Long term follow up of untreated primary hyperparathyroidism

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Abstract

Fourteen patients with primary hyperparathyroidism and whose initial serum calcium concentrations were 2.75 mmol/1 (110 mg/100 ml) or more were followed up for five to 23 years without operative treatment. One had osteitis fibrosa when seen and died with a fibrosarcoma 22 years later. The remaining 13 patients, who were followed up for a mean of 10 years, came to little obvious harm from not being operated on. Their serum calcium concentrations did not rise and there was no evidence of progressive renal impairment. In four patients who presented originally with renal colic there were three further episodes of renal colic in 54 patient years of follow up.

Conservative management of primary hyperparathyroidism is not an unreasonable option, and patients who do not have symptoms need not necessarily be pressed to accept surgery.

Introduction

Primary hyperparathyroidism is increasingly recognised as a common disorder, particularly in older women. Many patients are symptom free; the classic symptoms of bone disorders, renal stones, or abdominal pain are uncommon.1 In the past it was usual to advise an exploration for all patients with primary hyperparathyroidism to prevent an “inevitable” decline in renal function.2-4 Now, however, it is clear that progressive renal impairment seldom occurs in mild primary hyperparathyroidism2 and, since exploration of the parathyroids has a small morbidity and mortality,5 more and more patients are being treated conservatively.6-10

Some workers think that most patients should be treated surgically. The reasons given are that they really have symptoms, that there is a risk of acute hypercalcaemia, that progressive osteopenia may occur, that medical follow up is expensive, and that if surgery is deferred the patient may be unfit for operation when indications for surgery do appear.9 13-16

While these arguments continue in respect of patients with mild hypercalcaemia, most physicians advise an early parathyroid exploration for all, or almost all, patients with more severe hypercalcaemia. We describe a series of patients with hyperparathyroidism and serum calcium values of 2.75 mmol/1

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### Details of patients

<table>
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<th>Case No</th>
<th>Sex</th>
<th>Age initially</th>
<th>Years of hypercalcaemia</th>
<th>Presentation</th>
<th>Reason not explored</th>
<th>Serum parathyroid hormone (U/l)</th>
<th>Serum calcium (mmol/l)</th>
<th>Serum creatinine (μmol/l)</th>
<th>Outcome</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initial</td>
<td>Final</td>
<td>Initial</td>
<td>Final</td>
</tr>
<tr>
<td>1</td>
<td>F</td>
<td>54</td>
<td>9</td>
<td>Sarcoïdosis</td>
<td>Hypercalcaemia attributed to sarcoid</td>
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<td>2.89</td>
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<tr>
<td>2</td>
<td>F</td>
<td>49</td>
<td>23</td>
<td>Renal colic</td>
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<tr>
<td>3</td>
<td>M</td>
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<td>Ischaemic heart disease, duodenal ulcer, calculi 20 years before</td>
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<td>22†</td>
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<td>Misadventure</td>
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*All serum calcium values adjusted for serum albumin except where marked with asterisk.

†Misadventure used to describe patients who presented with typical symptoms of hyperparathyroidism but for whom no appropriate action taken at the time.  
Conversion: 1SI to traditional units—Calcium: 1 mmol/l = 4 mg/100 ml Creatinine: 1 μmol/l = 0.01 mg/100 ml.

(11-0 mg/100 ml) or more who for various reasons were left unoperated for five to 23 years and examine the clinical and biochemical consequences of such long periods of untreated severe hyperparathyroidism.

### Patients

Among 200 local patients with primary hyperparathyroidism, 13 (see table) had had initial serum calcium values of 2.75 mmol/l or more and had been followed up for at least five years (range 5-23 years; mean 10). All the patients in whom serum parathyroid hormone concentration was measured had detectable or raised values. None had a family history of hypercalcaemia, and none had the hypercalciuria typical of familial benign hypercalcaemia. Most of the patients were identified by chance after presenting with an unrelated illness, but four had renal colic.

One patient (case 14) presented with bone pain and a cystic lesion of the ilium. At that time the sole concern of the clinicians was the exclusion of malignancy, and no histological evidence of malignancy was found; when the blocks were reviewed afterwards osteitis fibrosa was obvious. Hypercalcaemia was not identified until 17 years later, and even then exploration of the parathyroids was not advised. She died aged 71 with fibrosarcoma of the ilium; a large parathyroid adenoma was found at necropsy.

### Results

In these patients serum calcium concentrations were remarkably stable over the long periods of follow up. The figure shows the values for serum calcium (adjusted for serum albumin concentration) in the nine patients for whom there were reasonably full data. Calcium concentrations remained remarkably constant, and no cases of acute hypercalcaemia were seen. The serum creatinine value remained normal in every case despite the long period of hypercalcaemia (table). Of the patients who died, all but two died of the progression of disorders known to be present when the hypercalcaemia was first found. Among the four patients presenting with renal colic there were only three further episodes of colic in 54 patient years of follow up. Skeletal symptoms were uncommon; two patients had longstanding arthropathies, which were troublesome throughout the periods of follow up. There was one fractured neck of femur (case 9, age 75). The only patient with vertebral collapse (case 14) was known to have had osteitis fibrosa.

### Discussion

In view of the initial serum calcium concentrations in these patients (2.75 mmol/l (11.0 mg/100 ml) or more) we have no doubt that ordinarily they would have been advised to have a parathyroid exploration. Some were not so advised because of other medical problems, others refused surgery, and the remainder were left untreated because of clinical misadventures. Despite their appreciable hypercalcaemia there was no change in serum creatinine concentrations over the long periods of follow up. These results are similar to those obtained for shorter periods by other workers. 15 17

The risk of progressive osteopenia is often regarded as a reason to recommend parathyroid exploration. In our series, with the exception of the patient with known osteitis fibrosa (case 14), skeletal symptoms were uncommon despite the fact that there were seven women aged more than 70 at the end of the study. The fatal sarcoma in case 14 may have been caused by longstanding osteitis fibrosa but may also have resulted from radiotherapy to the ilium 21 years before. 16 18 Whatever the
Loperamide in acute diarrhoea in childhood: results of a double blind, placebo controlled multicentre clinical trial

DIARRHOEAL DISEASES STUDY GROUP (UK)

Abstract

A total of 315 young children with acute diarrhoea were included in a double blind, hospital based multicentre trial of loperamide at two dose levels (0.8 mg and 0.4 mg/ kg/24 h), given with standard oral rehydration therapy versus placebo plus oral rehydration therapy. The overall recovery rate was slowest in the placebo group and fastest in the group given loperamide 0.8 mg. Comparisons between weights on admission and weights by day 3 showed that a larger proportion of children in the loperamide groups gained weight than in the placebo group. No serious side effects of loperamide were observed, but the drug was withdrawn in one infant because of mild abdominal distention. The results indicate that loperamide, in the doses employed, is safe and may in selected cases be a useful adjunct to oral rehydration in the management of acute diarrhoea in well nourished children.

Introduction

Glucose-electrolyte solutions are highly effective in treating dehydration in acute diarrhoea by stimulating glucose coupled sodium transport in the small intestine. The use of adjunct therapy in oral rehydration remains controversial, but agents that effectively inhibit the net secretion of fluid and electrolytes by the intestine without serious side effects may have a place.

Naturally occurring opioids have been used as anti diarrhoeal agents since antiquity but their central effects make them undesirable. Loperamide, a recently developed opioid analogue, differs from other, similar drugs in that it binds predominantly to intestinal tissue and when given by mouth has virtually no

References