CALCITONIN AND INSULIN SECRETION IN NORMAL MAN:  
STUDY WITH SOMATOSTATIN AND CALCIUM

Francesco Caviezel向下 
Ruggero Mangili

Cattedra di Clinica Medica Generale e Terapia Medica VIII
Cattedra di Endocrinologia Sperimentale
Università degli Studi di Milano - Ospedale S. Raffaele, Milano

Somatostatin inhibition of stimulated insulin secretion in vitro can be quickly relieved by increasing calcium ion concentration in the perfusate; however, this finding cannot be reproduced in vivo, neither in normal subjects nor in hypoparathyroid patients after restoration of calcium hemostasis.

This phenomenon might be partially explained by simultaneous stimulation of calcitonin (CT) secretion by calcium, despite somatostatin administration.

In this regard, it is important to note that: (a) the effect of somatostatin on CT secretion in normal man is still uncertain: though Metz et al. found no effects either on basal or on calcium-stimulated plasma CT levels, a recent report emphasizes a 40% inhibition of basal CT secretion; (b) salmon CT administration produces an inhibition of both glucose- and arginine-stimulated insulin secretion in normal man and in insulin-dependent diabetics; furthermore, endogenous CT is able to inhibit insulin secretion in normal man.

Thus, we aimed to ascertain whether the failure of calcium to reverse insulin secretion during somatostatin infusion is due, at least in part, to an unhampered CT secretion, which in turn induces further inhibition of insulin release.

Key-words: Calcitonin; Calcium; Insulin; Somatostatin.

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MATERIALS AND METHODS

Informed consent was obtained from 7 healthy human male subjects, aged 23 to 27; none of them was obese or suffered from endocrine or metabolic disease; all subjects were instructed not to take drugs for at least one week before the experiments.

All tests began between 08°0 and 09°~ after an overnight fast. A 19-gauge scalp vein needle was introduced into each antecubital vein and kept patent with a slow infusion of saline; two baseline samples were obtained in order to allow a 15-min equilibration period. Serum obtained from each specimen was kept frozen at −30 °C until assayed for CT, insulin, total calcium, phosphorus and magnesium; plasma glucose was determined shortly after sampling.

Calcium infusion test - Each subject was given calcium gluconate by i.v. infusion over a 10-min period (3 mg/kg elemental calcium from min 0 to min 10); blood samples were drawn from the contralateral antecubital vein at min −15, 0, 10, 15, 30, 45 and 60.

Somatostatin and calcium infusion test - In 3 subjects a calcium infusion test was repeated during somatostatin infusion. Somatostatin (cyclic somatostatin, Serono, Rome, Italy) was dissolved in saline and administered i.v. through a constant rate infusion pump; a priming dose of 33.3 μg/min from min 0 to 10 was followed by an infusion rate of 8.3 μg/min from min 10 to min 120. Calcium (3 mg/kg) was infused from min 60 to min 70. Specimens were obtained at min −15, 0, 15, 30, 60, 70, 75, 90, 105 and 120.

Assays - CT was assayed by RIA (I.R.E., Fleurus, Belgium); the sensitivity of this method is of 12 pg/tube; inter- and intra-assay variations are 20% and 10% respectively.

Insulin was also assayed by RIA (Serono-Biodata kit); its sensitivity is of 2 μU/ml.

Serum total calcium, phosphorus and magnesium were determined by spectrophotometric analysis; plasma glucose was determined by the oxdase method.

Data were statistically evaluated by paired Student's t-test.

RESULTS

In all subjects calcium administration (tab. 1, fig. 1) produced a prompt rise of calcemia (from 4.47 ± 0.06 to 5.81 ± 0.14 mEq/l, X ± SEM; p<0.001); serum CT increased significantly in 6 of the 7 subjects studied (from 77 ± 17 to 178 ± 31 pg/ml, X ± SEM; p<0.01); in one subject we observed negligible basal CT levels and no response to i.v. calcium; however, a positive and significant correlation between calcemia and serum CT was observed in each of the remaining subjects (0.69<r<0.94; 0.01<p<0.05). No significant variations of serum phosphorus and magnesium were seen. Serum insulin showed a reduction from basal levels, mostly at min 10 and 15 (~18.1% and ~32.8%, respectively; p<0.02), while plasma glucose levels showed a slight, but significant increase at min 30, 45 (p<0.02) and 60 (p<0.05).