

PAPERS

Changes in blood pressure and renal function after parathyroidectomy in primary hyperparathyroidism

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Summary

Changes in blood pressure and renal function were investigated in 62 patients with primary hyperparathyroidism treated surgically, in an attempt to assess whether or not hypertension and renal impairment should be regarded as important indications for parathyroidectomy.

29% were hypertensive pre-operatively and the blood pressure remained elevated after parathyroidectomy in all of these patients. Hypertension developed for the first time after parathyroidectomy in 45% of those patients who were normotensive before surgery.

Renal function was normal initially in 73% and mild renal impairment developed after surgery in 9% of these patients. At the end of the follow-up period, the prevalence of hypertension was higher in patients with renal impairment pre-operatively (88%) than in those with normal renal function (51%).

We conclude that hypertension alone should not be regarded as an indication for parathyroidectomy in asymptomatic hyperparathyroidism. No firm conclusions can be reached about the importance of mild renal failure as an indication for surgery and the question is unlikely to be resolved without conducting a prospective controlled trial.

KEY WORDS: hypertension, renal failure, primary hyperparathyroidism, parathyroidectomy.

Introduction

Measurement of serum calcium during routine biochemical screening has shown that primary hyperparathyroidism is a relatively common condition, especially in middle-aged and elderly women. A recent survey from Rochester, U.S.A. (Heath, Hodgson and Kennedy, 1980) indicated an annual incidence of 277 per million of the population. Similar results have been reported from Britain (Mundy, Cove and Fischen, 1980).

About half of these patients had mild hypercalcaemia and were asymptomatic. This poses a problem with regard to treatment, because the indications for surgery in such cases are uncertain (Scholz and Purnell, 1981; Coe and Favus, 1980). Both hypertension and impaired renal function have been considered important criteria (Hellstrom, Birke and Edvall, 1958; Pyrah, Hodgkinson and Anderson, 1966; Scholz, 1977; Blum, Kirsten and Worth, 1977).

We describe here the changes in blood pressure and renal function after parathyroidectomy in 62 patients with primary hyperparathyroidism due to a parathyroid adenoma.

Patients and methods

The series comprises 62 patients with primary

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hyperparathyroidism due to parathyroid adenoma treated in Cardiff between 1960 and 1980.

When these investigations were initiated in 1976, an attempt was made to trace all patients who had had a parathyroid adenoma removed up to that time. Thirty such patients were found and investigated, but 4 had to be excluded because of inadequate pre-operative data. We failed to trace another 23 patients; 16 are known to have died. The mean postoperative follow-up for the 26 patients included in the series was 9 years (range 2–20 years) and the mean age at the end of the follow-up period was 62 years.

Between 1976 and 1980, a further 40 patients had a parathyroid adenoma removed but 4 have had to be excluded because their medical records either cannot be traced or are incomplete. The mean duration of follow-up in this group of 36 patients investigated prospectively was 2.9 years (range 1–6 years) and the mean age at the end of the follow-up period was 60 years.

The diagnosis was made on the basis of persistent elevation of the serum calcium concentration (>2.60 mmol/litre) in the absence of any other obvious cause; an inappropriately high serum parathyroid hormone level (in patients seen after 1973); and histological evidence of a parathyroid adenoma at operation. Patients with parathyroid carcinoma, parathyroid hyperplasia and those in whom no abnormality was found on exploration of the neck have been excluded from the series. In all patients, the serum calcium concentration fell after parathyroidectomy.

Blood pressure measurements were made in the supine position after a period of rest. Diastolic readings were taken at phase five. Some patients were on antihypertensive drugs when first seen and for the purpose of this paper we have classified a patient as hypertensive if the diastolic blood pressure was persistently greater than 100 mmHg or if there was good evidence that this was the case before antihypertensive therapy was started. Renal impairment is defined as persistent elevation of plasma urea (>7.5 mmol/litre) and plasma creatinine (>120 μ mol/litre). At the time of surgery the 20 men had a mean age of 46 years (range 15–66) and the 42 women had a mean age of 59 years (range 31–77).

