Post-thyroidectomy hypocalcemia: The role of calcitonin, parathormone and serum albumin

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Serum calcium, inorganic phosphate, calcitonin, parathormone, albumin, triiodothyronine and thyroxine levels were measured during the surgical intervention and in the postoperative period to investigate the pathogenesis of post-thyroidectomy hypocalcemia in 25 female patients undergoing bilateral subtotal thyroidectomy for non-toxic nodular goiter. A highly significant fall in uncorrected serum calcium and albumin levels starting with the completion of lobectomies and a significant correlation between their gradient were observed. Early peak of calcitonin corresponded well with the falls in corrected calcium and inorganic phosphate levels. An overt parathyroid response to hypocalcemia was not encountered. On the basis of postoperative hypoalbuminemia, calcitonin leak triggered the early onset of hypocalcemia while insufficient parathyroid response contributed to post-thyroidectomy hypocalcemia. [Turk J Med Res 1994; 12(3): 127-130]

Key Words: Thyroid, Surgery, Post-thyroidectomy hypocalcemia

Though much work have been accomplished on the subject, the mechanism of post-thyroidectomy hypocalcemia still remains uncertain. Permanent hypocalcemia generally appears after 24-48 hours since the operation and related to ablation, devascularisation and infarction of the parathyroid glands (1-3). This is generally associated with radical thyroid surgery (2,4,5). The transient hypocalcemia occurring within 24 hours is seen more frequently. Many theories have been suggested to explain this complication. According to Michie’s (6) hypothesis, acute reversal of thyrotoxic osteodystrophy after thyroidectomy in thyrotoxic patients cause hypocalcemia (5,7,8). Many authors (9,10-13) object to this hypothesis which falls short in explaining the hypocalcemia seen in patients with non-toxic goiter or why the thyrotoxic patients become euthyroid by medication before the operation. It was first Suzuki (14) who suggested that the leak of calcitonin during the surgical manipulation of the thyroid gland may be the cause of hypocalcemia. Rasmusson (15) and Watson (16) showed strong evidences about the release of calcitonin during the manipulation causing hypocalcemia. Busetto (17) and Franz (12) found a postoperative rise in calcitonin levels but could not demonstrate a correlation between calcitonin and calcium. Although many others (3,5,10,12,13) opposed the thyrocalcitonin theory, Sawers (10), Franz (12), Falk (3) and Eforakopoulou (13) suggested that the fall in parathormone levels might be a contributing factor in the pathogenesis of transient post-thyroidectomy hypocalcemia. According to another hypothesis from Franz (12) and Falk (13), post-thyroidectomy hypoalbuminemia is the factor responsible from hypocalcemia. They found a significant correlation between the decline in serum calcium and albumin levels. However in all these previously done trials heterogeneous groups were used (eg: thyrotoxicosis versus euthyroid, total thyroidectomies versus nodulectomies, benign diseases versus malignancies). Thus, the results might have been influenced from the presence of many hypocalcemic factors.

The aim of this study is to investigate the possible role of calcitonin, parathormone and serum albumin on post-thyroidectomy hypocalcemia by using a homogeneous group.

MATERIALS AND METHODS

This prospective study was carried out to elucidate the pathogenesis of post-thyroidectomy hypocalcemia, in 25 consecutive female patients undergoing bilateral
The perioperative serum calcium (uncorrected and corrected), inorganic phosphate, calcitonin, parathormone, albumin, triiodothyronine and thyroxine figures are shown in Table 1.

**RESULTS**

The perioperative serum calcium (uncorrected and corrected), inorganic phosphate, calcitonin, parathormone, albumin, triiodothyronine and thyroxine figures are shown in Table 1.

Clinical hypocalcemia developed in only one patient (4%) with positive Chvostek’s sign that appeared on the 10th postoperative hour. Laboratory hypocalcemia, all within the first 24 hours, developed in 8 of 25 patients (32%).

**DISCUSSION**

Our patients undergoing bilateral subtotal thyroidectomy showed a transient fall in corrected serum cal-
Table 1. Perioperative mean (SE) serum calcium, inorganic phosphate, calcitonin, parathormone, albumin, T3 and T4 levels.

