our laboratory (mean 2060 mU/l; range 450-4050 mU/l). No patient had evidence of a prolactin secreting macroadenoma on computed tomography. No other endocrine abnormality was found after full endocrine assessment, and treatment was initiated with lysuride, the starting dose of 0.1 mg being taken at night in the middle of a snack. The dose of lysuride was then gradually increased by 0.1 mg in the middle of food until normoprolactinaemia was achieved, unacceptable side effects ensued, or a daily dose of 1.2 mg was reached. Patients seeking pregnancy were instructed to stop treatment within 48 hours of missing a period. Lysuride was the first dopamine agonist used in 22 patients, and in two it was introduced because of unacceptable side effects with bromocriptine. Treatment was continued for one to 40 months (mean 5.4 months).

In 23 cases lysuride (mean dose 0.4 mg daily; range 0.1-1.2 mg/day) appreciably reduced the serum prolactin concentration, values becoming normal in eight cases (figure). Symptoms and signs of hyperprolactinaemia improved in

Change in serum prolactin concentrations in 24 women treated with lysuride.
●-----● Patient with rapidly expanding pituitary lesion.

parallel with the fall in prolactin concentrations. In the remaining case failure to suppress was associated with a rapidly expanding pituitary lesion, which necessitated surgical intervention. Of 13 patients presenting with primary or secondary infertility, five became pregnant while receiving treatment. Gestation was uneventful and all babies were normal. In three cases lysuride was successfully reintroduced after delivery in order to suppress lactation. Of the eight patients who failed to conceive while taking lysuride, three had ovulation confirmed by serial progesterone estimations. The two patients intolerant of bromocriptine were successfully transferred to lysuride with return to normal of their serum prolactin values.

Sixteen patients (67%) given lysuride stopped treatment within one to four months before reaching a dose sufficient to lower prolactin concentrations to normal because of unacceptable side effects. In the whole series these included nausea (16 cases), drowsiness (17), dizziness (14), depression (12), lethargy (four), constipation (two), bloating (one), and headache (one).

Comment

These data confirm that lysuride is an effective prolactin lowering agent in hyperprolactinaemia, leading to arrest of galactorrhoea, resumption of ovulatory cycles, and hence fertility. The high incidence of side effects encountered in this study, however, which led to withdrawal of the drug in 16 of the 24 patients before an optimum dose was reached, appears to be a substantial disadvantage. Drowsiness was particularly common and may relate to the antiserotonergic properties of the drug. Other side effects were similar to those associated with bromocriptine. Interestingly, however, the two patients who had been intolerant of bromocriptine subsequently successfully changed to lysuride. Intolerance of one drug may not therefore necessarily lead to intolerance to another dopamine agonist.^{2,3} Structural analogues of lysuride, particularly transdihydrolysuride, may offer advantages over the parent compound, and a recent report suggests that this compound may be comparatively free of side effects.⁴

In conclusion, our findings confirm the efficacy and safety of lysuride as a prolactin lowering agent in hyperprolactinaemic hypogonadism and infertility. In view of the high occurrence of side effects we suggest that it represents a second line treatment in this condition but may be useful in patients intolerant of bromocriptine.

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Does atenolol have an effect on calcium metabolism?

Hypercalcaemia is often an incidental finding during biochemical investigation, being found in 1.1% of the general population¹ and 3.6% of patients in hospital.² The most common cause is primary hyperparathyroidism. Ten per cent of patients with sarcoidosis have hypercalcaemia, but hypercalciuria is much more common.³ It is therefore possible that β antagonists may be given to some patients with unsuspected disturbances in their calcium metabolism. I report on the effects of the β_1 antagonist atenolol on the calcium balance of two patients.

Case reports

Case 1—A 61 year old man with angina was treated with atenolol 100 mg/day. He had been under investigation for two years for mild but persistent asymptomatic hypercalcaemia, which was thought to be due to primary hyperparathyroidism. He was not taking any other drugs.

Case 2—A 51 year old woman with diabetes controlled by diet and with a diagnosis of sarcoidosis was prescribed atenolol 100 mg/day for hypertension. She was not taking any other drugs. After three weeks atenolol was stopped because of side effects.

The table shows the results of measurements of plasma concentration and urinary excretion of calcium and phosphate in both cases.

Comment

In both these cases atenolol caused decreases in plasma calcium concentration and urinary calcium excretion and an increase in plasma phosphate concentration. These changes appeared to be reversible in the patient studied after withdrawal of atenolol (case 2) and have not previously been reported.

It is not known how atenolol caused these changes. The non-selective β antagonist propranolol can reduce basal parathyroid hormone concentrations,⁴ and it has been successful in treating a case of hyperparathyroidism.⁵ Different mechanisms are responsible for hypercalcaemia in hyperparathyroidism and in sarcoidosis, which suggests that atenolol may have more than one action.