Results

Hypertension

Pre-operatively, 18 (29%) of the 62 patients were hypertensive. Six of these were from the pre-1976 group and 12 from the 1976–80 group. The blood pressure remained high after parathyroidectomy in all these patients.

Hypertension developed for the first time after parathyroidectomy in 20 of the 44 patients (45%) who

were initially normotensive. Eleven of these were from the pre-1976 group and 9 from the 1976–80 group.

At the end of the follow-up period, renal function was impaired in 10 of the 18 patients with pre-operative hypertension, compared with 9 of the 44 patients who were normotensive. The difference is statistically significant ($\chi^2 = 5.90$; $P < 0.05$).

Renal function

Renal function was normal initially in 45 of the 62 patients but deteriorated after surgery in 4 of them (9%). Renal function improved after parathyroidectomy in 2 of the 17 patients with impaired renal function, but in both of them, renal failure was attributable to inadequate correction of fluid and electrolyte depletion pre-operatively.

At the end of the follow-up period, 15 of the 17 patients (88%) with reduced renal function pre-operatively were hypertensive, compared with 23 of the 45 patients (51%) with normal renal function. The difference is statistically significant ($P < 0.05$).

Few patients had severe renal failure. Plasma creatinine exceeded 250 μ mol/litre in only 4 patients pre-operatively and in 5 patients at the end of the period. In the remaining 57 patients, the mean plasma creatinine was 109 μ mol/litre both pre-operatively and at the end of follow-up. No marked change in renal function occurred in individual patients other than the two in whom plasma creatinine fell from 230 μ mol/litre to 100 μ mol/litre and 190 μ mol/litre to 100 μ mol/litre respectively soon after surgery as a result of fluid repletion.

The initial serum creatinine in patients who developed hypertension (mean 146 μ mol/litre; s.d. 94 μ mol/litre) was significantly higher ($P < 0.02$) than in those who remained normotensive (mean 97 μ mol/litre; s.d. 19 μ mol/litre).

Serum calcium

The initial serum calcium in patients who developed hypertension (mean 3.10 mmol/litre; s.d. 0.35 mmol/litre) was slightly higher than in those who remained normotensive (mean 2.94 mmol/litre; s.d. 0.19 mmol/litre) (Fig. 1). However, although this difference is statistically significant ($P < 0.02$), initial serum calcium was of no value in predicting which patients would develop hypertension. Several patients with only slightly raised serum calcium eventually became hypertensive whereas others with severe hypercalcaemia pre-operatively remained normotensive throughout.

The initial serum calcium in patients with impaired renal function at the end of the follow-up period (mean 3.14 mmol/litre; s.d. 0.37 mmol/litre) was higher than in those with normal renal function

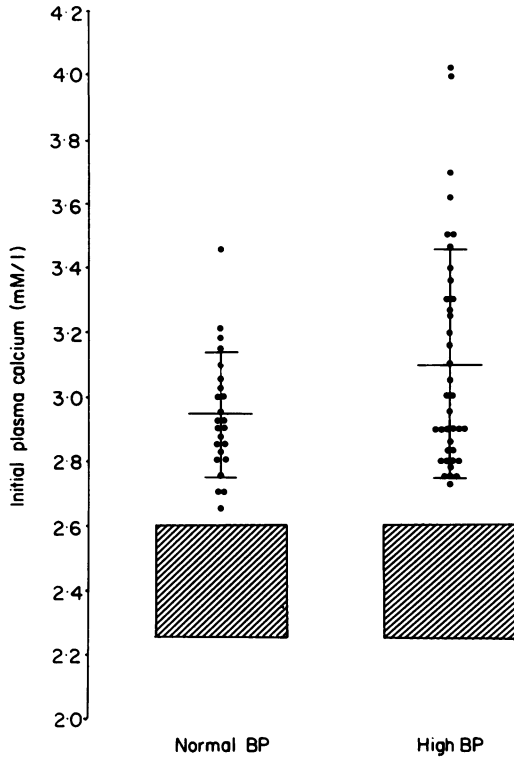


FIG. 1. Relationship between blood pressure (BP) at the end of the follow-up period and initial plasma calcium (Mean \pm s.d.). Hatched areas give normal range.