<table>
<thead>
<tr>
<th></th>
<th>t0</th>
<th>t1</th>
<th>t2</th>
<th>t3</th>
<th>t4</th>
<th>t5</th>
<th>t6</th>
<th>t7</th>
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<tbody>
<tr>
<td>Uncorrected Ca</td>
<td>9.3</td>
<td>8.4*</td>
<td>8.4*</td>
<td>8.8*</td>
<td>8.5*</td>
<td>8.6*</td>
<td>8.6*</td>
<td>8.6*</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>(0.1)</td>
<td></td>
<td></td>
<td></td>
<td>(0.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corrected Ca</td>
<td>9.3</td>
<td>9.0</td>
<td>8.9</td>
<td>9.1</td>
<td>8.8*</td>
<td>8.9*</td>
<td>9.1</td>
<td>9.2</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>(0.1)</td>
<td>(0.2)</td>
<td>(0.2)</td>
<td>(0.1)</td>
<td>(0.1)</td>
<td>(0.2)</td>
<td></td>
<td></td>
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<tr>
<td>I. Phosphate</td>
<td>3.7</td>
<td>3.2</td>
<td>3.3</td>
<td>3.00</td>
<td>3.5</td>
<td>3.6</td>
<td>3.4</td>
<td>3.4</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>(0.3)</td>
<td>(0.2)</td>
<td>(0.2)</td>
<td>(0.1)</td>
<td>(0.2)</td>
<td>(0.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcitonin</td>
<td>3.4</td>
<td>12.2*</td>
<td>14.8</td>
<td>6.5</td>
<td>6.3</td>
<td>6.1</td>
<td>4.2</td>
<td>4.0</td>
</tr>
<tr>
<td>(pg/ml)</td>
<td>(0.7)</td>
<td>(3.1)</td>
<td>(4.9)</td>
<td>(1.5)</td>
<td>(2.5)</td>
<td>(1.4)</td>
<td>(0.9)</td>
<td>(1.0)</td>
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<tr>
<td>Parathormone</td>
<td>27.4</td>
<td>24.7</td>
<td>39.8</td>
<td>25.0</td>
<td>23.2</td>
<td>18.5</td>
<td>41.6</td>
<td>26.0</td>
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<tr>
<td>(ng/ml)</td>
<td>(5.3)</td>
<td>(4.6)</td>
<td>(7.5)</td>
<td>(6.6)</td>
<td>(6.9)</td>
<td>(3.6)</td>
<td>(14.6)</td>
<td>(6.5)</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.5</td>
<td>4.0*</td>
<td>4.2*</td>
<td>4.3*</td>
<td>4.2*</td>
<td>4.2*</td>
<td>4.2*</td>
<td>4.1*</td>
</tr>
<tr>
<td>(g/dl)</td>
<td>(0.07)</td>
<td>(0.17)</td>
<td>(0.14)</td>
<td>(0.09)</td>
<td>(0.06)</td>
<td>(0.08)</td>
<td>(0.07)</td>
<td>(0.08)</td>
</tr>
<tr>
<td>T3 (ng/ml)</td>
<td>1.35</td>
<td>1.07*</td>
<td>1.05*</td>
<td>1.10*</td>
<td>0.94*</td>
<td>0.74*</td>
<td>0.83*</td>
<td>0.80*</td>
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<tr>
<td>(g/dl)</td>
<td>(0.5)</td>
<td>(0.4)</td>
<td>(0.5)</td>
<td>(0.4)</td>
<td>(0.4)</td>
<td>(0.4)</td>
<td>(0.5)</td>
<td>(0.4)</td>
</tr>
<tr>
<td>T4 (mg/dl)</td>
<td>10.4</td>
<td>10.6</td>
<td>11.1</td>
<td>10.0</td>
<td>9.3</td>
<td>9.3*</td>
<td>9.7</td>
<td>9.2*</td>
</tr>
<tr>
<td></td>
<td>(0.5)</td>
<td>(0.4)</td>
<td>(0.5)</td>
<td>(0.4)</td>
<td>(0.4)</td>
<td>(0.5)</td>
<td>(0.5)</td>
<td>(0.4)</td>
</tr>
</tbody>
</table>

t0: before the operation, t1: immediately after the resection, t2: one hour after the resection, t3: second postoperative hour, t4: sixth postoperative hour, t5: first postoperative day, t6: second postoperative.

*: significant difference, p<0.001
**: significant difference, p<0.01
*: significant difference, p<0.05

Calcium values; maximal at the sixth postoperative hour and regaining its normal level after 3 days. All the cases with clinical (4%) and laboratory (32%) hypocalcemia were detected within the first 24 hours.

Calcitonin is known as a serum calcium lowering hormone with a potentiated effect in hyperthyroidism. Its effect on post-thyroidectomy hypocalcemia is expected to be early and short, since its half life is only 2-15 minutes (18). In our study, the sharp peak in calcitonin and the marginal rise in T4 during operation suggests that the thyroid hormones may leak from the damaged thyroid remnant during surgical manipulation.

Although no statistically significant correlation between corrected calcium and calcitonin levels during t1-t7 were found, the significant rise at t1, t2 and the fall at t3 in calcitonin levels corresponded with the sharp decrease at t1, t2 and the fall at t3 in calcium.

While-Watson (16) demonstrated a significant correlation between calcium and calcitonin during the first 12 postoperative hours, Falk (13), Franz (12) and Eforakopoulou (13) disagree. This controversy was possibly because of the lack of early estimations of calcium and calcitonin in the latter group. Our results suggest that calcitonin may be a contributing factor on the early onset of postthyroidectomy hypocalcemia.

Serum inorganic phosphate levels during t1-t7 were all lower than the preoperative value, with elevations and falls. An overt parathyroid response to
hypocalcemia was not observed. In contrast to Franz (12), Falk (13) and Eforakopoulou (13) we could not find a correlation between calcium and parathormone in the early post-thyroidectomy hypocalcemia.

All the values for uncorrected serum calcium and albumin measured during the operation and postoperative period were significantly lower with respect to preoperative values. The highly significant correlation between their pattern within the first 24 hours (t1, t3, t4, t5) indicates the importance of postoperative hypoaalbuminemia on post-thyroidectomy hypocalcemia. Similarly in two different studies Franz (12) and Falk (3) demonstrated a strong correlation between post-thyroidectomy hypoaalbuminemia and hypocalcemia. Hypoaalbuminemia is also seen after nonthyroid surgery. Percival (11) has shown a marginal fall in serum calcium level in 11 patients who underwent minor abdominal surgery where the fall was less marked than in partial thyroidectomy. Falk (3) has reported a decline in serum calcium and albumin levels after nonthyroid surgery in 6 patients although the falls were not significant.

Postoperative hypoalbuminemia is possibly related to the hemodilutional effect of antidiuretic hormone and to the transcapillary leak accruing during the stress of surgery. Calcitonin leak played a trigger mechanism on the very early onset of hypocalcemia.

We conclude that postoperative hypoalbuminemia is the major factor in the pathogenesis of post-thyroidectomy hypocalcemia. On the basis of hypoaalbuminemia, trigger factors related to thyroid surgery or disease such as parathyroid damage, insufficient parathyroid response, calcitonin leak or thyrotoxic osseodystrophy result in post-thyroidectomy hypocalcemia.

**REFERENCES**


