines/hypertension/

2. Benazepril plus Amlodipine or Hydrochlorothiazide for Hypertension in High Risk Patients. Jamerson KD et al. N.Engl.J.Med. 2008;359:2417-2428