EDITORIAL

HOW I TREAT MY PATIENTS WITH HYPERTENSION

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The three main objectives of treating patients with hypertension are: (1) to reduce the incidence of complications such as cerebrovascular accidents (strokes), ischaemic heart disease, congestive heart failure and renal failure (2) to reduce the cardiovascular as well as the overall mortality and (3) to preserve the quality of life.

REDUCING THE RISK OF CORONARY ARTERY DISEASE

Reducing elevated blood pressure (BP) has been conclusively shown to significantly decrease the total cardiovascular mortality and the incidence of strokes, heart failure and renal failure. However, the incidence of ischaemic heart disease has remained disappointingly high. Indeed, in treated hypertensive patients, coronary artery disease is the major cause of mortality and morbidity.

The actual reasons why the reduction of ischaemic heart disease with antihypertensive treatment has not been fully achieved are at present unclear. The usual explanation which is given is that nearly all the previous major drug trials in hypertension have mainly involved either diuretics or beta-blockers. Diuretics elevate the serum total cholesterol, LDL cholesterol and triglyceride levels. They also cause hyperglycaemia and hypokalaemia. Beta-blockers (especially those without intrinsic sympathomimetic property) reduce the HDL cholesterol and elevate the serum triglyceride level. Therefore, it has been suggested that the potential anti-atherosclerotic effect of BP lowering on the coronary arteries by these two drugs is largely negated by their metabolic adverse effects. Today, the biggest challenge in antihypertensive drug therapy goes far beyond merely controlling the high blood pressure - it is to find pharmacological agents and regimes that will in addition significantly decrease the incidence of ischaemic heart disease and sudden death. Hopefully, this very important objective will be achieved in this present decade.

PRESERVING QUALITY OF LIFE

Preserving the quality of life is the second major issue in antihypertensive drug therapy. The great majority of hypertensive patients have mild or moderate hypertension and are totally asymptomatic. Many of the present drugs have important side effects such as fatigue, sexual dysfunction and a general lack of well being. Poor compliance to drug therapy is a major problem that is encountered all over the world. The fewer the side effects and the simpler the therapeutic regime, the more compliant the patient will be with his treatment. It has been reported that of all the currently available antihypertensive drugs, the ACE inhibitors probably have the lowest incidence of side effects and cause the least impairment to the quality of life. This statement is largely true except that in the Asean experience, cough is the single most important and disturbing problem with ACE inhibitors. It is seen in about 15% of patients who are given this class of agents.

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CLINICAL DECISIONS AND PERSPECTIVES

In all my patients with hypertension, the following approach is routinely adopted: (1) a detailed history and physical examination including a very careful measurement of the BP level (2) estimation of serum urea, creatinine, electrolytes, glucose, uric acid and lipids (total cholesterol, LDL and HDL cholesterol and triglycerides) (3) urine analysis and (4) ECG. In selected patients, it may be necessary to do more sophisticated tests such as 24-hour ambulatory BP monitoring, echocardiography, exercise stress test and investigations to exclude renal parenchymal disease, renal artery stenosis, phaeochromocytoma and Conn's syndrome.

After these initial steps, the 3 questions which should be routinely addressed are : (1) whom to treat? (2) when to treat? and (3) how to treat? A difficult problem which a clinician frequently has to solve is a patient with mildly elevated BP. Many such patients actually do not have hypertension but have spuriously elevated BP readings only at the clinic when they are examined by doctors (so called "office" or "white coat" hypertension). In apparently mildly hypertensive patients, it is extremely important to measure the BP repeatedly in many subsequent visits. A diagnosis of mild hypertension should only be made when the BP is consistently elevated. Home BP and non-invasive 24-hour ambulatory BP monitoring are both useful tools in the evaluation of mild hypertension. Blood pressure measurements using both these techniques have been frequently found to be lower than the clinic readings. However, the main limitation at present of both home and 24-hour ambulatory BP monitoring is the lack of adequate data regarding what values which are obtained with either of these tests truly represent normal or abnormal BP readings (ie normotension versus hypertension).