(mean 2.99 mmol/litre; s.d. 0.27 mmol/litre) but this difference is not statistically significant.

Discussion

Routine estimations of serum calcium can be expected to yield at least 250 new cases of primary hyperparathyroidism per million of the population per year. More than half of these patients are likely to be over the age of 70 and about half of them asymptomatic (Heath *et al.*, 1980; Mundy *et al.*, 1980). Because the potential workload is large and the cost of operating on all these patients would be very high (Heath *et al.*, 1980), there is a pressing need to establish definitive criteria for parathyroidectomy.

This high incidence of hypertension in primary hyperparathyroidism has long been recognised. Hellstrom *et al.* (1958) found that 70% of a series of 105 patients were hypertensive at some stage. Others have reported an incidence of between 20% and 50% (Pyrah *et al.*, 1966; Rosenthal and Roy, 1972). Of our patients, 29% were hypertensive pre-operatively. It has been suggested that the presence of hypertension in otherwise asymptomatic hyperparathyroidism should be regarded as an indication of surgery, in the

hope that parathyroidectomy may return the blood pressure to normal and prevent renal and cardiovascular damage (Hellstrom *et al.*, 1958; Pyrah *et al.*, 1966; Scholz and Purnell, 1977; Weidmann *et al.*, 1972). Coe and Favus (1980) consider that in any controlled trial, the appearance of hypertension should be regarded as an indication for parathyroidectomy. However, in the present series, parathyroidectomy appeared to have little effect on the blood pressure. All the patients who had high blood pressure initially remained hypertensive after parathyroidectomy, and 45% of pre-operatively normotensive patients developed hypertension subsequently. Similarly, Rosenthal and Roy (1972) found no significant drop in blood pressure after parathyroidectomy. On the basis of this evidence, and having regard to the high prevalence of hypertension in this age group, we do not consider that hypertension *per se* should be regarded as an indication for surgery in asymptomatic hyperparathyroidism.

The mechanism of the hypertension associated with hyperparathyroidism is uncertain (Scholz, 1977). Earlier reports attributed it to renal impairment (Hellstrom *et al.*, 1958), but recent studies have shown that hypertension often occurs in patients with no significant degree of renal impairment (Rosenthal and Roy, 1972). In this series, the prevalence of hypertension was significantly higher in patients with renal impairment pre-operatively than in those with normal renal function.

Hypercalcaemia, due to causes other than hyperparathyroidism, may be associated with hypertension, possibly due to a direct effect on calcium on vascular smooth muscle cells (Blum *et al.*, 1977; Weidmann *et al.*, 1972; Earl, Kurtzman and Moser, 1966). However, we found the severity of the hypercalcaemia to be of little value in predicting the development of either hypertension or renal impairment.

It is generally agreed that nephrolithiasis, nephrocalcinosis, severe hypercalcaemia and established renal failure are indications for parathyroidectomy because, although a significant improvement in renal function after parathyroidectomy is uncommon (Britton *et al.*, 1972), further deterioration may be arrested (Hellstrom *et al.*, 1958; Shaw and Cooper, 1969; Choudhary and Gray, 1973). The relevance of mild renal impairment in patients with asymptomatic hyperparathyroidism, however, is less clear. Progressive deterioration of renal function is by no means inevitable in patients treated conservatively, and a mild degree of renal impairment is in any case common in the elderly. Renal function was normal pre-operatively in the majority of our patients (73%). In 9% of these some degree of renal impairment appeared for the first time after parathyroidectomy but whether or not parathyroidectomy prevented the

development of renal failure in any of the others cannot be determined. The importance or otherwise of mild renal failure as an indication for surgery in asymptomatic primary hyperparathyroidism is unlikely to be resolved without conducting a prospective controlled trial.

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