Diabetic Association on reuse and insisted that they should be used only once.¹ Diabetic patients therefore received conflicting advice from the DHSS and high street chemists (who had an added financial incentive in advocating the single use of syringes) on the one hand, and from diabetic clinic staff on the other. Our present study shows that patients heeded the advice of clinic staff and continued to reuse syringes. Indeed, the frequency of reuse of syringes by these patients actually increased. No systematic advice was given to the patients and there is no obvious reason why the reuse of syringes increased over time. One possible explanation is that patients increased the reuse of syringes as their confidence and experience grew. This did not seem to be a conscious decision as most patients were unaware that they had increased their frequency

of reuse. The conflict should now be resolved as the Department of Health has recently issued Drug Tariff Specification No 39A bearing the heading "Sterile Single Use or Single Patient Use," although it seems likely that the labels on the syringes will continue to read "For single use only."

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Effects of parathyroid hormone on delayed renal allograft function

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Patients with chronic renal failure frequently have hyperparathyroidism. It has been suggested that high concentrations of circulating parathyroid hormone may result in an increased rate of delayed renal allograft function.¹ We have investigated this relation in a prospective study using an assay for intact parathyroid hormone.

Patients, methods, and results

We studied patients receiving a cadaveric renal allograft between April 1988 and September 1989. Each received cyclosporin 10 mg/kg with or without other immunosuppressive agents. Blood samples were obtained before surgery and assayed with a two site immunochemiluminescence technique to measure intact parathyroid hormone² (reference range 0.9-5.4 pmol/l). Delayed function was defined as the requirement for dialysis or failure of the graft to reduce the serum creatinine concentration by 15% within four days of transplantation without technical failure or accelerated rejection. Statistical significance was assessed by the χ^2 test and Mann-Whitney U test.

Eighty four patients received a cadaveric renal allograft, 18 of whom suffered delayed function. None of the grafts failed for technical reasons or as a result of

accelerated rejection. There were no significant differences between the immediate and delayed function groups in terms of recipient and donor variables (table). Serum calcium and phosphate concentrations were not significantly different, although the phosphate concentrations seemed to be higher in the delayed function group. Seventy two patients either had raised concentrations of intact parathyroid hormone or had previously had a parathyroidectomy (n=3). Fourteen patients had parathyroid hormone values within the normal range at the time of transplantation, and eight of these had delayed function.

The patients with delayed graft function had significantly lower concentrations of parathyroid hormone (median 5.9, quartile deviation 9.1, 95% confidence interval 5.8 to 32.4 pmol/l) than those with immediate function (median 25.9, quartile deviation 21.8, 95% confidence interval 31.4 to 52.1 pmol/l) (p=0.0018; Mann-Whitney U test).

Comment

This study has shown for the first time an association between delayed renal allograft function and low concentrations of circulating parathyroid hormone in recipients at the time of transplantation. This finding contrasts with a retrospective study by Varghese *et al*, who noted a relation between delayed function and high concentrations of parathyroid hormone.

There were important differences between the two studies. The assay used by Varghese *et al* was an immunoassay for C terminal parathyroid hormone, which detects inactive fragments of the molecule that are normally excreted by the kidney, as well as the intact hormone. This assay poorly reflects the biological activity of parathyroid hormone. The values obtained are more closely associated with duration of chronic renal failure and the degree of residual renal function. Information relating to the duration of dialysis before transplantation was not included by Varghese *et al*. The delayed function rate in our study was lower (21% compared with 46%) despite a less rigorous definition of delayed function (the requirement for dialysis).

Parathyroid hormone has been shown to have a vasodilatory action in various organs including the kidney.³ The vasodilator effect seems to be an intrinsic property of parathyroid hormone⁴ and to reside in the 24-28 amino acid fragment of the molecule whereas the calcaemic effect is a property of the 2-28 segment.⁵ We have noted that parathyroid hormone has a renal vasodilator effect in cyclosporin treated rats (unpublished observations).

Parathyroid hormone may act as a vasodilator and

Recipient and donor data and other factors. Figures are medians (quartile deviation; 95% confidence interval) and numbers of patients

	Immediate function (n=66)	Delayed function (n=18)
Recipient age (years)	44 (11.5; 39.1 to 45.6)	38 (15; 29.8 to 45.9)
Months of dialysis	12 (9; 12.4 to 18.7)	18 (13.5; 12.9 to 31.6)
Donor age (years)	37 (14; 31.8 to 40)	39.5 (19; 24.2 to 45.1)
Total ischaemic time (hours)	23.37 (4.82; 20.9 to 33.8)	23.65 (3.2; 20.2 to 26.4)
Serum calcium (mmol/l)	2.41 (0.11; 2.34 to 2.44)	2.49 (0.12; 2.32 to 2.7)
Inorganic phosphate (mmol/l)	1.89 (0.22; 1.84 to 2.06)	2.17 (0.24; 1.95 to 2.43)
Recipient sex (male)	40	14
Mode of dialysis:		
Haemodialysis	40	14
Continuous ambulatory peritoneal dialysis	26	4
Regrafts:		
Second	11	3
Third	2	0
Calcium channel blockers:		
Nifedipine	13	1
Diltiazem	22	6

