Renal tubular function in hyperparathyroidism

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Summary: Renal tubular function was assessed in a group of patients with mild hyperparathyroidism before and after a mean period of 2.7 years conservative management. It was also assessed, before and after a mean of 3.3 years following surgery in a group of patients with initially higher plasma calcium concentration.

Mean maximum urine osmolality was within the accepted range as was the maximum urine plasma hydrogen ion gradient in both groups at the time of diagnosis.

No significant change in renal tubular function was observed in either group over the periods of this study. Although deterioration after a long period cannot be excluded, we do not consider that regular assessment of renal tubular function is necessary in the conservative management of primary hyperparathyroidism.

Introduction

Severe impairment of renal glomerular function in primary hyperparathyroidism that was so frequently described in the past is now rarely seen, either at the time of diagnosis, or in mild cases that are managed conservatively.1

Impaired renal tubular function has also been reported in hyperparathyroidism2,3 but the relevance of this is difficult to assess because of impaired glomerular function in some cases. We were interested to discover whether there might be evidence of impaired tubular function in the absence of glomerular dysfunction, and also whether this could be an early marker of renal impairment in hyperparathyroidism. We have therefore done a prospective study of renal tubular function in conservatively managed primary hyperparathyroid patients and at the same time studied a group of surgically treated patients.

Patients and methods

Two groups of patients have been studied which by definition are not comparable. In the first, patients had mild primary hyperparathyroidism and were studied at diagnosis and after a mean of 2.7 years of conservative management. The diagnosis in this group was confirmed by the finding of a raised plasma 1–84 parathyroid hormone (PTH)4 on both occasions, no other cause of hypercalcaemia being found during the period of observation. The second group had initially higher plasma calcium concentrations and were studied before, and after a mean of 3.3 years following successful parathyroidectomy.

Renal tubular function was assessed in two ways. Urine concentrating ability was assessed by measurement of urine osmolality during 10 hours fluid deprivation. The maximum osmolality obtained was the reading used. The ability to acidify urine was assessed by the standard acidification test of the oral administration of ammonium chloride 0.1 g/kg body weight, and measurement of urine and plasma pH.5 Results are expressed as the maximum urine/plasma hydrogen ion gradient6 this being a more sensitive indicator of change than the lowest urine pH. These and relevant routine tests were performed before and at the end of the study.

Statistics

Results were compared using the paired t-test. To detect a difference of 1 standard deviation within the renal function tests power calculation for the paired t-test was shown to be in excess of 95%.

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Results

Because the two groups were, by definition, not comparable, patients were their own controls and comparison was made within the groups, i.e. before and after a mean of 2.7 years of conservative management, and before and after a mean of 3.3 years following surgery.

Mean maximum urine osmolality and maximum urine/plasma hydrogen ion gradient were within the normal accepted range at the time of diagnosis. There was no significant change within either group at the end of the periods of study (Table I).

As expected, both total ionized plasma calcium and PTH fell after surgery, but none of these measurements changed significantly in the conservatively managed group. Neither plasma creatinine nor creatinine clearance changed significantly in either group. Plasma alkaline phosphatase fell significantly following surgery.

Discussion

Impaired renal tubular function in hyperparathyroidism may be due to a reduction in tubular reabsorption of bicarbonate resulting in a fall in plasma bicarbonate and hyperchloroaemic acidosis.2,8 In some cases these abnormalities can be corrected by successful parathyroid surgery. Experimentally both in man and in dogs, administration of parathyroid extract induces a rise in urine pH and bicarbonate.9,10 Reduced urine concentrating ability has been reported in hyperparathyroidism3 and here again improvement may occur following successful surgery. In many of these reported cases there was also evidence of impaired glomerular function and the influence of this abnormality on tubular function is difficult to assess.

Nowadays normal renal glomerular function is present in most cases of primary hyperparathyroidism that are diagnosed. It is a usual requirement in those elderly patients where the decision is made to manage them conservatively.1 To date, review of these patients has not shown any significant deterioration in glomerular function following varying periods of follow-up.1,11–14

In the present series no abnormality of renal tubular function was found at the time of diagnosis and, perhaps not surprisingly, there was no change following surgery. Tubular function has not previously been studied in conservatively managed hyperparathyroidism. In this series there was no deterioration in tubular function following a period of conservative management. This does not exclude the possibility of tubular dysfunction occurring after a longer period, nor does it answer the question whether impairment of tubular function may be an early marker of more generalized renal impairment. To date, however, there is little evidence of development of more generalized impairment of renal function in

<table>
<thead>
<tr>
<th>Parameters (reference range)</th>
<th>Conservative management Before</th>
<th>After</th>
<th>Surgery Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>29</td>
<td>29</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Age, years</td>
<td>57.4 (10.1)</td>
<td>55.5 (10.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma total Ca (2.25–2.60 mmol/l)</td>
<td>2.76 (0.13)</td>
<td>2.78 (0.12)</td>
<td>2.95 (0.20)</td>
<td>2.42* (0.11)</td>
</tr>
<tr>
<td>Plasma ionized Ca (0.98–1.21 mmol/l)</td>
<td>1.32 (0.09)</td>
<td>1.30 (0.09)</td>
<td>1.41 (0.13)</td>
<td>1.04* (0.04)</td>
</tr>
<tr>
<td>1–84 PTH (1.5–6.4 pmol/l)</td>
<td>10.5 (4.9)</td>
<td>9.6 (3.2)</td>
<td>16.4 (10.6)</td>
<td>3.1* (1.9)</td>
</tr>
<tr>
<td>Plasma alkaline phosphatase (45–120 U/l)</td>
<td>104.0 (30.5)</td>
<td>104.9 (30.5)</td>
<td>114.1 (24.4)</td>
<td>88.6* (18.5)</td>
</tr>
<tr>
<td>Plasma creatinine (55–108 μmol/l)</td>
<td>92.3 (17.3)</td>
<td>91.5 (13.8)</td>
<td>97.6 (24.5)</td>
<td>95.5 (30.5)</td>
</tr>
<tr>
<td>Creatinine clearance (75–125 ml/min)</td>
<td>67.8 (20.3)</td>
<td>63.8 (21.3)</td>
<td>70.6 (25.4)</td>
<td>77.5 (32.0)</td>
</tr>
<tr>
<td>Max. urine osmolality (&lt;750 mOsmol/kg)</td>
<td>823 (147)</td>
<td>805 (175)</td>
<td>791 (197)</td>
<td>834 (164)</td>
</tr>
<tr>
<td>Max. urine plasma H⁺ gradient (126–1,000)⁶</td>
<td>271 (200)</td>
<td>244 (164)</td>
<td>235 (171)</td>
<td>197 (135)</td>
</tr>
</tbody>
</table>

Values are mean (s.d.); *P < 0.001
patients with mild hyperparathyroidism. In the routine review of these patients we advocated that the plasma creatinine be measured at six monthly intervals. In view of the negative results in this paper and, from the patients' aspect, the relative complexity of these tests, we do not advocate assessing renal tubular function routinely in the conservative management of hyperparathyroidism.

The significant reduction of plasma alkaline phosphatase following surgery was not pursued in this study. Although none of the patients had radiological evidence of osteitis fibrosa, it does raise the possibility of minor bone changes having been present. Whether patients with mild hyperparathyroidism are subject to progressive osteopenia, and whether this is clinically significant in terms of causing an increased tendency to fractures is a problem which requires separate examination. This is particularly important as the majority of patients found to have mild hyperparathyroidism are elderly women who are already prone to osteoporosis and fractures. If this tendency is demonstrated it will also need to be shown that it can be prevented by successful parathyroid surgery.

References