The D B A Stepcare System

A rational antihypertensive regime in black family practice

by Leonard van Gelder

Summary

Hypertension is common in the black population of the RSA. A five-step care system is given by the author. He discusses the drugs used, the effect of the combination of drugs and their experiences with a large group of patients.

KEYWORDS: Blood Pressure; Hypertension; Antihypertensive Agents; Vascular Resistance; Negroid Race — South Africa; Urban Population; Drug Therapy, Combination.

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Curriculum Vitae

Dr LW van Gelder graduated at the University of Pretoria in 1972. He then did a general rotating Internship at Cook Country Hospital, Chicago, Illinois (1973-1974). He obtained a M PRAX MED-degree (Pretoria 1978) and a MFGP (SA)-South African College of Medicine. During 1978 he passed both the VQE and FLEX examinations in the USA. He is presently working on a Masters degree in Pharmacology at the University of Pretoria. His main interest lies in family medicine, its whole spectrum including research aspects, pharmacology, theology, sexology, computer applications and hypertension. He has 11 years' experience in the Dept of Family Practice (Pretoria), 15 months' in the Dept of Family Practice, Cook Country Hospital (Chicago) and frequently visits the USA to keep in touch with family practice and research aspects there. He has also been certified in basic and advanced cardiac life support by the American Heart Association. Dr van Gelder has published various articles on his research work and is an active member of the American Academy of Family Practice, the Illinois Chapter of the AAFP, member of the Society for Clinical Trials and the Christian Medical Fellowship. He married Susan and they have two children.

RIGHT at the beginning I need to stress the fact that hypertension is extremely common in the black population in South Africa and is second only to violence as the most common cause of death in Johannesburg blacks 1-5.

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However, the treatment is usually a lifelong process and the decision to treat should not be taken lightly. I feel that a sustained diastolic blood-pressure of 100 mm Hg or higher in older people should be a practical base level from which to initiate treatment.

The W H O considers a systolic blood-pressure of 160 mm Hg or more and a diastolic blood pressure of 95 mm Hg or more as an established hypertension.

The treatment of high blood-pressure reduces the incidence of renal and cerebrovascular complications and increases survival; however, the incidence of hypertension and sudden death remains the same.

Factors that increase the need to treat a blood-pressure of less than 100 mm Hg are: a concomitant systolic blood-pressure, signs of target organ damage (left ventricular hypertrophy or congestion retinopathy or kidney damage), the male sex, smoking, diabetes and hyperlipidaemia.

A diagnosis of essential hypertension is made by the exclusion of organic causes (renal and adrenal pathology, intracranial pathology, eclampsia and coarctation of the aorta) and constitutes more than 50% of cases. The renin status of patients with essential hypertension, although not considered important any more, possibly points to a dysfunction in the sodium status.

Low renin hypertension is more common in the elderly patient and more common in black patients (40%) than in white patients (20%). These patients have a volumedependent hypertension that responds very well to diuretics. Normal and high renin hypertension are more common in young white patients.

Hypertension is very common in blacks in South Africa.

These patients have a vasoconstricting dependent hypertension which responds well to beta-adrenergic blockers and other drugs, which have a tendency to lower renin activity and/or the ability to reduce sympathetic tone through a central or peripheral mechanism.

In these cases blood-pressure is lowered in most patients regardless of the drug employed. The goal of any antihypertensive treatment is to stabilize the diastolic blood-pressure at less than 90 mm Hg with minimal side-effects. This can be attained in more than 80% of hypertensive patients, regardless of the original severity of the disease.

Initial therapy should consist of non-drug treatment including salt restriction and mass reduction (both important in urban blacks).

In white, normal or high renin, non volume-dependent hypertensive patients, Opie⁷ and others suggest by implication alpha or beta blockers as the first step in treatment of uncomplicated hypertension. Treatment should be started with either alpha or beta blockers, according to the individual patient.

Salt restriction and mass reduction are very important in the treatment of urban blacks.

In black patients a lot of confusion still exists largely due to false rumours that these patients do not respond to beta-blocker therapy. This has led to an avoidance of employing the most widely accepted method of treatment, ie starting with a diuretic, adding a betablocker and going on to a vasodilator as a third step in eventual control.

At the Kalafong and Mamelodi hospitals we currently treat between 2 800 and 3 000 black patients with hypertension per month.

