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Changes of the growth hormone level after a single small dose of somatostatin

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Growth hormone (GH) secretion was studied in children after a single small intravenous (i.v.) dose of somatostatin (Somatotropin Release Inhibiting Factor, SRIF). After a short decrease of the GH level there was a slow increase culminating at 60 minutes, then again a decrease with the lowest point at 90 minutes. During the third hour the GH level showed a second peak; this was more frequent than the first one. It is concluded that a single small dose of somatostatin during the third hour after its administration can cause an increase of the GH level.

Pituitary GH secretion is regulated by two hypothalamic hormones, a stimulatory (GH-releasing factor, GRF) and an inhibitory one (somatostatin, SRIF) [2, 4]. SRIF has been characterized as a tetradecapeptide and it is commercially available in synthetized form [6]. This inhibitory factor suppresses GH and TSH and outside the pituitary it does not only inhibit the secretion of insulin and glucagon but also that of a large number of other gastrointestinal polypeptides [9]. Considerable work has been done on the in vivo effects of exogenous SRIF, but little is known about the changes of the GH level after a single bolus administration of SRIF. Because of its very short half life (2–4 minutes) it is mostly applied in infusion [2] and the GH level was estimated only in the first hour after terminating the infusion.

We have studied the late effect of a single small i.v. dose of SRIF on the GH level during three hours.

Patients and Methods

Twenty-five healthy children and twelve GH deficient patients were studied. None of the healthy volunteers had a history of endocrine disease. GH was tested with the standardized RIA method of Pharmacia (Uppsala) 20 minutes and immediately before and 5, 10, 20, 30, 45, 60, 90, 120, 150 and 180 minutes after injecting 5 μg/kg of SRIF or physiological saline. After the first nine tests blood sampling was done only at –20 and 0 min and in the second and third hours. In the GH deficient children the GH level was studied at 0, 90, 150 and 180 minutes, and also at 210 minutes.

GH deficiency was diagnosed on the basis of short stature, bone age retardation, delayed growth, normal thyroid function, cytogenetic normality, negative insulin induced hypoglycaemia and DOPA tests (GH peak value-$<$ 14 mU/L).

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Results

The mean GH values of healthy children showed the inhibitory effect of SRIF on GH release during the first ten minutes, followed by a rebound during the next 50 minutes. The individual reactions were different in the second period; the peak occurred at 20 minutes in 7 children, at 30 in 3 children, at 45 in 6 children and at 60 minutes in 4 children, and the standard deviations were high (26.8—31.4). At 90 minutes there was a second low point with 5.8 ± 8.0 mU/L GH and then a second peak above 14 mU/L. (10 individual peaks out of 14 occurred at the last two samplings.)

Physiological saline did not provoke this undulation of the GH level except for an increase at 0 minute which was ascribed to the venous puncture.

None of the GH deficient patients had an increase of the GH level during the last period of the test (150—210 minutes).

Discussion

The rebound of GH secretion has been observed in adults at the end of SRIF infusion in studies of 30—60 minutes duration [1, 3, 5]. In our experiments SRIF was given in a single small dose and the GH level was followed for three hours, to study the late effect of exogenous SRIF. A single intravenous injection of 5 μg/kg provoked an undulation of the GH level with a second peak at 150—180 minutes; this peak was observed more frequently than the rebound during the first hour.

Table I

GH level (mean ± S. D.) before and after 5 μg/kg somatostatin or physiological saline

Minutes	GH mU/L					
	Healthy children				GH deficiency somatostatin	No
	No	Somatostatin	phys. saline	No		
—20	(16)	12.0±18.4	7.3±4.4	(5)	—	
0	(20)	14.6±17.0	12.3±0.5	(4)	1.9±2.0	(12)
5	(9)	7.6±7.6	—		—	
10	(11)	5.8±5.6	5.0±1.7	(2)	—	
20	(18)	9.8±7.4	4.0±1.9	(4)	—	
30	(10)	17.8±28.4	1.5±0.1	(2)	—	
45	(12)	19.0±26.8	4.4±2.6	(3)	—	
60	(9)	20.6±31.4	0.8±0.3	(2)	—	
90	(19)	5.8±8.0	3.3±1.6	(4)	2.3±1.9	(10)
120	(19)	7.2±5.8	2.6±1.8	(5)	—	
150	(13)	12.0±8.0	0.9±0.4	(3)	2.4±2.2	(12)
180	(14)	16.0±24.1	2.8±1.8	(5)	2.6±2.1	(12)
210		—	—		2.5±1.8	(8)

It has been assumed that SRIF upsets the balance of endogenous GH regulating hormones if their production is sufficient and we have found a significant difference in the GH curves of normal and GH deficient children [7]. On the basis of this observation we have studied the effect of combined administration of somatostatin and DOPA to estimate the GH capacity [8].

Our hypothesis has been supported by some recent results. During insulin-induced hypoglycaemia a rise in the plasma endogenous somatostatin level was seen, culminating at 60 minutes [10] or during the second hour [11]. One group hypothesizes that this change of the somatostatin level after insulin hypoglycaemia is related to alterations in metabolic stimuli [11], but Martin supposes [4] that the increases in the GH level are dependent on GRF release and cannot be accounted for by a rebound release from endogenous somatostatin inhibition.

We thus believe that the peaks in the first and third hours are caused by a predominance of GRF and the endogenous somatostatin is responsible for the low point at 90 minutes [7, 8].

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