SHORT REPORTS

Dopamine pretreatment in unstable kidney donors

Most kidneys that never function after transplantation are probably damaged by ischaemia, and a prolonged period of hypotension in the donor before death is almost certainly a contributory factor. Carroll *et al*[1] showed that avoiding such hypotension improves the quality of cadaveric kidneys. Often when the donating hospital contacts the transplant team a prolonged period of hypotension associated with oliguria may already have occurred, or it may occur while preparation is being made for donor nephrectomy. This paper reports on the use of dopamine (Intropin) in resuscitating the "unstable" kidney donor.

Patients, methods, and results

An unstable donor is defined as a patient who, despite adequate hydration, has persistent hypotension associated with oliguria. We have been notified recently of 15 such potential donors, in whom, despite intravenous fluids and diuretics, it has been impossible to maintain an adequate blood pressure and urine output. After ascertaining that the criteria of brain death had been satisfied and consent for donor nephrectomy obtained from the next of kin, our policy was to recommend to the team responsible for the primary care of the patient that an infusion of dopamine be started, initially at a rate of 2 μg/kg/min, and the dose titrated against the response in the patient's blood pressure. Before donor nephrectomy the following premedication was given intravenously to all patients: methylprednisolone 1 g; frusemide 120 mg; chlorpromazine 50 mg; phenoxybenzamine 100 mg; and heparin 10 000 units. Immediately before stopping ventilation 5 mg of phentolamine was given intravenously. After cardiac arrest the kidneys were initially perfused with Sach's solution at 4°C via the aorta, and after removal they were perfused with a modified plasma protein fraction[2] on a Gambro perfusion apparatus until transplantation. All 15 donors responded with a rise in blood pressure and urine output. The time elapsing before an increased urine output occurred varied from 30 minutes to 12 hours. In every case the urine output and blood pressure had increased before the premedication. The table shows the systolic blood pressures and urine outputs before and after dopamine was given. We transplanted 30 kidneys from these donors in our unit. Seventeen functioned immediately, no period of postoperative dialysis being required. Ten showed delayed function—that is, intermittent dialysis was required until the transplanted kidney could maintain a progressive daily increase in creatinine clearance. The three remaining kidneys never functioned, one owing to technical difficulties resulting in graft thrombosis within 24 hours after the operation, another to graft thrombosis without evidence of rejection, and the third to acute tubular necrosis complicated by severe irreversible acute rejection.

Mean systolic blood pressures and urine outputs before and after treatment with dopamine, and mean duration of hypotension

	Systolic blood pressure (mm Hg)	Urine output (ml/h)
Before dopamine (mean (range) of lowest value recorded)	55 (30–100)	6 (0–15)
After dopamine (mean (range) of average value recorded)	135 (100–220)	175 (50–500)
Mean duration of hypotension (and range) (min)	286 (30–780)	

Comment

Dopamine increases systolic and pulse pressures,[3] dilates the renal vasculature, and increases renal plasma flow and the glomerular filtration rate.[4] Talley *et al*[5] reported that dopamine, combined with diuretics but not alone, successfully reversed acute renal failure, resulting in an increased urine flow and a reduction in blood urea nitrogen and serum creatinine concentrations to preoliguric values. In an uncontrolled study such as this, in which we eventually obtained 27 functioning kidneys, it is impossible to predict what would have happened to the donors and the kidneys had dopamine not been used. Almost certainly several donors would have been refused owing to long periods of hypotension and oliguria, and in those in whom hypotension was profound cardiac arrest might possibly have occurred before the transplant team arrived.

On the basis of these results we suggest that in an unstable donor dopamine should be administered to improve renal function. Further, we wish to emphasise that donating hospitals should not be deterred from informing the local transplant team of a potential donor even when the patient has had a prolonged period of hypotension and oliguria, since treatment with dopamine may result in two viable kidneys for transplantation.

We gratefully acknowledge the help received from consultants in the Manchester region who have informed us of potential donors, and thank Mr Barry Chapman for technical help.