In the stepcare of hypertension of these patients we have found that diuretics, beta blockers and, as a third step, alpha-adrenergic blockers provide impressive, flexible as well as inexpensive treatment for all types of hypertension. After thorough and ongoing research with beta and alpha-adrenergic blockers, we are convinced of their place as second and third step antihypertensive agents respectively.

CARDIAC OUTPUT AND WELL-BALANCED ANTIHYPERTENSIVE THERAPY

Blood-pressure is dependent upon both cardiac output and peripheral resistance. However, the cardiac output should be maintained at adequate levels, if one is looking for well-balanced antihypertensive treatments.

In this respect there is no significant difference between the nonselective and selective beta-blocking drugs, neither having the edge in terms of haemodynamic changes. There is, however, a reduction in the cardiac

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output in both, mainly a reflection of a reduced pulse rate, as the stroke volume does not change. In addition there is a rise in the calculated peripheral resistance. These responses are in sharp contrast to combined alpha and beta blockade when there is a significant reduction in both systolic and diastolic blood-pressure, without any major change in cardiac output or pulse

The alpha blocker overcomes the acute rise in peripheral resistance and afterload which would be expected with the beta component alone and the nett result is a hypotensive effect without any major change in cardiac output or pulse rate^{8,9}.

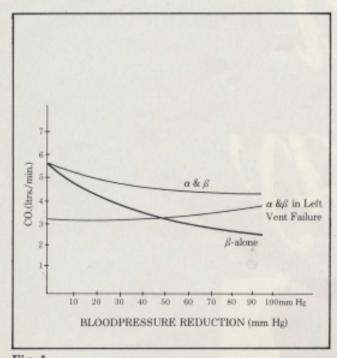


Fig. 1

CLINICAL USE OF THE DIURETIC/BETA-ALPHA REGIME (DBA REGIME) IN PATIENTS WITH VOLUME-DEPENDENT HYPERTENSION

In this triple drug regime (alpha and beta blockade plus diuretics), side effects such as cold extremities, asthma, impotence and diabetes can be controlled. This is achieved simply by adjusting the ratio of diuretics, beta and alpha-adrenergic blockers to suit the individual — it in fact amounts to the situation where one has three taps with which to regulate the blood-pressure and to minimize side-effects.

If a patient develops asthma or diabetes, for instance, a higher proportion of the alpha-blocking drug and less or none of the beta-blocking drug is used. Likewise, if postural hypotension develops, the beta-adrenergic component is increased and the alpha component reduced. WHO considers a systolic BP of 160mm Hg (or more) and a diastolic BP of 95 mm Hg (or more) as an established hypertension.

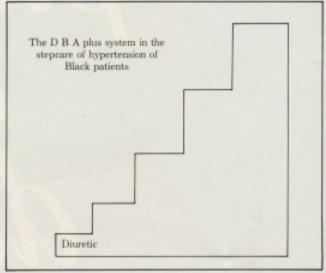


Fig. 2

DIURETICS (Fig 2)

Regarding diuretics, we are all aware of a lot of publications now appearing — with the message that the dosage of the drug should be kept as low as possible due to its effect on the blood lipids.

We found that beta blockers, and especially the nonselective, inexpensive beta blockers such as sotalol and nadolol, which do not have a flat dose response curve, were highly effective in the control of hypertension in black patients. Beta-blockers of this type are exceptionally effective in low renin patients, particularly in combination with a diuretic.

We currently have over 1500 patients on Sotazide (sotalol combined with thiazide) and we have achieved excellent results. This is mainly due to sotalol's broad therapeutic index — dosages of 640 mg or more being well tolerated and we have experienced no serious complications in over three years.

Antihypertensive treatment aims to stabilize the diastolic BP at less than 90mm Hg with minimal side effects. There is no significant difference between the non-selective and selective betablocking drugs, neither having the edge in terms of haemodynamic changes.

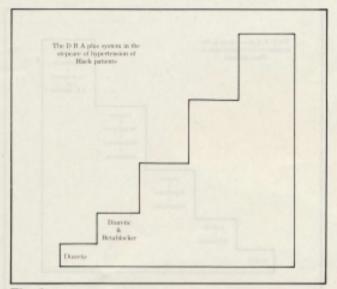


Fig. 3

A FEW POINTS OF INTEREST ON BETA BLOCKERS (Fig 3)

Bradycardia due to beta blockers

Little concern need be paid to bradycardia due to beta blockers even in elderly patients as long as the cardiac output is sufficient, even at a pulse rate of 45 to 50. If I am concerned about a patient's well-being, I cut back on the beta blocker. But by adding an alpha blocker the heart rate is automatically increased due to peripheral vasodilation. My advice is to add an alpha blocker without cutting down the beta blocker dosage. I feel that the concept of congestive cardiac failure as a result of beta blockers has been overstressed.