The recent observation that untreated asymptomatic hypercalcaemia constitutes a risk factor for premature death suggests that further studies on the effects of atenolol on calcium metabolism are indicated.¹

In summary, the results show that atenolol may have an effect on calcium and phosphate metabolism. Although the mechanisms of action remain unknown, in cases where plasma concentration and urinary excretion of calcium and phosphate are measured the effects of any concomitant use of β antagonists must be considered.

I am grateful to Dr W B Thomson for allowing me to report these cases.

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Plasma concentration and urinary excretion of calcium and phosphate before and after treatment with atenolol. (Normal values given in parentheses)

	Plasma concentration		24 Hour urinary excretion	
	Corrected calcium (mmol/l)	Phosphate (mmol/l)	Calcium (mmol/24 h)	Phosphate (mmol/24 h)
Normal range	2.12-2.62	0.8-1.45	2.5-7.5	15-40
<i>Case 1</i>				
Before treatment	2.77	0.67	16.2	29.9
After treatment for one week with atenolol 100 mg	2.65	0.95	11.2	22.6
<i>Case 2</i>				
Before treatment	2.43	1.12	12.5	27.9
After 10 days' treatment with atenolol 100 mg	2.27	1.45	8.6	35.9
Seven days after stopping atenolol	2.37	1.12	17.4	42.5

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Successful cadaveric renal transplantation from a donor who died of cyanide poisoning

Most kidneys used for cadaveric renal transplantation come from victims of fatal head injuries or cerebrovascular accidents. Patients who suffer other causes of irreversible brain death should also be considered as potential donors, even though they may at first appear unsuitable. We report a successful renal transplantation from a young man who died of cyanide poisoning.

Case report

A 24 year old man was cleaning a vat containing silver cyanide when he was overcome by fumes and collapsed into several inches of slurry. On arrival in the casualty department 15 minutes later he was unresponsive, apnoeic, and hypotensive. His skin was brick red, which is compatible with cyanide toxicity. After resuscitation 300 mg of dicobalt edetate was given at one, two, three, and seven minutes. Spontaneous respiration resumed, although he remained haemodynamically unstable. Twenty four hours after admission urine output and blood pressure were satisfactory. Electroencephalograms obtained at this time and 48 hours after admission showed no cerebral activity. As he remained haemodynamically stable and blood cyanide values were rapidly falling to non-toxic concentrations (table) the possibility of organ donation was considered. The criteria for brain death were satisfied four days after admission, and shortly afterwards donor nephrectomy was undertaken. Serum urea and creatinine concentrations were 10.7 mmol/l and 146 µmol/l respectively on the day the kidneys were removed. Urine output during the 24 hours before the operation was 2883 ml.

The recipients were a suitably matched 43 year old man and 52 year old woman. Both kidneys were perfused immediately after removal with ice cold Marshall's solution and transplanted within 24 hours. Renal transplant biopsy samples taken

Blood cyanide concentrations

	Day of admission			Day 1			Day 2
	Time: 1600	1800	1900	0400	0900	1400	0900
Blood cyanide (µmol/l)	804	819	607	23	15	15	8

30 minutes after transplantation showed acute moderate tubular damage only. Cyclosporin A (5 mg/kg daily intravenously for 48 hours followed by 15 mg/kg daily by mouth) and prednisolone (20 mg daily) were used as immunosuppressive agents. Neither kidney underwent a primary diuresis, necessitating maintenance dialysis for 11 days. Renal transplant biopsy samples taken on the ninth postoperative day showed acute mild to moderate tubular damage. Mild cellular rejection in one of the kidneys was treated with 200 mg of oral prednisolone for three days. Twenty one days after transplantation creatinine clearances were 33.4 ml/min and 36.7 ml/min. Six months after transplantation the recipients remained well; urea and creatinine concentrations were 9.7 mmol/l and 243 µmol/l and 20.9 mmol/l and 167 µmol/l, respectively.

Comment

We believe that this is the first report of successful organ transplantation from a donor dying of cyanide poisoning. Cyanides are rapidly absorbed by all tissues, particularly the lungs.¹ The cyanide ion combines intracellularly with the ferric ion in cytochrome oxidase, forming an inactive complex which blocks the electron transport system and cellular utilisation of oxygen. In sufficient dosage death is caused by respiratory failure because the nerve cells of the respiratory centre are particularly vulnerable to lack of oxygen. Blood cyanide concentrations of 8 µmol/l indicate substantial intoxication and a value of more than 38 µmol/l is usually fatal.²

It has been suggested that if cardiac output and respiration can be maintained, up to half of the cyanide in the circulation can be metabolised within one hour of exposure.³ Eighty per cent of cyanide is detoxified by the liver enzyme rhodanase to non-toxic thiocyanate, which is excreted in the urine.⁴ The high concentration of cyanide recorded during the first three hours in this case probably indicate continuing enteric or percutaneous absorption. Despite these values the patient's kidneys were successfully used for transplantation. This suggests that although victims of fatal cyanide poisoning suffer irreversible brain injury as a result of depression of the respiratory centre, other organs are only reversibly damaged and may be considered for transplantation. Careful evaluation of every patient dying of irreversible brain injury should increase the number of potential donors.

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