No significant differences by Mann-Whitney U test or χ^2 test.

prevent acute tubular necrosis by reducing vasospasm after reperfusion. Other renal vasodilators, particularly calcium channel blocking drugs, have been shown to reduce delayed function. It seems that the maintenance of renal blood flow after revascularisation is important for early graft function.

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Assessment of pain after subcutaneous injection of erythropoietin in patients receiving haemodialysis

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Intravenous recombinant human erythropoietin is effective for treating the anaemia of chronic renal failure.^{1,2} Subcutaneous erythropoietin is also effective.³ Moreover, it seems that the dosage requirements for subcutaneous administration may be lower than those of intravenous maintenance therapy.⁴

Subcutaneous administration is a convenient way of giving erythropoietin, particularly in predialysis patients and patients receiving peritoneal dialysis. Self administration at home is feasible. However, after subcutaneous injection of Eprex (Cilag, Belgium) several of our patients reported unexpected pain at the injection site, which occasionally precluded self administration.

We report the results of a double blind, placebo controlled, randomised crossover study, designed to assess differences between pain experienced after subcutaneous injection of one of two different erythropoietin preparations or saline 0.9%.

Patients, methods, and results

All adult patients regularly receiving subcutaneous erythropoietin in two haemodialysis centres (n=32) were invited to participate in the study. Two brands of erythropoietin were tested: Eprex (aqueous solution of 1 ml containing 2000 U/ml erythropoietin (epoetin alpha) and 2.5 mg/ml human serum albumin in a citrate buffer) and Recormon (2000 U erythropoietin (epoetin beta) as a lyophilisate, then made up to 1 ml with water: Boehringer Mannheim, The Netherlands). Saline 0.9% (Braun Melsungen, Germany) served as a placebo and control. Since in each of the centres all patients had been receiving either Eprex or Recormon they had not had the opportunity to compare both preparations with regard to pain. The solutions were equilibrated at room temperature before injection.

Percentage pain scores on visual analogue scale and patient's response on verbal descriptive pain scale after subcutaneous injection of Eprex, Recormon, or saline 0.9%

	Eprex	Recormon	Saline
Visual analogue scores (%):			
Median (second and third quartiles)	35 (13, 51)*	0 (0-1)	0 (0, 7)
Range	0-90	0-17	0-33
Verbal descriptive scale:			
No with very mild or no pain	10*	31	26
No with mild to very severe pain	22	1	6

* $p < 0.0001$ for difference between Eprex and Recormon or saline, by signed rank test for visual analogue scale and McNemar's test for verbal descriptive scale.

At intervals of one hour the 1 ml injections were given subcutaneously in the outer part of the upper arm by an experienced nurse. The sequence of the injections was randomised and blinded for both patient and nurse.

A visual analogue scale with no divisions and a six point verbal descriptive scale were used by the patients to define grades of pain after each injection.⁵ The end points of the 15 cm vertical line on the visual scale were "no pain at all" and "pain as bad as it could be." The horizontal verbal descriptive scale offered alternatives ranging from "no pain" to "very severe pain." The table shows that the median percentage score on the visual scale was higher after injection of Eprex than after injection of Recormon or saline. The proportion of patients having had very mild or no pain on the verbal scale was low with Eprex (0.31, 95% confidence interval 0.16 to 0.50) compared with Recormon (0.97, 0.84 to 0.99) or saline (0.81, 0.68 to 0.95). There was no significant difference between the scores for Recormon and saline.

In a separate questionnaire the patients were asked which injection was most painful. Five patients had felt no pain after each of the three injections. Twenty six of the remaining 27 patients indicated Eprex, and one indicated saline.

There were no differences in pain scores between patients from the two haemodialysis centres if they were classified according to the regular use of Eprex or Recormon.

Comment

The results show that pain after subcutaneous injection is typically associated with Eprex. The pain was usually described as burning or itching and was different from the pain occasionally felt after saline or Recormon. In most patients the pain had disappeared after 10 minutes.

The absence of pain after subcutaneous injection of Recormon suggests that the inactive ingredients of the formulation are the cause of the pain. Further study is needed to elucidate whether the citrate buffer or perhaps human serum albumin in the Eprex solution is involved in this troublesome phenomenon.

We thank the patients and the nursing staff in the participating haemodialysis wards for their cooperation and Ms C Pans for her skilful assistance.

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