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SHORT REPORTS

RESPONSES OF ADRENAL GLAND TO LITHIUM DURING HYPOTHYROIDISM IN AN AVIAN SPECIES.

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ABSTRACT

The effect of lithium on adrenal hormones was studied during experimental hypothyroid condition in pigeon. The investigation revealed that experimentally altered thyroid function had a depleting effect on the adrenomedullary catecholamines. Normally, lithium depleted the catecholamine level but had no effect on the corticosterone contents of the pigeon adrenals. However, lithium was found to counteract the effect of hypothyroidism but showed no effect on corticosterone contents of the pigeon adrenals. This suggested that lithium differed in function on the adrenals during hypothyroid condition in pigeon.

Keywords: Lithium, adrenal hormones, hypothyroidism, pigeon

INTRODUCTION

Lithium is frequently used in the treatment of manic-depression. It requires chronic administration for its therapeutic efficacy. One of the main concerns is the wide range of endocrine related side effects due to prolonged lithium injection (Mannisto, 1980). The extra-hypothalamic pathway of lithium action is fairly well documented in mammals. Thus lithium chloride is found to cause inhibition of hormonogenesis in the thyroid gland and decreased secretion of thyroid hormones into the blood (Semenov *et al.*, 1981; Bistriceau *et al.*, 1986), stimulation of adrenomedullary secretion (Terao *et al.*, 1992; Chauloff *et al.*, 1992). The activity of the adrenal cortex has also been found to be increased in a dose-dependent manner by lithium in rats (Ghosh *et al.*, 1990). On the other hand, in birds, very scanty information is available regarding lithium induced changes in the thyroids. A solitary report by Ghosh *et al.*, (1999a) in pigeon showed that lithium differs in function on the adrenal during hyperthyroidism by showing non responsiveness to catecholamines but increased activity of the cortex. As a sequel to the previous study, the present experiment has been performed in order to examine what changes do lithium cause in the adrenal gland during hypothyroidism in pigeon (*Columba livia*).

MATERIALS AND METHODS

After collection, domestic pigeons (*Columba livia*) with average body weight of 200 g, were acclimatized to uniform laboratory conditions with *ad libitum* food and water prior to experimentation. Birds were divided into four groups. A thyrohormone inhibitory drug, Neo-mercazole (carbimazole, I.P., Nicholas Piramal Limited, India) was given orally to the birds belonging to the first group at a dosage of 0.5 mg/bird/day continually for 10 days. Lithium chloride (Fisher Laboratory, USA) was injected intraperitoneally at a dosage of 3 meq/kg body weight to the second group of birds and autopsied after 4 hrs. To the third group, Neo-mercazole, in a similar dosage was given for 10 days and on the 11th day, at 4 hrs. prior to autopsy, lithium chloride was given following the manner as adopted for only lithium treated group. The remaining group served as untreated control. All the birds were sacrificed by cervical dislocation, both the adrenals and the thyroids were processed for biochemical estimations. Catecholamine and corticosterone were estimated spectrofluorometrically by the methods of Laverty and Taylor (1968) and Glick *et al.*, (1964) respectively. Spectrophotometric estimation of thyroid peroxidase was done following the method of Bergmeyer (1980). Level of significance was calculated by students' t-test (Snedecor and Cochran, 1967) at $P<0.05$.

RESULTS

The biochemical data are presented in Table 1. Lithium chloride treatment significantly decreased the glandular level of epinephrine, norepinephrine and peroxidase. Neo-mercazole, when applied exclusively, was found to respond in a similar manner as found during lithium chloride alone, but in the latter case, the rate of depletion is more pronounced. In contrast to exclusive lithium chloride treatment, those receiving a combined treatment of neo-mercazole and lithium were found to show an unaltered level of glandular epinephrine, norepinephrine and peroxidase. Corticosterone remained non-responsive in all the treatments.

Table 1 Effect of Neomercazole and lithium chloride on adrenal catecholamines and corticosterone and thyroid peroxidase in *Columba livia*. Values are expressed as mean ± standard error. Figure in parenthesis indicate the number of birds used.

Group	Epinephrine (µg/mg tissue weight)	Norepinephrine (µg/mg tissue weight)	Corticosterone (µg/g tissue weight)	Peroxidase (ΔO.D./min/ mg protein)
1. Control	0.665±0.08 (5)	0.133±0.01 (5)	7.82±1.38 (5)	1.51±0.47 (4)
2. Lithium treated	0.405±0.05 (4) *i P<0.025	0.099±0.01 (3) *i P<0.050	6.98±2.55 (5) *i NS	0.43±0.01 (4) *i P<0.050
3. Neomercazole treated	0.224±0.04 (5) *i P<0.001 *ii P<0.025	0.074±0.01 (4) *i P<0.005 *ii NS	5.98±1.22 (5) *i NS *ii NS	0.38±0.09 (5) *i P<0.050 *ii NS
4. Neomercazole + Lithium Treated	0.294±0.06 (5) *i P<0.005 *iii NS	0.099±0.01 (5) *i P<0.050 *iii NS	7.38±0.79 (5) *i NS *iii NS	0.51±0.07 (5) *i NS *iii NS

*i Normal VS groups 1, 2, 3 *ii Lithium VS Neomercazole *iii Lithium Vs Neomercazole + lithium

DISCUSSION

It is known lithium chloride stimulates the secretion in adrenal medullary cells and triggers a dose-dependent increase in plasma epinephrine and norepinephrine level (Terao et al., 1992; Chouloff et al., 1992). In pigeon, lithium treatment is able to reduce the tissue store of catecholamines significantly (Ghosh et al., 1999b). Similarly, depleting trend of glandular catecholamines (though not statistically significant except in case of epinephrine) was also found during neo-mercazole induced hypothyroidism. Thus experimentally induced thyroid hypoactivity appears to interfere with the medullary function. It is to be mentioned here that during eltroxin induced hyperthyroid condition, adrenomedullary catechol hormones were found to remain normal in the same avian species (Ghosh *et al.*, 1999a). When compared to birds with hypoactivity of the thyroids (i.e. Group 2), lithium was found to elevate the tissue store of epinephrine (+31%) and norepinephrine (+33%) in hypothyroid birds (i.e. Group 4). Whereas, lithium failed to change the tissue stores of catecholamines in pigeon during hyperactivity of the thyroids. Hence it can be assumed that lithium may counteract the effect of Neo-mercazole induced catecholamine depletion.

Corticosterone, on the other hand, remained normal in all the treated groups showing nonparticipation of adrenal cortex in hypothyroid condition during lithium regimen. In contrast, hyperthyroidism increased the glandular titre of corticosterone reflecting a greater quantity of synthesis/storage of this corticoid during lithium administration (Ghosh *et al.*, 1999a). In future, it may be a concern to the therapeutists when administering lithium to the hypo / hyperthyroid patients.

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