Improvement in renal function in primary hyperparathyroidism following parathyroidectomy

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Summary

Glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) were measured pre- and post-parathyroidectomy in 9 patients with primary hyperparathyroidism. Radiological studies had shown no sign of renal calculi or nephrocalcinosis in these patients. Before operation, GFR ranged from 98.5 to 23.4 ml/min/1.7 m² and ERPF ranged from 510 to 127 ml/min/1.7 m². After operation, GFR rose to a range of 108.8 to 48.7 ml/min/1.7 m², and ERPF ranged from 556 to 189 ml/min/1.7 m².

The results suggest that early diagnosis and surgery are important, both to prevent progressive renal damage and to improve the possibility of recovery where functional damage has occurred.

Introduction

Relatively few studies have been reported in which renal clearances were performed in primary hyperparathyroidism (1°HPT) before and after parathyroid surgery. Edvall (1958) estimated glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) in severe 1°HPT, and observed a fall in both variables when these tests were repeated shortly after parathyroidectomy. However, Freaney, Casey and Muldowney (1978) demonstrated relatively stable creatinine clearances after parathyroidectomy in a group which included severe and mild 1°HPT. The authors have measured renal function for periods of from 3 months to 4.5 years after ablation of a single adenoma causing hyperparathyroidism, and observed GFR and ERPF in a selected group of 9 patients, from which those presenting with renal calculi were excluded.

Patients and methods

The patients under consideration presented at Singleton Hospital, Swansea, with a variety of complaints, and were found to have hypercalcaemia on routine biochemical screening. Diagnosis of 1°HPT was further investigated by measuring serum calcium and inorganic phosphate concentrations, alkaline phosphatase and immunoreactive parathyroid hor-

mone concentration (carboxy terminal fragment). Any patient who had a history of renal calculus, or who had radiological evidence of renal calcification was excluded. Nine patients fulfilling these criteria were studied, 5 female and 4 male, with ages ranging from 16 to 61 years. Two of these patients, M.T. and D.E., admitted to generalized skeletal pains.

Skeletal X-rays and i.v. urogram were performed in all patients. Skeletal survey was normal in these patients with the exceptions of M.T. and D.E. in whom peri-osteal resorption was present. No nephrocalcinosis or nephrolithiasis was noted in the urinary tract.

Mid-stream urine cultures were sterile in all patients.

Sustained hypertension, if present, was treated with anti-hypertensive drugs to achieve good BP control.

Parathyroid exploration led to the finding of single parathyroid tumour in all patients, the 3 remaining parathyroid glands having been identified and shown to be normal macroscopically and histologically. Serum calcium, inorganic phosphate, alkaline phosphatase and creatinine concentrations were measured by Technicon Auto-analyser. Venous blood was obtained in the fasting state from an unobstructed vein. Serum immunoreactive parathyroid hormone was assayed by a radio-immunometric technique which measured the biologically inert carboxyl fragment of the parathyroid molecule. 0.05 ng/ml was the upper limit of normal using this method (Addison *et al.*, 1971). GFR and ERPF were estimated simultaneously after intravenous administration of ⁵¹Cr EDTA and ¹²⁵I sodium iodohippurate, taking venous blood samples at 2 and 4 hr after injection (Morgan *et al.*, 1977).

Results

Pre-operative clinical and biochemical details are summarized in Table 1. Serum calcium concentration fell into the normal range within 24 hr of parathyroidectomy. Pre- and postoperative values for serum calcium concentration GFR and ERPF are

given in Table 2. Using Student's paired *t* test the postoperative fall in serum calcium concentration was significant ($P=0.001$), and the increase in GFR ($P=0.005$) and ERPF ($P=0.02$) were also significant. There was no significant relationship between pre-operative serum calcium concentration and GFR. Mean pre-operative values of GFR and ERPF were

reduced to 65 and 73% respectively of the values expected for subjects of the corresponding age and sex. Postoperatively, GFR and ERPF increased to 81 and 86% respectively.

Table 2 shows the postoperative/pre-operative percentage change in GFR and ERPF. In 6 of the 9 patients the postoperative GFR rose by 27% or more

TABLE 1. Initial serum biochemistry on patients with primary hyperparathyroidism (normal ranges in brackets)

	Sex and age (years)	Clinical presentation	Serum calcium mmol/l (2.2-2.6)	Serum inorganic phosphate mmol/l (0.8-1.5)	Serum alkaline phosphatase u./l (35.5-106.5)	Serum parathyroid hormone ng/ml (0-8.0)
MT	F(52)	Hypertension	3.74	0.9	198.8	6.5
DE	M(62)	Dyspepsia without peptic ulceration	2.84	0.7	184.6	5.0
JH	M(25)	Aching jaw	3.40	0.5	127.8	0.7
EM	F(55)	Paraesthesia in fingers	3.16	0.9	54	0.9
CG	M(62)	Chest pain	3.38	0.7	139.2	0.9
VH	F(58)	Fatigue and weight loss	3.13	0.6	56.8	2.5
EP	F(48)	Pain and swelling in left knee	2.93	0.9	120.7	0.6
KG	M(16)	Recurrent abdominal pain	3.33	0.5	106.5	0.6
MB	F(38)	Hypertension	2.93	0.7	46.9	2.4

