Hypertension and raised serum lipids

About 30% of patients seen in our lipid clinic during 1976 had raised blood pressure, and many patients attending the hypertension clinic have hyperlipidaemia. This apparent association between hypertension and hyperlipidaemia could have arisen because hypertensives tend to have lipid concentrations measured more frequently than people with no risk factors for vascular disease, or might have been due to treatment. We examined the association further by studying fasting lipid, glucose, and insulin concentrations in untreated hypertensives and in controls.

Patients, methods, and results

Untreated subjects with raised arterial pressure were sought from among the staff of the Atomic Energy Research Establishment at Harwell and from two general practices. Blood pressures were measured by the London School of Hygiene sphygmomanometer. Some 89 subjects (71 men, 18 women; aged 30-67) whose diastolic pressure exceeded 100 mm Hg on each of four occasions were arbitrarily designated to have hypertension. None had received antihypertensives. Age- and sex-matched controls were selected for each hypertensive from among those with diastolic pressures below 90 mm. No women were taking oral contraceptives.

Weight, height, and skinfold thickness (mean of mid-triceps, subscapular, and anterior superior iliac spine) measurements were recorded. Measurements of cholesterol, triglyceride, glucose, and insulin concentrations and lipoprotein electrophoresis were carried out on a fasting blood sample.¹ The results are shown in the table. By using arbitrary upper limits of normal (cholesterol > 7.3 mmol/l (282 mg/100 ml) and triglyceride > 2.03 mmol/l (177 mg/100 ml)), and electrophoresis to confirm the type of lipoprotein abnormality, 41% of hypertensives and 21% of controls had hyperlipoproteinaemia: 9% of the hypertensives had type IIa, 6% IIb, and 26% IV. Among the controls 7% had type IIa, 3% IIb, and 11% IV.

Fasting cholesterol, triglyceride, glucose, and insulin concentrations in hypertensives and controls

	Hypertensives* (89) (mean : SEM)	Controls* (89) (mean : SEM)	P†
Weight (kg)	77.3 : 1.7	72.6 : 1.1	<0.05
Height (cm)	170.8 : 0.8	170.1 : 0.8	NS
Mean of three measurements of skinfold thickness (mm)	16.9 : 0.7	15.3 : 0.5	NS
Cholesterol (mmol/l)	5.9 : 0.2	5.8 : 0.1	NS
Triglyceride (mmol/l)	1.70 : 0.07	1.41 : 0.06	<0.01
Glucose (mmol/l)	5.1 : 0.08	4.8 : 0.08	<0.05
Insulin (μU/ml)	5.27 : 0.3	4.37 : 0.3	<0.05

*Mean (: SEM) systolic blood pressure for hypertensives 162 (: 2.1) and for controls 123 (: 1.3). Diastolic pressures were 104 (: 0.9) and 78 (: 1.4), respectively. †According to Student's unpaired *t* test.

Conversion: SI to traditional units—Cholesterol: 1 mmol/l $\approx$ 38.6 mg/100 ml. Triglyceride: 1 mmol/l $\approx$ 88.5 mg/100 ml. Glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

A low-grade, but significant association was present between body weight and both glucose and insulin concentrations when considering hypertensives and controls separately and together ($r \approx 0.3$, *P* values ranging from 0.01 to 0.001). A similar association was present when considering Quetelet's index ($\frac{\text{weight}}{\text{height}^2}$) rather than weight. A significant association between body weight (or Quetelet's index) and triglyceride concentrations was present when considering cases and controls together ($r = 0.2$, $P < 0.01$). Within arbitrarily defined groups determined by ranges of Quetelet's index, triglyceride concentrations were significantly higher among hypertensives than controls. For example, the mean triglyceride concentration for the 21 hypertensives with Quetelet's index 2.0 to 2.4 was 1.59 mmol/l (141 mg/100 ml) and for the 42 controls in this range 1.32 mmol/l (117 mg/100 ml).

Discussion

Raised concentrations of triglyceride and insulin and glucose intolerance are often seen in association with obesity, and hyperinsulinism and glucose intolerance have been reported in hypertensives.² We are still uncertain about the causal sequence, though obesity is often associated with insulin resistance and weight reduction tends to reverse these abnormalities.³ Obesity is also associated with

raised blood pressure. Our data suggest that obesity may be the common factor which explains the excessive prevalence of raised lipid concentrations among patients with hypertension, but there is some evidence also of an effect of raised blood pressure on triglyceride concentrations which is independent of obesity. These results are also relevant to earlier work claiming that raised triglyceride concentrations in treated hypertensives could be attributed to the hypertriglyceridaemic effect of thiazide diuretics.⁴ Reciprocal relationships between the data cannot be examined in detail, but the results underline the importance of searching for other factors that increase the risk of vascular disease in hypertensive patients. Risk factors for ischaemic heart disease appear to exert a synergistic effect.⁵ The combination of hypertriglyceridaemia and hyperglycaemia may therefore greatly increase the risk of vascular disease in a hypertensive patient.

