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CALCITONIN ACTIVITY OF THE THYROID GLAND IN PRIMARY HYPERPARATHYROIDISM

By

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ABSTRACT

The thyroidal content of calcitonin was investigated in patients with euthyroid goitre, patients undergoing laryngectomies or neck operations and finally patients with primary hyperparathyroidism using method of biological titration. Patients with primary hyperparathyroidism had markedly decreased content of calcitonin in the thyroid gland when compared with the content of calcitonin of both groups of patients without calcium metabolism disturbance. Decreased content of calcitonin in patients with primary hyperparathyroidism can be explained by long lasting hypercalcaemia during which the rate of biosynthesis of calcitonin in the C cells does not keep up with the rate of release of calcitonin into the circulation.

Primary hyperparathyroidism is a generalized disorder of calcium, phosphate and bone metabolism that results from an increased and autonomous secretion of parathyroid hormone. The excessive concentration of circulating hormone usually leads to hypercalcaemia and hypophosphataemia. The role of calcitonin in this system has not been defined. Calcitonin lowers serum calcium and counteracts hypercalcaemic stress by inhibiting bone resorption. Although certain studies (Hirsch & Munson 1969) have established that calcitonin plays a role in protecting animals from hypercalcaemia the physiological role of calcitonin in man has not been clearly elucidated.

The concentration of calcitonin measured by the bioassay method in thyroid tissue was not detectable in 5 cases of primary hyperparathyroidism (Aliapoulis & Watts 1966). In later studies reported by Tashjian & Voelkel (1967) 6 of 8 patients with primary hyperparathyroidism showed negative concentrations and 2 were stated to be in the normal range. LiVolsi et al. (1973) found...
hyperplastic calcitonin containing parafollicular cells in 36% of 14 hyperparathyroid patients studied. For the first time Heynen & Franchimont (1974) using a radioimmunoassay method established that plasma calcitonin levels are statistically significantly increased in primary hyperparathyroidism. The plasma levels of calcitonin are increased in a manner proportional to the serum calcium and parathormone levels.

In the present study we have used the biological assay of calcitonin to determine the content of calcitonin present in the thyroid glands of patients with primary hyperparathyroidism, patients with euthyroid goitre and patients undergoing laryngectomies or neck operations.

**MATERIAL AND METHODS**

The human thyroid tissue collected was from 6 male and 2 female patients, aged 20–50 years undergoing laryngectomies or neck operation and 8 female and 2 male patients, aged 30–60 years with euthyroid nodular goitre. In addition to the 18 normal thyroid samples there were thyroid samples from 3 male and 16 female patients, aged 30–60 years with primary hyperparathyroidism. From all patients undergoing operation we had consent for removing of thyroid tissue. The mean duration of primary hyperparathyroidism was 2–5 years.

The diagnosis of primary hyperparathyroidism has been verified by surgery and histopathology. In all patients blood samples were taken before operation for the determination of plasma alkaline phosphatase and calcium.

Specimens of thyroid glands were obtained in the operating room at the time of operation. All specimens were taken from the same site of the thyroid lobe. Within a few minutes after excision the specimens (0.5–1.0 g) were frozen in dry ice at −20°C. The tissues were sliced into thin sections and homogenized for 30–60 seconds in 0.1 N HCl (5 ml) per g fresh tissue at 4°C in a Waring blender. The insoluble material was separated by centrifugation (8000 × g) 15–20 min at 4°C. The supernatant solutions obtained from centrifugation were assayed biologically for calcitonin using 100–120 g male rats according to method of Cooper et al. (1967). The extracts and standard (Calcitare, Armour) were injected subcutaneously into parallel groups of test rats. The control rats received the 0.1 N HCl only. The calcitonin content of thyroid glands was estimated by comparison with the calcitonin standard and was expressed as MRC mU/g fresh thyroid tissue.

The mean and 95% confidence limits were calculated for all the values obtained and the results were evaluated statistically by analysis of variance (Duncan 1955).