Pharmacological therapy should routinely be given if the diastolic BP is 105 mm Hg or higher. However, with regard to mild hypertension (diastolic BP between 90-104 mm Hg), there is today tremendous controversy regarding the level of diastolic BP above which drug treatment is unequivocally indicated. All patients with mild hypertension should initially be treated with non-pharmacological measures such as weight reduction, decrease in salt and alcohol intake, aerobic exercise and stopping cigarette smoking. If the diastolic BP persists around 100 mm Hg or higher despite the non-pharmacological treatment, most experts will recommend that drug therapy be started[1]. However, it is at present uncertain whether drug treatment is beneficial if the diastolic BP is between 90-100 mm Hg. All the trials so far have shown that the value of drug therapy in mild hypertension is small. I will consider pharmacological therapy in this situation if the patient shows target organ damage or has other risk factors for atherosclerosis such as diabetes mellitus or hyperlipidaemia.

In recent years, there has been a great deal of interest in

lderly patients with hypertension. Contrary to earlier beliefs, lderly patients with diastolic hypertension, like their younger ounterparts, have been shown to benefit from drug therapy. lowever, since these patients are sometimes sensitive to even mall dosages of drugs, it is my practice to start drugs in lderly patients at a low dose and to increase the dosage very radually and gently. Isolated systolic hypertension is usually een in the older population. Unlike diastolic hypertension, the reatment of systolic hypertension has not yet been demonstrated o be beneficial. Indeed, some authorities believe that isolated ystolic hypertension should not be treated irrespective of its everity. However, in the renowned Framingham study, isolated ystolic hypertension was demonstrated to be even more mportant than diastolic hypertension[2]. I will consider drug herapy if the systolic blood pressure is consistently greater han 180 mm Hg.

CHOICE OF ANTI-HYPERTENSIVE AGENTS

Today, the practising physician is deluged as never before sometimes even almost drowned) by the plethora of drugs hat are surrounding him. In my opinion, there are currently oo many classes of antihypertensive agents and too many lrugs within the same class of agents. For example, there are it present five ACE inhibitors available in Singapore, with a ew more to come in the near future. Despite what the harmaceutical companies would have us believe, in the light f our present knowledge, all of them are essentially similar in linical practice except that captopril is short acting whilst all he others are longer acting and thus can be given once a day. Despite this abundance of drugs, there is as yet still no harmacological agent that fulfils all the criteria of an ideal ntihypertensive agent. All the current drugs that are widely rescribed have certain advantages as well as disadvantages. None can be considered clearly and decisively superior to the thers in every clinical situation that may be encountered within he wide spectrum of potential problems that are seen in ypertensive patients. Over and above clinical efficacy and afety, the cost factor is also extremely important especially in leveloping countries. Some drugs (eg. ACE inhibitors) are nuch more expensive than others (eg. diuretics).

Today, the 4 major groups of antihypertensive agents that re widely used and recommended are: (1) thiazide diuretics (2) beta-blockers (3) calcium antagonists and (4) ACE nhibitors. The alpha-blockers (eg. prazosin) are also sometimes rescribed. Indapamide, which is currently fairly popular in Singapore, has both diuretic as well as vasodilator properties. Although it has been reported that indapamide has minimal netabolic side effects, in my experience severe hypokalaemia nay occasionally occur.

INDIVIDUALIZED STEPPED-CARE APPROACH

The stepped-care approach has been widely used with success for about ten years. In this method, a single drug is given initially and the dosage is increased gradually. If there is inadequate control of the hypertension, other drugs are added or substituted one at a time (in steps) until the target BP is achieved. Until recently, either a thiazide diuretic or a beta-blocker was routinely started in step 1. Either of these drugs will adequately reduce the elevated BP in about 40% of patients. In the remaining cases where the response was not optimal, it was recommended that both these drugs should be given together in step 2. This combination therapy will usually result in adequate control of the hypertension in another 40% of patients. In the last 20% of cases, a third drug, usually a vasodilator, was added in step 3.

