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Preliminary reports

EFFECTS OF CENTRALLY APPLIED SANDOSTATIN ON THE PITUITARY GH CELLS IN MALE RATS

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INTRODUCTION

Sandostatin is a synthetic somatostatin (SRIH) analogue, which consists of 8 amino acid residues (BAUER *et al.*, 1982). It exerts very strong inhibitory effect on growth hormone (GH) secretion. Due to the much longer half-life (around 110 minutes) (WASS 1990) in comparison with natural SRIHs (SRIH-14 and SRIH-28), Sandostatin was first that was used in the treatment of GH-secreting adenomas. It is also used in cancer therapy as well as in therapy of various gastrointestinal disorders. Sandostatin interacts primarily with somatostatin receptors (sstr) 2 and 5 (SCARPIGNATO 1996) and with greater stability than native somatostatins.

In this report, the effects of intracerebroventricular (i.c.v.) Sandostatin administration on immunocytochemical and stereological properties of GH cells in adult male rats are demonstrated.

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MATERIALS AND METHODS

In our experiment 3 months old Wistar male rats (210-230 g) were used. The animals were implanted with a headset later serving for i.c.v. injections. A minimum recovery time of 5 days was permitted before the onset of experiment. The animals were divided into two experimental groups each including five rats. Those from the first group were i.c.v. given three 1.0 mg doses of Sandostatin (Novartis Pharma AG, Basle, Switzerland) dissolved in 10 mL saline, every second day. The second group serving as a control was treated in the same way and by the same schedule with saline only. All animals were sacrificed in deep anaesthesia by decapitation, 5 days after the last injection. The pituitary glands were excised, fixed in Bouin's solution and embedded in paraffin. Pituitary GH cells were localized by the peroxidase-anti-peroxidase-complex (PAP) method of STERNBERGER *et al.* (1970). Measurements were performed on the widest portion of the pituitary gland. Immunocytochemically-labelled GH cells were analyzed by the M42 test system after WEIBEL (1979). For the calculations of the cellular (Vc; mm^3) and nuclear (Vn; mm^3) volumes as well as the volume density (Vvc; %) of GH cells, formula of WEIBEL (1979) was used. Stereological data obtained from each rat were averaged *per* experimental group and standard deviation of the mean (S.D.) was calculated using Student's *t-test*. A probability value of 5% or less was considered statistically significant.

RESULTS

Data on body weight, absolute and relative weights of the pituitary glands in Sandostatin-treated group and the controls is summarized in Table 1. As seen,

Table 1. - The effects of Sandostatin on body weight, absolute and relative pituitary weight in adult rat males

Experimental Group	Body weight (g)	Absolute pituitary weight (mg)	Relative pituitary weight (mg%)
Control	234 ± 15.1	12.1 ± 2.3	4.1 ± 0.7
Octreotide-treated	228 ± 8.3 (-3%)	10.6 ± 0.6 (-12%)	3.9 ± 0.2 (-5%)

The values represent the means ± SD. (n=5/group).

body weight, absolute and relative pituitary weights were not significantly changed in comparison with corresponding controls ($p>0.05$). Immunocytochemically identified GH cells in control rat pituitaries ranged from ovoid to pyramidal in shape, with a spherical centrally located nucleus. GH cells were usually situated along blood capillaries. In the pituitaries, of Sandostatin-treated rats, GH cells were smaller, irregularly shaped, with more intensely stained cytoplasm. All measured stereological parameters were significantly ($p<0.05$) decreased in Sandostatin - treated group compared with controls (Fig 1). The volume of GH cells and their

nuclei were significantly ($p<0.05$) decreased by 15%, 12% respectively, in comparison with control values. The volume density of GH cells and decreased by 12% ($p<0.05$) in the pituitaries of Sandostatin treated rats, compared to the controls.

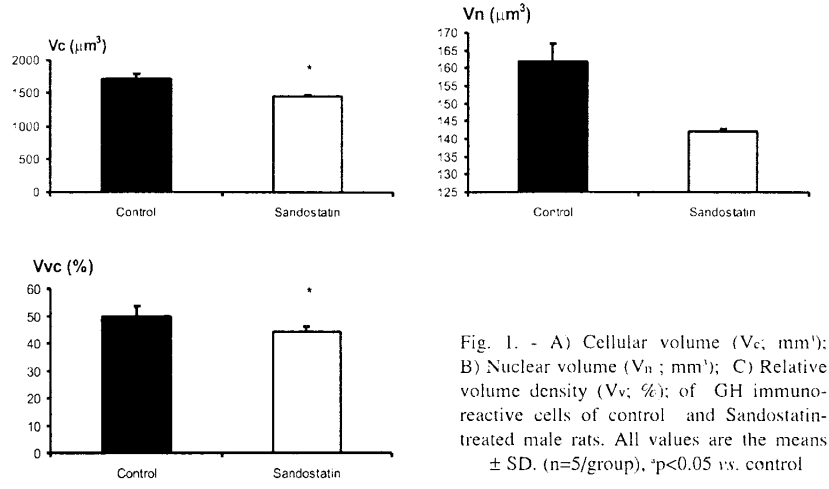

Fig. 1. - A) Cellular volume (V_c; mm^3); B) Nuclear volume (V_n ; mm^3); C) Relative volume density (V_v; %); of GH immunoreactive cells of control and Sandostatin-treated male rats. All values are the means ± SD. (n=5/group), *$p<0.05$ *vs.* control

DISCUSSION

The results presented above demonstrate that repeated i.c.v. bolus injections of Sandostatin significantly decreased all measured stereological parameters and altered immunocytochemical properties of GH cells in adult male rats. The biological actions of SRIH are mediated through its five distinctive receptor subtypes (sstr1-5) (PATEL AND SRIKANT 1994). Sandostatin primarily interacts with sstr2 and sstr5 and binds with a moderate affinity to sstr3 (ÖSAPAY AND ÖSAPAY, 1998). O'CARROLL and KREMPELS (1995) proved the presence of all five somatostatin receptor subtypes in somatotrophs, thyreotrophs, mammotrophs, corticotrophs and gonadotrophs in the pituitaries of male rats.

In conclusion, our results indicate that i.c.v.-applied Sandostatin, exerts significant inhibitory effects on the immunocytochemical and stereological characteristics of GH cells in adult male rats.

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