Cleardreams

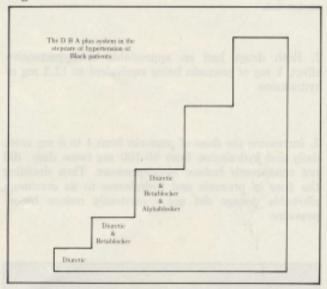
With hydrophilic beta blockers there were very little or no dream side-effects.

Alpha blockers are the drugs of choaice in cases with asthma, congestive cardiac failure, heartblock and peripheral vascular problems.

• Torsade de Pointes not seen in over 1 500 cases

|Torsade de Pointes — or twisting along the electrical axis; dysrhythmias due to the administration of many drugs and to hyperkalaemia| In over 1500 to 2000 cases on sotalol plus the thiazide combination we have not encountered Torsade de Pointes and our patients are regularly monitored by ECG and electrolyte evaluations. Although we are aware of a very select group of patients in an intensive care setting, where renal failure and concomitant therapy could have been contributary to Torsade de Pointes, in our group of patients we have not seen Torsade de Pointes and we are constantly on the lookout for it.

Fig. 4



ALPHA BLOCKERS

Prazosin has no effect on the blood-lipids, maintains high cardiac output and low peripheral resistance. The biggest problem experienced has been that some black patients have shown a first-dose syncopic attack as well as postural hypotension. We have also had some experience with indoramin and have been satisfied with it. It does, however, cause a mild transient sedation in patients.

Alpha blockers, like indoramin and prazosin, are the drugs of choice in cases with asthma, congestive cardiac failure, heartblock and peripheral vascular problems. Alpha blockers are also indicated in young patients who are physically active — in whom a high cardiac output is required.

THIRD STEP CARE

Oral vasodilators are recommended for the treatment of hypertension if the combination of a diuretic and betablockers fails to produce a satisfactory reduction of blood-pressure. Such triple therapy is very effective at lowering blood-pressure and both hydralazine and

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prazosin have been shown to reduce diastolic pressure effectively when used in combination with beta blockers.

STEP FOUR

In support of the fourth step the following study was done by MJ Vandenburg et al on hydralazine and prazosin¹⁰.

- This was an observer-blind crossover trial in 31 patients with essential hypertension comparing the efficacy of low dose combinations of prazosin and hydralazine (Apresoline) in the treatment of hypertension.
- Both drugs had an appreciable antihypertensive effect, 1 mg of prazosin being equivalent to 12,5 mg of hydralazine.
- 3. Increasing the dose of prazosin from 4 to 8 mg twice daily and hydralazine from 50-100 mg twice daily, did not consistently reduce blood-pressure. Thus doubling the dose of prazosin and hydralazine to its maximum allowable dosage did not consistently reduce bloodpressure.

I feel that the concept of congestive cardiac failure as a result of beta blockers has been overstressed.

- The combination of the two drugs at low doses resulted in the blood-pressure of more patients being controlled than when either drugs was used alone at high dose.
- The symptoms reported by patients were similar for both drugs. The combination did not lead to an increased reporting frequency.

Thus the effect of prazosin and hydralazine is additive, the combination at low dose producing a greater fall in blood-pressure than either drug used alone at its maximum dose. The combination of a diuretic beta blocker and alpha-blocking drug plus hydralazine follows logically to be the fourth step of this stepcare approach in the care of the volume-dependent hypertensive patient.

STEP FIVE

The fifth step includes the use of a calcium antagonist, A E inhibitor or centrally acting drug in addition to the D B A drugs.

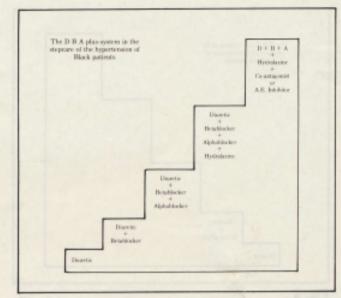


Fig. 5

CONCLUSION

In conclusion, the three main components of this D B A system, namely diuretics, beta blockers and alpha blockers (vasodilators) lead to a situation where almost any drug-related symptom could easily be corrected by adjusting the ratio between the three main drugs, namely diuretics, beta blockers and alpha blockers (D B A — regulation).

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