Choosing the Correct Drug for the Individual Hypertensive Patient

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Summary

With the availability of a wide selection of antihypertensive drugs acting by different mechanisms, it should be possible to match the requirement of individual patients with the pharmacological and clinical properties of an appropriate agent. Although the concept of stepped-care therapy is now largely outdated, therapy must be initiated with one agent. Diuretics remain a first-choice option in the elderly and in Black patients, as do calcium antagonists. In patients with ischaemic heart disease or enhanced adrenergic drive, β-blockers are preferred. Calcium antagonists or ACE inhibitors are finding increasing use as initial therapy when quality of life is important and metabolic neutrality is required. The choice of antihypertensive agent may be limited by adverse effects, e.g. pedal oedema with nifedipine, constipation with verapamil, and cough with ACE inhibitors.

Certain advantages are evident for both calcium antagonists and ACE inhibitors. Calcium antagonists are more likely to be effective first-line therapy than ACE inhibitors in Black patients, in those with a high salt intake, in patients with Raynaud’s disease, and when angina pectoris is present. ACE inhibitors are preferred for use in combination with diuretic agents, and in the presence of congestive heart failure or low salt intake. Combination therapy between these 2 drug classes is finding increasing acceptance because of its many theoretical advantages, and may provide a means of maximising benefit.

About 15 years ago, the Joint National American Committee on the Detection, Evaluation and Treatment of High Blood Pressure (1977) recommended the use of thiazide diuretics as step 1 therapy for hypertension, with step 2 requiring the addition of either propranolol, methyldopa, or reserpine. Step 3 entailed the addition of the vasodilator hydralazine, and step 4 a ganglion-blocking agent such as guanethidine. The following year, the WHO Expert Committee on Arterial Hypertension (1978) presented a different point of view. Both β-blockers and diuretics were recognised as first-line therapy, with second-line therapy defined as addition of a vasodilator to the β-blocker (hydralazine or prazosin) or addition of β-blocker, reserpine or methyldopa to the diuretic. Third-line therapy then introduced either the diuretic (patients first started with β-blocker) or hydralazine (patients first started with the diuretic).

Recently, even such modified versions of traditional stepped-care have been challenged. Some years ago, Zanchetti (1985) proposed that diuretics, β-blockers or ACE inhibitors could be used as first-line therapy, and by 1987 calcium antagonists had also been included (Zanchetti 1987). Logically, α-blockers are yet another choice. A broader approach to stepped-care has been advocated by Laragh (1984), and Kaplan (1986) stressed that the
choice of initial therapy should be tailored to the individual patient. I propose to call this principle ‘choice care’.

The principle of choice care is to match the qualities of the drug to the requirements of the patient. Thus, for each category of antihypertensive agent, certain patients can be identified who best suit treatment with that agent as first-choice therapy.

1. Diuretics

Diuretics remain agents of choice in elderly patients, in the Black population and possibly in obese patients (table I).

In elderly patients, a diuretic was the basis of therapy in the large European Working Party for Hypertension in the Elderly (EWPHE) study in which cardiovascular but not total mortality was reduced (Staessen et al. 1990). In the Systolic Hypertension in the Elderly Program (SHEP) study (SHEP Cooperative Research Group 1991), therapy was initiated with low dose chlorthalidone, which could be doubled, and then atenolol added. Over nearly 5 years, the stroke rate fell by over one-third and the incidence of left ventricular failure by about one-half but, again, total mortality did not decline. An added advantage of diuretic therapy is a lessened risk of hip fracture and osteoporosis (LaCroix et al. 1990), which are often disabling problems in the elderly.

Black patients respond better to diuretics as first-line therapy than to conventional β-blockade (Weinberger 1990), possibly because of their low-renin status. Combination diuretic and β-blockade treatment is, however, effective (M’Buyamba-Kabangu & Tambwe 1990), as is combination ACE inhibitor-diuretic therapy (Weinberger 1990). In obese subjects, who as a group tend to have an increased extracellular volume, diuretics are a logical choice and have proven antihypertensive benefit when combined with dietary weight reduction (Langford et al. 1991).

Diuretics are conventionally combined with a β-blocker or an ACE inhibitor. Diuretics are agents of second choice when therapy has already been started with a β-blocker (with the exception of sotalol) or an ACE inhibitor, but not with a dihydropyridine calcium antagonist (Cappuccio et al. 1991). When added to a β-blocker, only a very low dose of diuretic (such as 12.5mg of hydrochlorothiazide) is required (MacGregor et al. 1983). Higher doses should be avoided to minimise the possibility of impaired glucose tolerance (Swislocki et al. 1989). The administration of low dose diuretic plus ACE inhibitors represents a logical choice because the ACE inhibitors offset diuretic-induced hypokalaemia, changes in glucose tolerance and renin-releasing effects (Leary & Reyes 1987; Weinberger 1990).

There are numerous relative contraindications to the use of diuretics (table I). Additionally, cotherapy with agents prolonging the cardiac action potential duration (e.g. sotalol and ketanserin) predisposes the patient to the possible additive effect of diuretic-induced hypokalaemia with risk of developing ventricular arrhythmias of the torsade de pointes type. In general, young patients should not be treated with diuretics, because they are more likely to have high-renin hypertension and to require long term antihypertensive therapy, with greater risk of developing metabolic complications including diabetes or gout.

High-dose diuretics carry a real risk of a variety of nonspecific effects such as loss of energy, impotence or muscular fatigue (Medical Research Council Working Party on Mild to Moderate Hypertension 1981). Thus, the initial dose of di-