Meeting Report


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The 11th Congress of the Southern Africa Hypertension Society was held in Dunbar, Natal, South Africa on March 21–24, 1999. Lawrence Ramsay (Head Clinical Pharmacology and Therapeutics, Royal Hallamshire Hospital, Sheffield, UK) opened the meeting with a discussion of the problems in managing hypertension in clinical practice. He pointed out that the “rule of halves” is alive and well: only one-half of all hypertensive people are detected, only one-half of them receive treatment and only one-half of those treated achieve optimal blood pressure control. He also pointed out that, while most classes of antihypertensive agents are reasonably satisfactory, no single drug alone controls hypertension adequately in a majority of patients with even mild hypertension. Most patients need at least two drugs to attain target blood pressure, and about one-third of them need three or more drugs in a combined regimen.

Michelle Beevers (City Hospital, Birmingham, UK) discussed the pitfalls in blood pressure measurement. She pointed out that 15% of all hypertensives have an arm circumference greater than 33 cm, necessitating a wider cuff (12.5 × 36 cm). The conventional cuff (12 × 23 cm) is suitable only for nonobese arms. Regarding diastolic blood pressure, the view of all guideline committees is that it should be taken at the disappearance (K5), not muffling (K4), of sounds and that phase 4 (K4) should be abandoned even in obstetric patients. Beevers also highlighted the role of weight reduction, pointing out that the 1 kg weight loss results in a 1 mmHg fall in diastolic blood pressure. The recently completed TONE study in the United States has shown that in randomized controlled trials patients can lose between 4–5 kg if they are suitably counseled.

A special session was devoted to the management of hypertension in special situations. A. Motala (University of Natal, Durban, South Africa) stressed the importance of tight control of blood pressure in slowing the progression of diabetic nephropathy. S. Naiker

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Naicker pointed out that thiazides are generally not effective when serum creatinine is greater than 220 μmol/L. In this situation, a combined regimen of frusemide (furosemide) and metolazone is usually effective, even when the creatinine clearance is less than 10 mL/min.

Y. Veriawa (Helen Joseph Hospital, Gauteng, South Africa) discussed stroke and hypertension. Strokes account for 7% of all deaths in South Africa compared to 5% for ischemic heart disease. He pointed out that blood pressure is often elevated at presentation in patients with an acute stroke. This blood pressure elevation may be a physiological response to brain ischemia to maintain blood flow in the ischemic peri-infarction zone. There is a failure of cerebral autoregulation to this area, which is now totally dependent on systemic blood pressure to maintain perfusion. Lowering of the blood pressure during this crucial period may decrease perfusion and increase ischemic cerebral damage. Acute stroke blood pressure reduction should, therefore, not be attempted if the blood pressure level is <220/120 mmHg.

Arya Sharma (Free University of Berlin, Germany) stressed that the attributes of the ideal antihypertensive agent should include 24 hour efficacy with a once daily dose and a trough peak ratio of at least 50%. While most physicians begin with a low dose of the drug of choice and gradually titrate the dose, dependent upon the patient’s response, newly developed combinations offer an alternative approach. Combinations of drugs from different classes may provide greater efficacy with a lower risk of dose-dependent side effects. Recent studies, including the Hypertension Optimal Treatment (HOT) trial, lend support to this approach, since the majority of patients in this trial required two or more drugs to achieve target blood pressure.

Y. K. Seedat (University of Natal, Durban, South Africa) and Norman Kaplan (University of Texas, Dallas, TX, USA) discussed different hypertension guidelines. Seedat expressed concern about the guidelines and whether they reflect consensus views or simply the views of the panel rather than of the broader clinical community. Nevertheless, guidelines are surprisingly in agreement on several important issues, such as the urgency of the early treatment of severe or malignant hypertension, the need for lower target values in patients with an increased cardiovascular risk, the importance of treating isolated systolic hypertension, and the benefits of treating the elderly.

