Modulation of serum cortisol by Substance P in albino rats: Evidence of a direct effect on adrenal gland

Anita Prasad, Ranu Naskar, Rakhi Dubey, Dipali Raha & M Firoz Ahmed*
Department of Zoology, Ranchi University, Ranchi 834 008, India

Received 1 April 2005; revised 12 July 2005

Effect of prolonged administration of substance P on the plasma cortisol level in the albino rats has been investigated. An inhibitory impact on intact individuals and a stimulatory effect in pharmacologically annulled rats has been observed. It is concluded that in normal conditions substance P presumably acts as a preventive agent for any excess secretion of cortisol while during stress or disturbed HPA or RAS conditions, it stimulates the secretion of cortisol. An intraglandular modulatory role of substance P has been suggested.

Keywords: Cortisol, Regulatory role, Substance P

The mechanism of regulation of cortical hormones has occupied a central stage of probing in adrenal research resulting in a quantum change in the perception of regulatory mechanism. Now the concept and information have travelled to a long distance from the early dogma of classical regulation by ACTH, RAS and Na⁺/K⁺ to a multifactorial regulatory mechanisms. Recently, a number of findings have accumulated to suggest that cortical hormones are also influenced by intraglandular peptides and systemic factors of diverse origin. The increasing list of such agents has been described amply in several reviews.

The tachykinins have been identified in both chromaffin cells and nerve endings within the adrenal complex of various vertebrates. Substance P belongs to a highly conserved family of regulatory peptides of tachykinins. Nussdorfer has recorded the involvement of substance P in the regulation of aldosterone section. The present study was undertaken to assess the role of substance P in the secretion of cortisol. The aim was achieved by estimating serum cortisol concentration in normal and pharmacologically annulled albino rats.

For the present study, 50 adult albino rats were selected and maintained on a standard diet in laboratory conditions for 15 days. After acclimatization, they were divided into two equal groups. On the first day of experiment, 1 ml of blood from the retro-orbital veins of each individual of both groups was collected to determine the normal level of cortisol. This level of cortisol was always considered as normal cortisol value for comparison with values of subsequent treatments. The animals of first group were given subcutaneous injection of substance P (0.1 mg/kg) for 7 days. Blood samples were collected one hour after the last injection to assess the level of cortisol as a result of substance P administration in intact animals. Simultaneously, the individuals of second group were given subcutaneous injection of dexamethasone (2.5 mg/kg) and captopril (8.3 mg/kg) daily for 7 days to suppress hypothalamo-pituitary-adrenal axis and rennin-angiotensin system. On the 7th day of the treatment the blood samples were collected to determine the effect of pharmacological annulation by the inhibitors. From the 8th day onwards the individuals of second group continued to receive the same amount of dexamethasone and captopril coupled with Substance P (0.1 mg/kg) for the next 7 days. On the 14th day the blood samples were collected and assayed for the cortisol level as these values depict the effect of Substance P on pharmacologically annulled individuals.

The cortisol level of these samples was estimated using competitive enzyme immunoassay (EIA). The enzyme penicillinase was used as marker for the “Trace” F-21-HS Pen (Cortisol-21-Hemisuccinate Penicillinase conjugate). The estimation was done by double antibody method. The detailed protocol has been given elsewhere. Data in relation to cortisol level in normal and variously treated individuals obtained during the present study and the interpretation have been presented in Table 1.

A large number of intraglandular adrenocortical factors (regulatory molecules) influencing the secretion of various zones of adrenal cortex has been identified. A close relationship between tachykinin and hypothalamo-pituitary-adrenal axis has also

*Correspondent author
Phone: 0651-2233806 (O); 2562786 (R)
E-mail: nisargasen2003@yahoo.co.in
been demonstrated\textsuperscript{13}. The probable role of substance P in the adrenal functioning has been investigated only in relation to aldosterone, a secretory product of zona glomerulosa and both stimulatory\textsuperscript{14,15} and inhibitory\textsuperscript{16} effects on aldosterone release has been recorded. The present result has extended the functional domain of this tachykinin from zona glomerulosa to zona fasciculata-reticularis, as its influence on cortisol secretion is very conspicuous. During the present study, it was noticed that in intact animals, substance P inhibits the secretion of cortisol whereas in pharmacologically annulled cases, it plays a stimulatory role. It appears that in traglandular substance P acts as fine tuner for cortisol secretions from adrenal complex and assumes important role in circumstances. It is concluded that in normal condition the substance P inhibits steroidogenesis in the inner zones of cortex and acts as preventive agent for any excess secretion of cortisol, while during stress or malfunctioning of HPA axis, Substance P assumes a stimulatory role for cortisol section.

One of us (RN) is thankful to CSIR, New Delhi for financial assistance in the form of an SRF (NET).

**References**