**RESULTS**

The thyroid samples from patients undergoing laryngectomies or neck operations without any changes in plasma calcium and plasma alkaline phosphatase had average content of calcitonin in the thyroid gland 38.1 ± 19.5 mU MRC/g fresh tissue (Table 1). The group of patients with euthyroid nodular goitre had
Results of experiment. Mean ± sd of plasma calcium, plasma alkaline phosphatase and thyroid content of calcitonin. The number of the groups with statistically significantly different means is given in brackets.

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<tr>
<th></th>
<th>No.</th>
<th>Calcium mEq./l plasma</th>
<th>Alkaline phosphatase KAU/100 ml plasma</th>
<th>Thyroid calcitonin MRC mU/g gland</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>8</td>
<td>4.8 ± 0.2</td>
<td>7.5 ± 1.2</td>
<td>38.1 ± 19.5</td>
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<td>(3)</td>
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<tr>
<td>Euthyroid nodular goitre</td>
<td>9</td>
<td>4.8 ± 0.1</td>
<td>8.5 ± 1.6</td>
<td>37.5 ± 14.7</td>
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<tr>
<td>(3)</td>
<td></td>
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<tr>
<td>Primary hyperparathyroidism</td>
<td>19</td>
<td>6.5 ± 0.4</td>
<td>39.6 ± 45.8</td>
<td>11.2 ± 4.0</td>
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an average content of calcitonin in the thyroid gland 37.5 ± 14.7 mU MRC/g fresh tissue (Table 1). Moreover this group of patients did not have any changes in plasma calcium and plasma alkaline phosphatase.

On the contrary, patients with primary hyperparathyroidism had markedly decreased content of calcitonin in the thyroid gland 11.2 ± 4.0 mU MRC/g fresh tissue when compared with the content of calcitonin in the thyroid gland of both groups of patients without calcium metabolism disturbance as shown in Table 1. In patients with primary hyperparathyroidism there was a statistically significant elevation in plasma calcium and in plasma alkaline phosphatase. Inside patients with primary hyperparathyroidism we did not observe any positive correlations between the content of calcitonin in the thyroid gland and plasma calcium and alkaline phosphatase levels.

**DISCUSSION**

Calcitonin can be measured in extracts of human thyroid tissue either by bioassay or radioimmunoassay (Tashjian & Voelkel 1974). The human thyroid has been found to yield much less hypocalcaemic activity per unit of weight than thyroid tissue obtained from most other mammalian species (Gray & Ontjes 1975).

The thyroidal content of calcitonin can be altered in a variety of pathological conditions. Dramatic increases are seen with primary C cell neoplasms in which concentrations of 100 to 5000 times the normal are commonly ob-
served (Anast & Conway 1972). Less dramatic increases in hormone stores are seen in thyroid tissue from pseudohypoparathyroid patients (Hirsch & Munson 1969). This increase is probably secondary to chronic hypocalcaemia since it is known that experimental hypocalcaemia can cause increased calcitonin content in the thyroid glands of rats.

On the basis of our experiments we conclude that the amount of calcitonin that is stored in the thyroid glands of a number of patients with hyperparathyroidism is markedly decreased when compared with the content of calcitonin of two groups of patients without hypercalcaemia. Decreased content of calcitonin in the thyroid gland of patients with primary hyperparathyroidism can be explained by long lasting hypercalcaemia during which the rate of biosynthesis of calcitonin in the C cells does not keep up with the rate of release of calcitonin into the circulation. Low content of calcitonin in the thyroid gland in primary hyperparathyroidism might be a secondary effect of the accelerated release of calcitonin into the circulation during long lasting hypercalcaemia. This is in good agreement with the levels of plasma calcitonin in patients with primary hyperparathyroidism as assayed by Heynen & Franchimont (1974) using radioimmunoassay.

The thyroid gland through calcitonin may protect patients against hypercalcaemia occurring during primary hyperparathyroidism. Calcitonin may also serve to protect the skeleton against excessive resorption by the parathyroid hormone.

REFERENCES


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