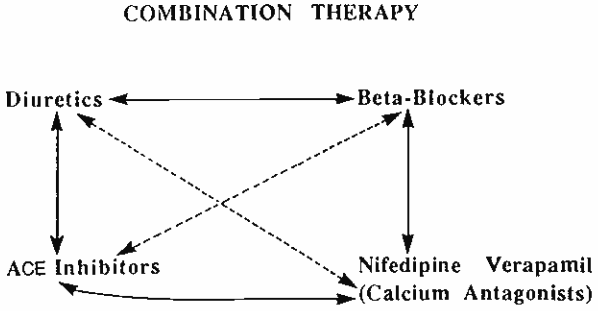
However, in recent years it has become clear that it is important not to adopt a rigid and a routine pattern of drug therapy, but to individualize treatment whenever this is possible or appropriate because hypertensive patients frequently have different problems which have to be considered[3]. Certain conditions may be present where specific drugs may be specially indicated or contraindicated. Therefore it is essential that a more intellectual, sophisticated and a broader approach to stepped-care therapy should be adopted. The initial choice of drugs should not be restricted to only the diuretics or beta-blockers but should routinely also include the calcium antagonists and ACE inhibitors. For example, a beta-blocker is specially indicated in a patient who has both hypertension and a previous myocardial infarction, since this drug not only lowers his blood pressure, but will also significantly reduce the risk of a further coronary event. On the other hand, a beta-blocker is contraindicated in a patient who has hypertension as well as either bronchial asthma or bradycardia. Instead, a diuretic, ACE inhibitor or a dihydropiridine class of calcium antagonist should be given. Diuretics may be undesirable in a hypertensive patient who also has diabetes mellitus or hyperlipidaemia. In this situation, a calcium antagonist or an ACE inhibitor should be prescribed. Finally, if a patient suffers from both hypertension and congestive heart failure, diuretics and/or ACE inhibitors are the preferred drugs because of their hypotensive and anti-heart failure effects. In the many hypertensive patients who have none of the diseases mentioned above, there is at present no consensus in opinion as to which drug should be given as the initial therapy. Diuretics and beta-blockers have been traditionally used as routine step one agents, with beta-blockers being preferred in younger patients. However, their popularity in the last few years has greatly decreased as their side-effects have become more apparent. Diuretics are today seldom used as monotherapy but have remained useful as combination therapy with other drugs. At present, the other agents which are more frequently prescribed in step 1 are the calcium antagonists and ACE inhibitors. In my practice, many of my patients are given beta-blockers or calcium antagonists because of associated ischaemic heart disease.

Approximately 60% of hypertensive patients (especially those with moderate or severe hypertension) will require 2 or sometimes even 3 drugs. Theoretically, any 2 different classes of antihypertensive agents can be combined. However, it has been established that certain combinations are much more effective and useful than others. Figure summarizes my preference in the choice of combination therapy. It is important to note that with regard to the calcium antagonists, the dihydropiridine class of agents (eg nifedipine, felodipine and isradipine), unlike verapamil and diltiazem, do not depress sinoatrial nodal function and atrio-ventricular conduction and can therefore be combined safely with beta-blockers. For many years, I have used the combination of beta-blockers and nifedipine (more recently felodipine) with considerable success. It is also important to stress that non-pharmacological intervention should not be ignored in patients who are treated with drugs, but should be carried out as a form of adjunct antihypertensive therapy.

THE 'J' CURVE PHENOMENON

The last issue I would like to address is the question of the 'J' curve phenomenon. Cruickshank et al recently reported that there is an increase in mortality from myocardial infarction when the diastolic BP of hypertensive patients with preexisting ischaemic heart disease are lowered below 85 mm Hg[4]. Despite current controversies, it is very likely that the 'J' curve phenomenon genuinely exists and that below a certain critical diastolic BP level, the harmful effects of antihypertensive

Figure. Recommended combination therapy. Solid lines indicate effective and well tested combinations :
(1) beta-blockers and diuretics/calcium antagonists (dihydropiridine class eg. nifedipine)
(2) ACE inhibitors and diuretics/calcium antagonists.
Broken lines indicate less effective combinations :
(1) beta-blockers and ACE inhibitors
(2) diuretics and calcium antagonists (see text).



therapy will exceed the beneficial effects. However, what this exact level is remains unknown at present. It is probably different for varying subsets of hypertensive patients.

CONCLUSION

There is little doubt that there has been tremendous progress in our understanding and management of hypertension in the past 30 years. Although none of the present antihypertensive agents are exactly ideal agents, they are all highly effective with a small and acceptable incidence of side effects[5,6]. In treating hypertension in the 1990s, it is important not to be overwhelmed by the enormous numbers of antihypertensive agents that are currently available nor the countless seminars and symposia on hypertension that are routinely organized. To be successful, it is essential for every practitioner to be completely familiar with only the main classes of antihypertensive agents and to be comfortable with just a few selected drugs within each class. Finally, the importance of adopting a flexible and individualized rather than a rigid therapeutic approach in the drug therapy of hypertensive patients cannot be over-emphasized.

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