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Effect of Synthetic Salmon Calcitonin on Iodine Metabolism in Rabbits (38042)

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Calcitonin (CT) or thyrocalcitonin, a polypeptide hormone synthesized and released by the C-cells of the thyroid gland in mammals, is known to decrease calcium and phosphorus serum levels in most species (1). Some recent reports indicate an interrelationship between thyroxine (T_4), the hormone synthesized by the follicular cells of the thyroid gland, and CT. Thus, Yasumura *et al.* (2) reported a significant decrease of thyroidal CT following the administration of T_4 in rats; however, the hypocalcemic effect of exogenous porcine CT is also dependent of the T_4 administration to rats (3).

In a previous report, we found that the long-term administration of salmon calcitonin to rabbits induced a hyperplastic goiter (4). In order to clarify this goitrogenic effect, the present study was undertaken to investigate the action of synthetic salmon calcitonin (SCT) on different parameters of iodine metabolism in rabbits.

Materials and Methods. Long-term investigations were carried out in adult New Zealand rabbits. In the first group, SCT-treated, 8 rabbits of an average body weight of 4 kg, were injected im 3 times weekly, for 1 mo, with SCT (Armour Pharmaceutical Company; lot #K 640-046) dissolved in 16% gelatin solution. The specific activity of this calcitonin preparation was 4758 MRCU/mg. Each rabbit received daily 50 MRCU (Medical Research Council Units), in 0.8 ml gelatin, a total dose of 600 MRCU for a month. Parallel studies were performed in order to compare the effect of synthetic salmon cacitonin with its vehicle (16% gelatin solution).

Thus in the second group, treated with vehicle alone, 8 rabbits of 4 kg body weight received the same treatment for 1 mo, except for SCT, a total dose of 10 ml gelatin. A third group of 8 rabbits of the same body weight served as controls. All rabbits were fed during the period of experiments with Purina Chow Checkers and tap water was given *ad libitum*. At 2 hr following the injection of calcitonin and radioiodine (^{131}I) (10 μCi injected iv for each rabbit), blood was withdrawn from the jugular vein and the heart and urine from the bladder. Renal iodine (^{131}I) clearance was evaluated in each experimental group at 2 hr employing the following formula: $C_k = UV/P$. According to this formula, the renal iodine clearance (C_k) was determined by measuring the (^{131}I) concentration in urine (U) and the volume (V) and then it was divided by its concentration in plasma (P) (5). After pentobarbital anesthesia, rabbits were sacrificed and both thyroid lobes were removed. Radioiodine (^{131}I) studies were carried out on thyroid, blood and urine. Samples were counted in a standard Picker Na I-Th activated crystal well counter with a spectroscale III pulse height analyzer and the results were expressed as counts per minute (cpm) and per mg or ml. Serum thyroxine (T_4) determinations were performed with a standard Mallinckrodt Nuclear Res-O-Mat and protein-bound iodine (PBI) was estimated according to Riley's and Gochman's procedure (6). All results were presented as mean $\pm$SE and significant differences (P values) between all groups were evaluated by Student's test.

Results. The effect of SCT and its vehicle

TABLE I. Effect of Synthetic Salmon Calcitonin (SCT) on Iodine Metabolism in Rabbits.[a]

Groups	^{131}I Thyroid uptake (cpm/mg)	^{131}I Plasma uptake (cpm/ml)	^{131}I renal clearance (ml/min)	PBI (μg/100 ml)	T_4 (μg/100 ml)
SCT- (8) Treated	1250 ± 92[b]	2900 ± 100[b]	0.89 ± 0.009[b]	2.01 ± 0.01[c]	1.64 ± 0.01[c]
Vehicle (8) (16% gelatin)	2690 ± 150	7000 ± 220	0.12 ± 0.008	4.45 ± 0.02	2.80 ± 0.02
Controls (8)	2680 ± 120	7090 ± 150	0.11 ± 0.002	4.50 ± 0.02	2.82 ± 0.01

[a] Data are presented as Mean ± SE and the number of animals per group is in parenthesis.
[b] Represents $P < 0.005$ as compared to controls and vehicle groups.
[c] Represents $P < 0.01$ as compared to controls and vehicle groups.

(16% gelatin) on different parameters of iodine metabolism are shown in Table I. At the end of the 4 wk treatment period and at 2 hr after the last injection, SCT markedly reduced the ^{131}I uptake in thyroid gland as well as in plasma of treated rabbits as compared to controls or to the vehicle alone. Thus, the thyroid uptake was 1250 ± 92 cpm/mg as compared to 2680 ± 120 cpm/mg of controls, and plasma uptake of ^{131}I was 2900 ± 100 cpm/ml as compared to 7090 ± 150 cpm/ml found in controls. PBI and T_4 serum levels were also decreased, respectively 2.01 ± 0.01 μg/100 ml as compared to controls 4.50 ± 0.02 μg/100 ml and thyroxine 1.64 ± 0.01 μg/100 ml as compared to controls 2.82 ± 0.01 μg/100 ml. Conversely, the renal iodine clearance was much elevated (8 times higher) in calcitonin-treated rabbits as compared to controls, respectively 0.89 ml/min after calcitonin and 0.11 ml/min in controls. No changes in radioiodine metabolism were observed in rabbits treated with the vehicle alone (Group II) or in the controls (Group III).

Discussion. The results of this study demonstrate that the chronic administration of SCT significantly reduces the ^{131}I incorporation in the thyroid gland as well as in the plasma of rabbits ($P < .005$). Also PBI and T_4 levels are effectively decreased ($P < .01$). Meanwhile, the radioiodine renal clearance is 8 times higher following calcitonin administration ($P < .005$). This means that synthetic salmon calcitonin induces a decrease of radioiodide uptake in the thyroid gland and in plasma and a marked increase of iodine excretion through urine in rabbits. This ioduric effect of salmon calcitonin is not mentioned by other investigators and it can explain the goitrogenic process induced by this hormone. It is known from earlier observations than an increased renal clearance of iodine leading to iodine depletion can produce a nontoxic goiter in some patients (7). Thus, in addition to its calciuric, phosphaturic and natriuric effects as previously reported (8), salmon calcitonin in large doses exerts a strong ioduric effect in rabbits. The present work emphasizes that calcitonin, except for its role in calcium and phosphorus significantly affects the iodine metabolism and can exert an important role in thyroid physiology.

Summary. Long-term administration of synthetic salmon calcitonin to rabbits markedly decreases the radioiodine (^{131}I) uptake in the thyroid gland as well as in the plasma. Protein-bound iodine and thyroxine serum levels are also decreased. In contrast, the renal iodine clearance is much increased in calcitonin-treated rabbits as compared to controls or to vehicle alone. This ioduric effect of salmon calcitonin can explain its role in goiter induction.

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