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[2] Johnson, R W G, *et al*, *Transplantation*, 1972, **13**, 270.
[3] Goldberg, L I, *Pharmacological Reviews*, 1972, **24**, 1.
[4] McDonald, R H, jr, *Journal of Clinical Investigation*, 1964, **43**, 1116.
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Hypercalcaemia induced by oestrogen withdrawal in vitamin D-treated hypoparathyroidism

Low serum calcium values and tetany have been described in a hypoparathyroid patient treated with oestrogens.[1] We report a patient with hypoparathyroidism treated with dihydrotachysterol (DHT) who developed hypercalcaemia after ceasing to take an oral contraceptive at the menopause.

Case report

A 52-year-old woman was admitted to hospital because of increasing weakness. She had suffered from hypoparathyroidism since a complete thyroidectomy 15 years previously. Since then she had been taking thyroid extract 100 mg/day, DHT 1 mg/day, and Stederil-d (0·25 mg norgestrel, 0·05 mg ethinyloestradiol). Serum calcium concentration was maintained at about 2·33 mmol/l (9·3 mg/100 ml). She stopped taking Stederil-d on her own accord at the age of 51. Thereafter she became increasingly asthenic. Her body weight remained stable. On examination her general condition was good. Serum calcium concentration was 3·0 mmol/l (12 mg/100 ml) and phosphate 1·29 mmol/l (4 mg/100 ml). Thyroid replacement treatment was satisfactory, judged by normal concentrations of plasma TSH, T3RIA, and T4RIA. Plasma FSH, LH, and oestradiol concentrations were of the postmenopausal type. Dietary calcium intake, sodium excretion, and exposure to sunlight had not altered over the period that she became hypercalcaemic. The preparation of DHT used and its dose were unchanged. Endogenous creatinine clearance was 60 ml/min. Her serum calcium concentration fell gradually when DHT was temporarily stopped and was maintained at about 2·30 mmol/l (9·2 mg/100 ml) with DHT 0·35 mg/day. Plasma parathyroid hormone was undetectable even after a fall in serum calcium to 1·75 mmol/l (7 mg/100 ml) had been induced by infusion of sodium edetate.

In order further to evaluate the effect of oestrogens on calcium metabolism ethinyloestradiol 0·10 mg/day was given for 40 days in addition to thyroid extract and DHT. During this time the serum calcium fell from 2·30 mmol/l to 1·68 mmol/l (6·7 mg/100 ml), with a simultaneous fall in urinary calcium and hydroxyproline excretion (table). Calcium absorption, as measured by a slight modification of the method of Rinsler *et al*,[2] was reduced one month after starting oestrogens. As oestrogen was stopped tetany developed and DHT had to be increased.

Comment

Our data clearly show that oestrogens can cause wide variations in serum calcium concentrations in hypoparathyroidism. First the stopping of oral contraception and the menopause resulted in vitamin

Effect of oestrogen (ethinyloestradiol) on calcium metabolism in patient with hypoparathyroidism treated with dihydrotachysterol (DHT)

	24 April	16 May	19 May	5 June	12 June	21 June	22 June	29 June	10 July	17 July	24 July	31 July	4 Sept
	DHT												
	0·35 mg/day								0·5 mg/day		0·37 mg/day		
			Ethinyloestradiol (0·1mg/day)										
Serum Ca (mmol/l)	2·33	2·33	2·30	2·05	2·03	1·80	1·78	1·68	1·63	1·93	2·13	2·33	2·35
Serum P (mmol/l)	1·26	1·26	1·45	1·16	1·32	1·58	1·45	1·58	1·68	1·65	1·52	1·32	1·23
Urinary Ca/creat $\left(\frac{mol}{mol}\right)$		0·62	0·71	0·57	0·28	0·14	0·06			0·31	0·23	0·40	0·71
Urinary OHP/creat $\left(\frac{mol}{mol}\right)$		0·028	0·034			0·018	0·014			0·029	0·020	0·023	
Calcium absorption (%) (n = 40% ± 13)		40					25						

Conversion: SI to traditional units—Calcium: 1 mmol/l ≈ 4 mg/100 ml. Phosphate: 1 mmol/l ≈ 3·09 mg/100 ml.

