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REGULATION OF SERUM CORTISOL BY SOMATOSTATIN: EVIDENCE OF NEUROENDOCRINE CONTROL OF ADRENAL GLAND IN AMPHIBIA

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ABSTRACT

The role of somatostatin in plasma cortisol level in *Rana tigrina* (amphibia,anura) has been investigated. An inhibitory impact on both, intact (16.32%) as well as pharmacologically annuled frogs(23.27%) has been recorded. It is concluded that in both the conditions, it act as a preventive agent to counteract any excess secretion of cortisol due to the failure of classical regulatory mechanism.

INTRODUCTION

Somatostatin is one of the several hypothalamic peptides which has been localized in the adrenal of many vertebrates (Delarue *et al.,* 2001,Lesouhaitier *et al.,* 1995) .Somatostatin bearing neurons and chromaffin cells have been identified in the adrenal of many vertebrates including amphibians (Gilliemen, 1992, Epelbaum *et al.,* 1994, Gillies, 1997) Despite its wide occurrence, its role in the regulation of cortical hormones has not been ascertained even in major vertebrate taxa (Mazzocchi *et al.,* 1985, Delaure *et al.,* 1990, Hanke and Kloa, 1995). The study was undertaken to know the neuroendocrine regulation of cortisol by somatostatin in an amphibian, *Rana tigrina*.The objective was achieved by estimating serum cortisol level in normal and somatostatin treated intact and pharmacologically annuled individuals.

MARETIALS AND METHODS

Seventy five frogs (*Rana tigrina*) were taken from their natural habitat and acclimatized in laboratory conditions.They were divided into five groups each consisting of 15 individuals. On the first day of the experiment the individuals of 1st group were sacrificed to assess the normal level of cortisol in the blood. Members of 2nd group were kept untreated for the entire period of the experiment (i.e.14 days) and the blood was collected on the last day of the experiment to see the effect of environment on cortisol profile if any. Members of the group 3 were treated with dexamethasone (@2.5mg/kg body weight) and captopril (@8.5mg/kg body weight) for seven days to inhibit the effect of ACTH and RAS, the classical regulatory factor. From the eighth day, 4th group of frogs were injected somatostatin (@5μg/kg body weight) along with the same dose of inhibitors to see the effect of somatostatin on annuled frogs. The last group of frogs were treated with the same dose of somatostatin for seven days and the cortisol profile was recorded to assess the effect of somatostatin on normal individuals.

All the samples from each set of experiment were assayed together to minimize the inter-assay variation. The cortisol profile was determined by ELISA with the help of cortisol kit.The data obtained were statistically evaluated with the help of paired sample t-test at 95% confidence level (Zar 2004).

RESULTS

The normal range of cortisol in frog is 16.80-31.50μg/dl with an average of 24.88 $\pm$ 1.80 μg/dl. The pharmacological annulation has shifted the range to 12.70-25.50μg/dl with an average of 18.39 $\pm$1.44 μg/dl. The depressive effect on cortisol is 26.09% as a result of dexamethasone and captopril treatment.The administration of somatostatin in these annulated frogs has further brought down the range to14.16-20.10μg/dl with an average of 14.11 $\pm$1.11 μg/dl. The inhibitory effect is 23.27% when compared to annuled condition. The administration of somatostatin alone in intact animals have also evoked a responsive action of 16.32% when compared to normal level of cortisol. The somatostatin has depressed the range to 13.90-27.10μg/dl with an average of 20.80 $\pm$1.62 μg/dl.Data of cortisol level in normal and variously somatostatin treated individuals were obtained during the

study and the interpretation have been presented in Table1, Fig.1.

In recent days, a number of neuropeptides have been screened for their adrenocorticotropic activities(Toth *et al.,* 1997, Mazzocchi *et al.,* 1998) but the effect of somatostatin on the secretion of glucocorticoids has not been investigated. The earlier reports concern mostly the regulation of mineralocorticoids, the aldosterone. Mazzochi *et al.,* (1998) and Pawlikowski *et al.,* (1990) noted depressed steroidogenesis in zona glomerulosa of rats. A direct inhibitory effect on aldosterone secretion has also been observed (Kasprzak *et al.,* 1991). Inhibition of growth and secretory capacity of zona fasciculata as a result of somatostatin infusion has been recorded by Rebuffat *et al*., (1994). Somatostatin has been recorded to be a potent and specific inhibitory factor for zona glomerulosa.The data involving somatostatin in the regulation of cortical hormones in sub mammalian vertebrates is also scant and restricted to aldosterone only.An inhibitory effect of somatostatin on corticosteroid and aldosterone in turkey (*Meleagris gallopavo*) has also been documented (Mazzocchi *et al.,* 1997). Interestingly in domestic turkey, adrenocortical cells have been noted to be unresponsive.The effect of somatostatin on the regulation of cortisol, a glucocorticoid has not been investigated. The results clearly depicts an inhibitory action on cortisol secretion in frog. The present result further extend the involvement of somatostatin in the domain of glucocorticoid at least in amphibian. The inhibitory influence of somatostatin is more pronounced in annuled frogs i.e 23.27% while in intact, it is only 16.23%. The author believes that somatostatin acts only during special circumstances as a fine tuner when there is a failure of classical inhibitory factors for adrenal to prevent or counteract excessive secretion of cortisol.

Table 1: Highly significant effect of somatostatin treatment on cortisol level(*µg*/dl) in frog *Rana tigrina*

Treatment Types	Range in *µg*/dl	Mean in *µg*/dl	Standard Deviation	SEMwith 95%C.L.	Stimulation/ Inhibition	Stimulatory/ Inhibitory in%
Normal	31.25-16.80	24.88	4.48145	1.80	-	-
Dexa+Capt.	25.50-12.70	18.39	3.5569	1.44	Inhibition*** t= 20.89623	Inhibitory 26.09%
Dexa+Capt+ Somatostatin	20.10-8.20	14.11	2.7404	1.11	Inhibition*** t=18.0006	Inhibitory 23.27%
Somatostatin only	27.10-13.90	20.80	4. 0409	1.62	Inhibition*** t= - 3.6940	Inhibitory 16.32%

*** $p < 0.001$; C.L. =Confidence Limit

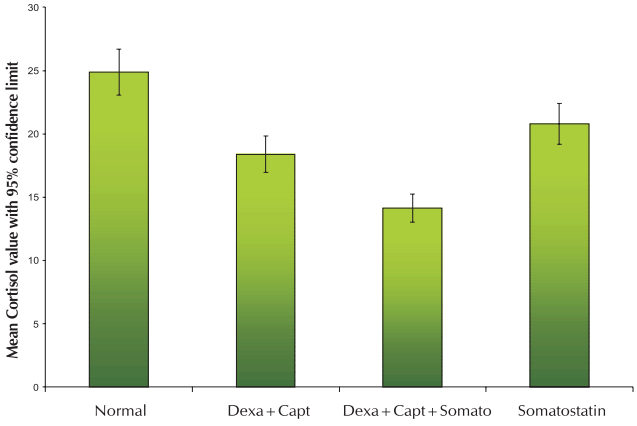

Figure1: Mean cortisol value in different treatment groups (somatostatin treated frogs)

The author further believes that somatostatin acts directly on cortisol producing cells and not via ACTH or RAS system since use of inhibitors exclude these possibilities. Regarding the pathway it is suggested that being a neuropeptide, it can always communicate with the effector cortisol producing cells or influence these cells in paracrine manner, a pathway suggested for other signaling biomolecules of adrenal tissues (Nussdorfer, 1996).

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