

## Hyperinsulinemia and hypertension in the Seychelles Cardiovascular Diseases Survey

Luc Tappy, Institute of Physiology and Medical Polyclinic, University of Lausanne

Apart from its major actions on carbohydrate, lipid and protein metabolism, insulin stimulates renal sodium reabsorption and increases the activity of the sympathetic nervous system by mechanisms incompletely understood. It is currently hypothesized that the resultant hyperinsulinemia found in insulin resistance may lead to constant overstimulation of renal sodium reabsorption and/or of sympathetic nervous system activation.

Several studies have been performed to determine if plasma insulin concentration bear a relationship with blood pressure and may be a causative factor in the genesis of hypertension. The results reported were discrepant between studies: insulin was observed to be independently correlated with blood pressure in some studies, whereas such a relationship was not observed in others.

In order to test the hypothesis that insulin plays a role in the control of blood pressure, the interrelationships of anthropometric features, age, glycemia and serum insulin levels were studied in people having participated in the Seychelles Cardiovascular Diseases Survey carried out in 1989. The survey involved 1081 residents from a randomly selected age- and sex-stratified sample of 1251 Seychellois aged 25–64. The study was however restricted to the 839 people for whom remaining plasma was available for insulin determination (the remaining 214 plasmas being no longer available). Most results are presented above (see Tables 9–19 and Figures 8–20).

It was observed that:

1. The proportion of hypertension was higher in subgroups of individuals with diabetes mellitus (52.4%) and with overweight (33.2%) than in the general population (22.5%). The proportion of diabetes mellitus was higher in the

subgroups of individuals with hypertension (11.6%) and with overweight (12.6%) than in the general population (5.0%). The proportion of individuals with overweight was higher in subgroups of individuals with diabetes (66.7%) and with hypertension (40.7%) than in the general population (26.6%).

2. Subgroups of individuals with overweight, diabetes or hypertension had higher mean ( $\pm$  SD) fasting plasma insulin ( $13.6 \pm 7.9$ ,  $14.0 \pm 8.0$ ,  $10.9 \pm 9.6 \mu\text{U}/\text{ml}$ ) than individuals not affected with these conditions ( $8.1 \pm 4.6 \mu\text{U}/\text{ml}$ ). Similarly, plasma glucose and triglyceride concentrations were also higher in these three conditions.
3. Both systolic and diastolic blood pressures were independently correlated with age, body mass index and fasting blood glucose in the whole population while no correlation was found with insulin. In contrast, in the subgroup of 223 overweight individuals, age, blood glucose and plasma insulin were each independently correlated with blood pressure.

It is concluded that hypertensive, diabetic and overweight individuals have several metabolic similarities, including hyperinsulinemia. Insulin was not independently correlated with blood pressure except in a subgroup of overweight patients. However, only a few percent of the variance of blood pressure was explained by insulin in this subgroup of overweight individuals. These observations do not support the hypothesis of a significant role of hyperinsulinemia in the genesis of hypertension. It is concluded that a link other than insulin is likely to exist between metabolic alterations and increased blood pressure.

## Workshops

### Detection, evaluation and treatment of hypertension

High blood pressure, a major risk factor for cardiovascular disease, has been found in as many as 34% of Seychellois men and 31% of Seychellois women aged 35–64. These prevalence rates, issued from the Seychelles Cardiovascular Diseases Survey, are among the highest when compared with those observed in industrialized countries

which participated to the WHO MONICA Project and had therefore similar blood pressure measurement protocol.

Among subjects with hypertension, about half of the men and one third of the women were unaware of having high blood pressure, while only 9% of men and 15% of women were presently on an anti-

hypertensive drug therapy. Furthermore, only 21% of men and 40% of women on antihypertensive treatment had a controlled blood pressure (i.e. < 160/95) at the time of the survey.

These findings are to be set in relation with the high incidence rates of cardiovascular diseases in the Seychelles, among which cerebrovascular disease incidence being one of the highest in the world. There is therefore an urgent need to stimulate all further diagnostic and treatment procedures to better control hypertension, presently a major health issue in the Seychelles.

#### *Detection of hypertension*

Around one third of the population aged 35–64 was found to have high blood pressure from which one half of men and one third of women being unaware of this condition.

**Population based screening.** Routine yearly screening for hypertension should be initiated early in life in order to detect and treat the disease from age 20, thus reducing the incidence of complications. People should be made aware of the necessity for regular blood pressure (BP) checks. One suggestion was that a bus with trained staff should call at each district regularly on specific dates and that people should be made aware of this service through the media. Another suggestion was that all subjects should be screened for hypertension when they visit the clinics for any other reason, since Seychellois adult population tend to frequently use this free of charge health service. Screening should also be done at school for students aged 15 years and over. This will not only be a good way to detect hypertension early, but also be a good opportunity to prompt them into leading a healthier lifestyle.

**High risk subjects.** Women who are hypertensive during pregnancy should be regularly followed up for hypertension after delivery. Relatives of hypertensive individuals should be systematically screened for hypertension because of the familial tendency to develop hypertension.