TABLE 2. Pre- and postoperative serum calcium concentration, GFR and ERPF

Pre-operative results				Postoperative results		
Serum calcium mmol/l <i>n</i> = 2.0-2.6	GFR ml/min/1.7 m ² <i>n</i> -(see note)	ERPF ml/min/1.7 m ² <i>n</i> -(see note)	Time interval	Serum calcium mmol/l <i>n</i> = 2.2-2.6	GFR ml/min/1.7 m ² <i>n</i> -(see note)	ERPF ml/min/1.7 m ² <i>n</i> -(see note)
3.74	23.4	136	1.5 years	2.45	37.9	175
			4 years		37.2	192
2.84	34.1	127	4.5 years	2.50	48.7	189
3.40	80.2	-	1 month	2.27	108.8	556
			0.5 year		107.3	475
3.16	60.4	510	1.5 year	2.39	79.5	413
3.38	70.0	402	1 month	2.32	89.9	413
			3 month		80.3	353
3.13	60.0	325	5 years	2.50	76.2	484
2.93	71.3	351	6 months	2.38	77.3	426
3.33	91.5	480	4.5 years	2.35	98.2	633
2.93	98.5	455	1 year	2.32	94.7	441
Mean (± one s.d.)	3.20 ± 0.29	65.5 ± 24.6	348 ± 148	2.39 ± 0.08	79.0 ± 23.0	397 ± 151

n = normal range/value.

GFR (Glomerular filtration rate): Normal male value = $157.8 - 1.16 \times (\text{age in years})$. Normal female value = $146.0 - 1.07 \times (\text{age in years})$.

ERPF (Effective renal plasma flow): Normal male value = $841.0 - 6.44 \times (\text{age in years})$; Normal female value = $760.0 - 6.44 \times (\text{age in years})$.

above the pre-operative value, in one case (M.T.) increasing by 62.0%. In the other 3 there was no significant change.

In 5 of the 8 patients in whom ERPF was measured pre- and postoperatively these values rose by 21.4 to 49%. In the other 3 cases there was either a fall or no significant change. There is no predictable correlation between GFR and ERPF percentage changes.

TABLE 3. Post- and pre-operative percentage change in renal function

Patient	GFR ml/min/1.7 m ² n - (see note)	ERPF ml/min/1.7 m ² n - (see note)
M.T.	62.0	28.6
D.E.	48.2	48.7
J.H.	35.7	-
E.M.	31.8	-19
C.G.	28.4	-2.5
V.H.	27.0	+49
E.P.	8.4	+21.4
K.G.	7.3	+31.9
M.B.	-3.9	-2.5

n = normal range/value.

GFR (Glomerular filtration rate): Normal male value = $157.8 - 1.16 \times (\text{age in years})$;

Normal female value = $146.0 - 1.07 \times (\text{age in years})$.

ERPF (Effective renal plasma flow): Normal male value = $841.0 - 6.44 \times (\text{age in years})$;

Normal female value = $760.0 - 6.44 \times (\text{age in years})$.

Discussion

It is striking that the 2 patients M.T. and D.E., with evidence of osteitis fibrosa and with the highest levels of circulating PTH, had the worst renal function pre-operatively and showed the greatest increase in GFR following surgery. Presumably, correction of serum calcium concentration was not the most important factor as the pre-operative serum calcium concentration was 2.84 mmol/l in D.E., and 3.74 mmol/l in M.T. The factors concerned with the postoperative improvement in renal function cannot be ascertained. No renal histology was obtained in these patients and therefore it cannot be established that regression of structural changes occurred. Furthermore, although correction of serum calcium concentration, of PTH and of serum alkaline phosphatase occurred postoperatively, it is not clear as to which of these factors were important in the reduction of renal function.

A wide range of renal dysfunction was noted at presentation in these patients. Reduction in GFR and ERPF is likely to result from structural changes within the kidney, although direct effects of excessive

PTH or hypercalcaemia may be contributory. Percutaneous renal biopsy findings have been described from a patient with 1°HPT who presented with a creatinine clearance of 17 ml/min. Intravenous urogram, as in the present patients, showed no sign of nephrocalcinosis or nephrolithiasis. Renal histology showed marked destruction of renal parenchyma with fibrosis, patchy infiltration and chronic inflammatory cells, and numerous amorphous calcium deposits. Tubules were severely atrophied, but glomerular changes were also marked, with hyalinization, tuft congestion, and fibrous thickening of Bowman's capsule (Evans and Zutshi, 1962).

Parathyroidectomy was associated with an impressive rise in GFR in 6 patients. When only slight reduction of renal function was initially present, it was apparent that complete recovery of renal function was possible but not inevitable after operation. Likewise, of Edvall's (1958) 20 patients who were studied pre- and postoperatively, there were 4 with minimal renal dysfunction who were restored to normal renal function after parathyroidectomy. Sixteen of Edvall's patients with moderate or severe renal impairment showed a decline in renal function after parathyroidectomy, yet 4 of these patients who were re-studied at a later date demonstrated some improvement.

Significant recovery of renal function is possible in 1°HPT after parathyroidectomy, and early parathyroid exploration is advocated to conserve and improve existing renal function.

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