In view of the increased frequency of these metabolic abnormalities among hypertensives and their probable reversal by dietary modification,³ it would seem prudent to measure lipid concentrations of all patients with a raised blood pressure and to pay more attention to achieving ideal body weight.

¹ Mann, J I, and Thorogood, M, *British Heart Journal*, 1975, **37**, 790.

² Kohner, E M, *et al*, *Lancet*, 1971, **1**, 986.

³ Butterfield, W J, Hanley, T, and Wichelow, M J, *Metabolism*, 1965, **14**, 851.

⁴ Johnson, B, *et al*, *Clinical Science and Molecular Medicine*, 1974, **47**, 9P.

⁵ Mann, J I, *et al*, *British Medical Journal*, 1975, **1**, 241.

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Lithium used with a diuretic

The combined use of lithium salts and diuretics has been said to be contraindicated.^{1,2} Nevertheless, there are occasions when the need arises to give a diuretic to a manic-depressive patient who is on long-term lithium treatment. This might be for coincidental disease such as hypertension,³ or to control lithium-induced effects, such as the diabetes-insipidus-like state it occasionally causes. The dangers of prescribing lithium salts and diuretics together in states such as these have been emphasised,⁴ particularly as the serum lithium concentration rises as the urine volume falls.⁵

This case history shows the successful long-term treatment of a manic-depressive patient with lithium carbonate, and the eventual development and treatment of a diabetes-insipidus-like state.

Case report

A woman, now aged 64, was first admitted with depression in 1955. She had two further depressive episodes in 1955 and 1956, and in the latter year a further period of six months in hospital, during which she went through two manic-depressive cycles. Between 1955 and 1964 she had ten hospital admissions with eight depressive and two manic episodes. In 1963 and 1964 she was treated as an outpatient with a regular cycle of hypomania and depression, each phase lasting 24-37 days. In June 1964 she was started on lithium carbonate, 250 mg four times daily, and her serum lithium concentration has remained between 0.8 and 1.2 mmol/l (0.6-0.83 mg/100 ml) throughout the whole of her treatment. She had remained well-controlled from 1964 until 1975, when she started to complain of thirst and polyuria, and began to have mild mood swings similar to those before 1964. Nevertheless, these were of low amplitude and did not require hospital admission.

In October 1976 she was admitted to hospital and started on a diuretic, in an attempt to control her polyuria. On admission, she had urinary frequency of the order of day/night = 15-20/5-7. Her psychiatric state was stable. She was started on bendrofluzide 5 mg daily and potassium chloride 600 mg (Slow-K) twice daily, in addition to her lithium carbonate, 250 mg

Serum lithium concentrations in relation to treatment.

Conversion: SI to traditional units—Lithium: 1 mmol/l $\approx$ 0.69 mg/100 ml.

four times daily. Serum lithium concentrations were monitored over the next few weeks (see figure). In the three days after starting the diuretic the concentrations rose steadily to 1.7 mmol/l (1.18 mg/100 ml), at which level her lithium intake was halved. After this the concentrations showed a slow decline and by day 28 she was back to her original dose of lithium carbonate. On day 36 she was discharged home and since then over a four-month follow-up her lithium concentrations have remained within the therapeutic range. She has improved symptomatically in that her urinary frequency has decreased to day/night = 3-4/0-2 and her mood has remained stable.

Comment

In a patient who is well-controlled on long-term lithium the development of a state requiring diuretic treatment presents a problem. In the case reported here bendrofluazide was successfully combined with lithium to control this patient's diabetes-insipidus-like state. Nevertheless, a clinician prescribing a diuretic to a patient on long-term lithium should bear in mind the following: (1) fairly close laboratory control of the serum lithium concentration is required, possibly as an inpatient; (2) an immediate increase in the serum lithium concentration should be anticipated, thus avoiding toxic effects which might make the patient lose confidence in the treatment³; (3) restabilisation may be at a lower lithium dose,⁵ or, as in this case, at the original dose level.

¹ Kerry, R J, in *Lithium Research and Therapy*, ed F N Johnson, p 162. London, Academic Press, 1975.

² Weinstein, M R, and Goldfield, MD, in *Lithium Research and Therapy*, ed F N Johnson, p 259. London, Academic Press, 1975.