**Devices.** Mercury sphygmomanometers should be used for screening purpose because of better reliability. As a rule, mercury sphygmomanometer should be used in the clinics and on the wards. Aneroid devices should be reserved for blood pressure monitoring in theater, in medical kits for home visiting or for patient's self monitoring. BP levels are to be measured and recorded to the nearest 2 mm Hg. The patient should be in a sitting position, with the arm comfortably lying on a table, at the level of the heart. It was stressed that a correct cuff is used (i.e. standard or big

cuff), as standard cuffs may over-estimate BP in people with big arms. At least 2 BP measurements are necessary at each visit; the second measurement should be done after a 10 minute rest. At least 3 different BP checks on different days should be done within a 3 month interval before hypertension is diagnosed, unless there is clinical evidence to treat the subject earlier. More values are even required over a longer period (6 months) for patients showing borderline BP values, in order to confirm the diagnosis of hypertension.

**Normal values.** Hypertension is defined according to the following criteria:

- Under age of 40: 140/90
- Between age of 40 to 70: 160/95
- Above age of 70: 180/95

#### *Evaluation of hypertensive subjects*

**Clinical assessment.** Patients with diastolic BP between 90 and 150 mm Hg; Na, K, creatinine, glycemia. Lipids should be done especially if hypertension is associated with other cardiovascular risk factors.

Patients with a diastolic BP greater than 105 mm Hg; same tests, in addition to an electrocardiogram (ECG) and a chest X-ray. An intravenous pyelogram or a renal ultrasound (assessment of an unilateral small kidney) may be performed to rule out a reno-vascular cause to hypertension, especially if hypertension does not respond to treatment, and in young people (e.g. under 40). As a general rule, control of other risk factors need to be achieved in hypertensive patients.

**Diabetes.** Hypertension is frequent in diabetics and is to be treated more aggressively because of particularly deleterious vascular complications of hypertension in diabetics. The aim of antihypertensive treatment should be to lower diastolic BP to a level lower than 90. Appropriate drugs include beta-blockers, calcium antagonists and especially ACE inhibitors as ACE inhibitors have been proved to reduce proteinuria, (which may reduce the progression of the underlying nephropathy). Thiazide diuretics should be used with caution because of their tendency to accelerate hyperglycemia and other possible metabolic disturbances. The anti-aldosterone spironolactone has no deleterious effect on glucose and lipid metabolism and may therefore be useful in diabetics.

**Smoking.** Smoking should be firmly prohibited.

**Obesity.** Obesity is strongly associated with hypertension. Obese hypertensives should therefore

be encouraged to reduce their weight. Moreover, they should take regular exercise, which not only helps to reduce weight but has also been proved to reduce blood pressure (when practised 30 min for at least 3 times a week).

*Pregnancy.* Methyldopa and beta-blockers are advisable. Labetolol is of special interest because of its alpha- and beta-blocker properties.

*Stroke.* Hypertensive patients with acute stroke should not be overtreated during the first 24 hours, as low blood pressure may aggravate the cerebral ischaemia.

#### *Non pharmacological therapy*

Reducing obesity and practising regular physical exercise help to control high blood pressure. Consumption of fruit ensure an adequate intake of potassium which may help to reduce blood pressure. Avoiding excess use of salt is advisable. Smoking should be stopped. Excess alcohol consumption may cause hypertension and should therefore be avoided.

#### *Drug therapy*

*Choice of drugs.* In general, initial treatment should be started with diuretics or beta-blockers in monotherapy. Other effective monotherapies are now available as first step therapy but are still expensive and should be used in appropriate specific clinical situations. When combinations are to be used, diuretics should be part of them, because of their low cost and proven effectiveness in any possible combination.

Beta-blockers with an intrinsic sympathicomimetic activity may be useful in bradycardic patients and should be available in Seychelles.

ACE inhibitors are powerful drugs. They are particularly useful in diabetics, as they reduce proteinuria. Combination with diuretics is very effective and has been also proven to prolong life of patients with congestive heart failure and allow blood pressure control in patients with refractory hypertension.

Calcium antagonists, particularly nifedipine, is useful in the treatment of hypertensive crisis. Slow-release formulation should be used for this indication to avoid too abrupt decrease of BP, (especially in patients with acute stroke). They are often effective in patients with refractory hypertension, in combination with beta-blockers.

Methyldopa may have disagreeable side effects (neurologic troubles, impotence) which may be found only through a thorough examination of the patient. It is not recommended for patients with orthostatic hypotension. It should be interrupted many days in advance when urine is collected for assessing pheochromocytoma diagnosis, because of interference with the analysis. Because of its low price and demonstrated effectiveness, this drug may still be recommended.

In patients with refractory hypertension, any combination of drugs may be used. In patients who still do not respond to therapy, it may be advisable to test compliance to the prescribed drugs. A way to do it is to give to the patient triamterene (a potassium-sparing diuretic) as a part of the treatment. The compliance to this treatment is then easily assessed by checking the presence of a fluorescent metabolite of triamterene in the urine, using a special but inexpensive light device (available in the Seychelles).