Disagreements exist in the management of mild hypertension. Seedat felt that estimation of cardiovascular risk is an attractive approach but may have the disadvantage of complexity in the discussion with patients from some racial groups. D. J. Ramsay (University of Maryland, Baltimore, MD, USA) held the opposite view: he felt that decisions regarding treatment of patients with blood pressure around 160/100 mmHg require 3–6 months of observation but are simple and straightforward. Decisions become more difficult when the blood pressure averages 140–159/90–99 mmHg. It is here that treatment decisions (in uncomplicated, mild hypertension) should be based on the formal assessment of cardiovascular risk using, for example, the New Zealand chart. All patients with a risk of 2% per year (equivalent to a coronary risk of 1.5% per year) should be offered antihypertensive treatment. Ramsay agreed, however, that the New Zealand chart is only applicable to the white population.
**Norman Kaplan** (University of Texas, Dallas, TX) showed that excellent results can be achieved with fixed drug combinations containing a very-low-dose diuretic. The fixed combination of bisoprolol (10 mg) and hydrochlorothiazide (6.25 mg) (CONCOR) is included in the JNC-V1 guidelines as a firstline antihypertensive treatment because of its proven efficacy and the low-dose composition, which tends not to cause side effects. He supported the algorithm that advocates for diuretics or β-blockers for patients with uncomplicated hypertension, which, he maintained, is based on randomized clinical trials. The only exception (when diuretics are not adequate or inappropriate) is the recommended use of a long-acting dihydropyridine-type calcium antagonist in elderly patients with systolic hypertension. This recommendation is based primarily on the recently published SYST-EUR trial, which was fully discussed later by J. A. Staessen. N. Kaplan felt that referral to a hypertension specialist was needed if blood pressure remained uncontrolled after multiple drugs. At present such an individual is not identifiable, other than by colleagues who know of the expertise of some practitioners in dealing with difficult hypertension. The American Society of Hypertension has begun an accrediting process towards this end.

In the symposium on calcium channel blockers, **J. A. Staessen** (University of Leuven, Belgium) addressed the problem of treating isolated systolic hypertension (ISH), which is a major modifiable risk factor in the elderly and affects up to 15% of people older than 60 years. He discussed the results of 3 randomized controlled trials on ISH: the Systolic Hypertension in the Elderly Program (SHEP) in the United States, the Systolic Hypertension in Europe (Syst-Eur) trial, and the Systolic Hypertension in China (Syst-China) trials. The outcomes of these trials were pooled. The treatment results were compared with those for placebo. The treatment reduced all-cause mortality by 17%, cardiovascular mortality by 25%, all cardiovascular endpoints by 32%, stroke by 37%, and death due to myocardial infarction, including sudden death, by 25%. These results demonstrated that elderly with systolic hypertension should be treated, if on repeated measurements systolic blood pressure is 160 mmHg or higher. Staessen also pointed out that according to the latest results from the Syst-Eur trial, the risk of cardiovascular complications can be effectively reduced in hypertensive diabetic patients by initiating drug treatment with a calcium channel blocker. The Syst-Eur trial investigated whether antihypertensive drug treatment, starting with a twice-daily dose of the long-acting dihydropyridine calcium channel blocker, nitrendipine, could reduce cardiovascular morbidity and mortality in older patients with isolated systolic hypertension. In diabetic patients, active treatment reduced all-cause mortality by 55%, fatal and nonfatal strokes by 73%, and all cardiac endpoints by 63%. Staessen concluded that nitrendipine-based antihypertensive treatment is particularly beneficial in older patients with diabetes and isolated systolic hypertension.

**P. Sareli** (University of Witwatersrand, Gauteng, South Africa) reported the results of the BAHAMA study. This study compared the blood pressure lowering effect of seven antihypertensive combinations using a prospective, randomized, open-label design with a 2-week placebo run-in phase. Three hundred forty-four black South African patients with mild to moderate hypertension participated in the study. Blood pressure control and dose titrations were based on ambulatory blood pressure monitoring. This study showed that long-acting calcium channel blockers controlled blood pressure in the majority of these patients, whereas hydrochlorothiazide, reserpine, or angiotensin converting enzyme (ACE) inhibitors resulted in satisfactory blood pressure control in only about a half of the...
patients. When hydrochlorothiazide was used, 75% of patients required combination therapy. Sareli concluded that in black patients with severe hypertension, long-acting dihydropyridine calcium channel blockers produce a significant and a predictable fall in blood pressure.