³ Macfie, A C, *British Medical Journal*, 1975, **1**, 516.

⁴ MacNeil, S, et al, *Lancet*, 1975, **1**, 1295.

⁵ Levy, S T, Forrest, J N, Heninger, MD, *American Journal of Psychiatry*, 1973, **130**, 1014.

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Assessment of sympathetic overactivity in tetanus

Overactivity of the sympathetic nervous system is thought to contribute to the still considerable mortality from severe tetanus,¹ and improved results have been reported after the use of adrenergic blocking agents.² Unless these agents are to be given to all patients with tetanus prophylactically, however, sympathetic activity will have to be monitored so that adrenergic block can be induced at an appropriate time. Plasma and urinary catecholamine concentrations, if measured at all, are usually measured in retrospect so that the results are not available to guide treatment on the hour-to-hour basis necessary in severe tetanus.

Various clinical indicators of sympathetic activity have been proposed, including increases in (a) the level and variability of the blood pressure, (b) the blood pressure response to aspiration of secretions from the trachea (tracheal suction),³ and (c) heart rate.² These clinical indices were compared with serial measurements of plasma catecholamine concentrations during severe tetanus in a 29-year-old farmer.

Methods and results

Blood pressure was measured every half hour by nursing staff using a standard cuff and mercury sphygmomanometer. The mean blood pressure was calculated from all the observations obtained within 24 hours and the blood pressure variability was calculated by averaging the absolute difference between successive readings of systolic pressure.³ A mean heart rate was calculated from corresponding readings. The increase in blood pressure during tracheal suction was the difference between the presuction systolic pressure and the highest systolic level recorded during or within one minute of the procedure.³ Blood samples were collected at least once a day before suction and within 30 seconds of the recommencement of artificial ventilation. Plasma adrenaline and noradrenaline concentrations were estimated using the radioenzymatic method of Hörtnagl et al.⁴

Until the eighth day after the onset of trismus, plasma catecholamine concentrations were relatively normal and the cardiovascular system fairly stable (see table). On the eighth day, despite unchanged treatment and in the absence of any indication of infection, there were significant increases in heart rate, mean blood pressure (largely due to an increase in diastolic pressure), and plasma catecholamine concentrations. Both adrenaline and noradrenaline concentrations reached abnormally high values. Blood pressure variability was slight throughout the illness and changes in pressure and catecholamine concentrations induced by tracheal suction were minimal. Treatment with the beta-adrenergic blocking agent propranolol (40 mg/8 h) was started because of the tachycardia, and no further plasma catecholamine estimations were carried out. The patient's subsequent course was uneventful and he recovered fully after three weeks of artificial ventilation.

Assessment of sympathetic activity in a 29-year-old man with severe tetanus

Day after onset of trismus:	3	4	5	6	7	8
Curare dosage (mg/24 h)	330	270	300	330	360	330
Average mean blood pressure (mm Hg)	85	86	96	88	90	102
Blood pressure variability (average absolute systolic difference) (mm Hg)	9	12	14	8	7	8
Average heart rate	71	84	82	83		
Resting plasma concentrations:						
Adrenaline (nmol/l)	0.71	0.44	1.2	1.8	2.46	9.01
Noradrenaline (nmol/l)	1.71	1.3	2.72	2.01	1.83	5.50
Responses to tracheal suction:						
Systolic blood pressure (mm Hg)	+10	+10	+20	+13	+11	+13
Adrenaline (nmol/l)	-0.05	+0.93	+0.87	+0.33	+0.33	0.00
Noradrenaline (nmol/l)	+0.19	+0.65	+0.12	+0.18	+0.71	+1.24

Conversion: SI to traditional units—Adrenaline: 1 nmol/l $\approx$ 183 ng/l. Noradrenaline: 1 nmol/l $\approx$ 169 ng/l.

Comment

Our experience with this patient suggests that the appearance of an unexplained tachycardia in a patient with tetanus shows that there is an increase in sympathetic activity and that careful monitoring of the heart rate may indicate when adrenergic blocking agents can be introduced to lessen the possibility of catecholamine-induced myocardial damage.⁵

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¹ Kerr, J H, et al, *Lancet*, 1968, **2**, 236.

² Lazar, M, *Schweizerische medizinische Wochenschrift*, 1970, **100**, 1486.

³ Kerr, J H, in *Third International Conference on Tetanus*, p 128. Special Scientific Publication No 253. Washington, Pan American Health Organisation, 1972.

⁴ Hörtnagl, H, et al, *British Journal of Clinical Pharmacology*. In press.

⁵ Rose, A G, *Suid Afrikaanse Mediese Tydskrif*, 1974, **64**, 1285.

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