D intoxication. Giving ethinyloestradiol, on the other hand, caused a dramatic fall in a previously well stabilised serum calcium concentration. The hypocalcaemia might have been due to decreased bone resorption, as suggested by the fall in hydroxyproline excretion. Oestrogens could have antagonised DHT-induced bone resorption, since this is the case with other vitamin D metabolites.[3] The osteolytic effect of parathyroid hormone is not inhibited in hypoparathyroidism. On the other hand, a direct inhibitory effect of oestrogens on bone resorption cannot be excluded, as suggested by studies in rats.[4] The decrease in intestinal calcium absorption under oestrogens is at variance with the increase noted in postmenopausal women treated with oestrogen.[5] But in their case secondary hyperparathyroidism is thought to cause the increased absorption. A direct inhibitory effect of oestrogens on calcium absorption may therefore be considered.

Since oestrogens are often spontaneously taken or discontinued by patients themselves those with hypoparathyroidism should be warned of the consequences. Moreover, serum calcium concentrations should be monitored during the menopause in patients with hypoparathyroidism and vitamin D treatment adapted accordingly.

[1] Burckhardt, P, *et al*, *Hormone Research*, 1975, **6**, 321.
[2] Rinsler, M D, *et al*, in *Radioaktive Isotope in Klinik und Forschung*, ed K Fellinger and R Höffer, vol 4, p 19. Munich and Berlin, Urban and Schwarzenberg, 1960.
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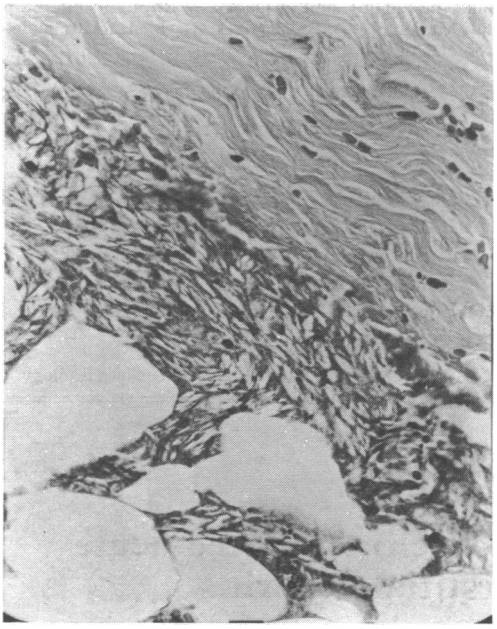
Probable toxic necrosis after prolonged fluspirilene administration

Nursing staff at one psychiatric hospital have had no difficulty in administering two of the three main long-acting intramuscular antipsychotic drugs—namely, fluphenazine decanoate and flupenthixol decanoate—both of which are held in a vegetable oil base. The third, fluspirilene (Redeptin), which has been commercially available for over three years, is held in aqueous suspension, 2 mg/ml; injections are given once-weekly. The maintenance dose in schizophrenia varies widely but should not exceed 20 mg/week. In recent months nurses have reported that in several patients increased pressure has been needed to give the injection and lumps have appeared at injection sites. We decided to examine the problem in more detail.



Crystalline clefts between connective tissue and fat at fluspirilene injection site. (H and E. ×275.)

Methods and results

All patients receiving fluspirilene under the care of two consultant psychiatrists were reviewed; there were 15 women and nine men. In eight cases deep subcutaneous lumps up to 9 × 3 cm were palpable at the injection sites, the upper and outer quadrants of the buttocks; their presence was confirmed by the consultant psychiatrists. The lumps, which persisted throughout the week, compelled the nurses in some cases to hunt for a suitable injection site. In a further four patients increased pressure was necessary to give the injection. Nine patients, two with palpable lumps, reported pain or discomfort at the injection site.

One man gave informed consent to excision biopsy of a lump in his buttock. At operation the subcutaneous tissue was hard and contained fibrous gritty material extending down to muscle, the superficial layers of which were affected by a similar process. Routine microscopy of haematoxylin and eosin sections showed numerous sheaves of crystalline material with surrounding hyaline necrosis of fat and connective tissue (see figure). The crystals, not optically active under polarised light, presumably represent spaces left after dissolution of the deposits during processing for microscopy. There were a few small foci of inflammatory-cell infiltrate, possibly related to previous injection tracks, but there was a noticeable absence of infiltrate in the necrotic area surrounding the deposit. The deposits were not intramuscular, and little muscle was present in the specimen.