Martha Hill (The Johns Hopkins School of Nursing, Baltimore, MD, USA) reported the results of a trial of losartan hydrochlorothiazide (Cozaar Comp) in a black urban community under difficult social circumstances. Significant blood pressure lowering was achieved in 300 young men in both, the special- and normal-care groups, probably because of the very low side effect profile of this drug combination.

Albert Mimran (University Hospital, Montpellier, France) reported on two studies conducted in healthy volunteers which showed that the angiotensin II receptor blocker, irbesartan, had superior receptor blocking activity. In one study conducted by M. Burnier and Hans Brunner (Lausanne, Switzerland), blockade of the renin-angiotensin system was evaluated at 4, 24, and 30 hours after drug intake. At 4 hours, irbesartan caused 88% blockade of the angiotensin II-induced blood pressure increase, whereas losartan and valsartan produced only 43% and 51% blockade, respectively. Irbesartan maintained a significant blockade versus placebo at 30 hours. These data suggest that there are differences between various drugs in the angiotensin II antagonist class that might have potential implications for the management of hypertensive patients.

The symposium on moxonidine evoked a lot of discussion. Moxonidine, a selective, centrally acting, imidazoline-1 receptor agonist, acts by reducing central sympathetic outflow. It acts on α2-adrenoceptors in the periphery and in several areas of the brainstem to decrease the central sympathetic outflow. A sustained release (SR) formulation of mononidine has been developed to minimize symptomatic hypotension initially seen with the immediate release formulation. Concerns about the safety of the drug were raised because the MOXCON heart failure trial had to be stopped early due to the increased mortality in the moxonidine group. This finding may be related to the potential of the drug to cause arrhythmias. Furthermore, abrupt discontinuation of centrally acting agents (e.g., clonidine) is known to result in a rebound phenomenon that is typically manifested within days of discontinuation. In studies in hypertensive patients neither arrhythmias nor rebounds have been observed with this agent. The clinical trials with monoxidine indicate that this drug is safe in the treatment of hypertensive patients.

P. A. van Zwieten (University of Amsterdam, The Netherlands) reviewed the management of heart failure and discussed the role of angiotensin II receptor blockade in heart failure. The results of the ELITE study which compared captopril and losartan in patients with heart failure showed marked reduction in mortality with losartan. Since this was not a predetermined endpoint in the study and the study was not powered to detect differences in mortality, a new trial, ELITE II, is underway to confirm these findings. Several new studies are looking at the angiotensin II receptor antagonists in heart failure. The largest to date, VALHEFT using valsartan, has completed recruitment and the results are eagerly awaited. According to van Zwieten the major attraction of these drugs in the treatment of hypertension is the freedom from side effects.

Three awards of R5,000 each were given to the best papers presented at the meeting. A. Daniels (MRC) presented an audit, performed in the primary care setting, of attitudes to national guidelines. He found that the guidelines were poorly implemented because of the attitudinal barriers and rather passive dissemination of guidelines. G. Norton (Uni-
versity of Witwatersrand, Gauteng, South Africa) presented interesting findings on pressure overload hypertrophy in rats. He showed that the onset of left ventricular failure in pressure overload hypertrophy was accompanied by deleterious chamber remodeling rather than myocardial dysfunction. Anita Naicker (University of Natal, Durban, South Africa) took biopsies of placental tissue from deliveries involving hypertensive mothers and found that defective trophoblastic invasion could be due to an altered expression of the transforming growth factor $\beta_1$.

Conclusion: The guiding theme of the symposium: “Hypertension: Yesterday, Today and Tomorrow,” clearly reflects the significant strides in the management of hypertension during the past decade. Clinicians now know what target blood pressure to aim for. The discovery of newer, efficacious, and better-tolerated drugs makes this target level an achievable goal using multiple drugs at lower doses and in combinations.