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Effect of Lithium chloride on the Endocrine Pancreas of Domestic Pigeon (*Columba livia*)

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Abstract : Though there are numerous antis - psychotic drugs, currently Lithium salts are therapeutically used for the treatment of many depressive illnesses in psychiatry. Lithium acts through the hypothalamic pathway, but it also produces side effects on the peripheral endocrine glands. Our knowledge is still limited regarding the latter aspect, so mechanism of lithium action through the extra - hypothalamic pathway is, still in some way, unexplored and must be elucidated for a better insight.

The present investigation deals with the action of lithium chloride (LiCl) on the endocrine pancreas, *i.e*. Islets of Langerhans regarding histological and certain biochemical parameters. Our study revealed that, high dosage of LiCl treatment initiates high mobilization of alpha cell granules,- indicating a storage of the hormone glucagon. It also increased the blood glucose and slightly depleted the liver glycogen of the pigeons. The probable mechanism behind these results was briefly discussed.

Key words : Lithium chloride, islets of Langerhans, domestic pigeon

Introduction :

Though there are a number of anti - psychotic drugs, lithium salts are therapeutically used nowadays for the treatment of many depressive illnesses in psychiatry, especially manic depression. Lithium acts through the hypothalamic pathway (Banerji *et al.*, 1984), but it also produces side effects on the endocrine glands including the adrenals, pancreas, thyroid and the gonads (Jacobs, 1978; John *et al.*, 1979; Mannisto, 1980). Our knowledge is still limited regarding the latter aspect, so mechanism of lithium action through the extra - hypothalamic pathway is, still in some way, unexplored and must be elucidated for a better insight.

As the endocrine pancreas (*i.e*. islets of Langerhans) is concerned, lithium has been found to produce marked changes in glucose metabolism. Weiss (1924) initially reported that lithium had a favorable action in diabetic patients. Later reports suggested that, lithium may exacerbate diabetes mellitus (Saran, 1982), and the conflicting reports as to whether or not glucose tolerance is decreased (Shopsin *et al.*, 1972), increased (Vandesborg, 1978) or unchanged (Lazarus *et al.*, 1981) remains to be resolved.

The present investigation deals with the effect of lithium on the islets of Langerhans. Specifically, its effect on blood glucose and gluconeogenesis (from estimation of liver glycogen) were studied. Histological

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observation of endocrine pancreas was also performed regarding this treatment. Our experimental model is the domestic pigeon (*Columba livia*).

Materials and Methods :

Adult domestic pigeons were used for the present investigation. Birds were obtained from local bird dealer and acclimatized in laboratory condition for, at least, a week before the experiment. Food and water were given *ad libitum*. Finally, birds were divided into four groups : (I) Control, (II) 3 m.eq. (= milli equivalent) lithium treated, (III) 6 m.eq. lithium treated and (IV) 9 m.eq. lithium treated. Lithium chloride (LiCl) [Fisher Scientific Lab., USA] was injected intra-peritoneally. For group (II),- LiCl was injected at a dosage of 3 m.eq. / kg. body weight for 4 hours; for group (III),- LiCl was given in 6 m.eq. / kg. body wt. for 4 hours and for group (IV),- 3 m.eq. / body wt. LiCl was injected twice on the first day (= 6 m.eq.). Further, 3 m.eq. of the salt was given to this group (total = 9 m.eq. / kg. body wt.) on the second day and after this third dose, birds were kept for 4 hours and then sacrificed. All the pigeons were fasted for 12 hours prior to autopsy.

All the birds were killed by cervical dislocation. Blood was collected by puncturing the wing veins and, after autopsy, ventral lobe of the pancreas and a portion of liver were dissected out. Blood glucose was estimated by Nelson and Somogyi's method (Oser, 1979). Following usual microtechnique, 7 m sections of pancreas were stained by Masson's Trichrome stain method. Glycogen was estimated biochemically from liver (Plummer, 1990). Statistical analysis was performed by Student's t test (Snedecor and Cochran, 1967).

Results :

Histological : The ventral lobe of the pancreas contains the highest number of islets. Each section contains one or two very large islets which are mostly oval in shape and have regular margins. These islets are made up mostly of alpha cells, which secrete Glucagon. The smaller islets are of the mixed type, containing both alpha and beta (secreting Insulin) cells. The large islets are extensively supplied by the fibrous ramifications of the connective tissues.

Control : The alpha cells are large and the cellular outlines are usually well delineated. Some of the cells are polygonal and some are columnar in shape. The alpha cell nuclei are round or oval with prominent nucleoli. These cells are seen to be almost uniformly covered by large, course granules. The beta cells are mostly tall, columnar and touch the basement membranes. The nuclei are situated at one end, opposite to the membranes. It was also observed that the nuclei are either round or oval, though at times, they are irregular.

Treated : No perceptible changes were noted after 3 m.eq. and 6 m.eq. LiCl treatments. However, cytomorphological alteration became prominent in alpha cells after 9 m.eq. lithium treatment. Granules among these cells became large and densely packed when compared to the cells of control pancreas (*i.e*. storage of granules was clearly evident). Alterations in beta cells were not so profound.

Biochemical : Results of the blood glucose and liver glycogen estimations are given in Table - 1. Regarding the control values, both blood glucose and liver glycogen levels were seen to be slightly altered, - only after 9 m.eq. LiCl treatment. The former slightly increased, while the latter was found

Table 1 : Effects of Lithium chloride treatment (in 3 doses) on blood glucose and liver glycogen of domestic pigeon (*Columba livia*).

Groups	Blood glucose (mg %)	Liver glycogen (mg / mg tissue)
Control	254.83 ± 11.26	3.14 ± 0.06
(Group I)	(n = 6)	(n = 6)
LiCl treated *	251.89 ± 10.94	3.45 ± 0.04
(Group II)	(n = 6)	(n = 6)
	N.S.	N.S.
LiCl treated *	214.76 ± 12.16	3.92 ± 0.07
(Group III)	(n = 6)	(n = 6)
	N.S.	N.S.
LiCl treated *	286.85 ± 14.61	2.68 ± 0.07
(Group IV)	(n = 6)	(n = 6)
	N.S.	N.S.

* See text
Figures in parentheses represent number of specimens.
(+) Mean ± standard error N.S. : Not significant

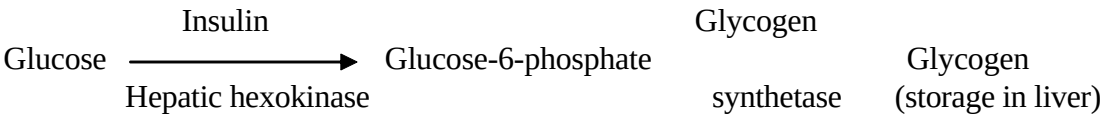
to be decreased a little. Though, both the values were not statistically significant.

Discussion :

Our present investigation revealed that, acute but high dosage of lithium treatment initiates a high mobilization of alpha cell granules (indicating a storage of glucagon) along with an increase of blood glucose and slight depletion of liver glycogen. glucagon converts glycogen into glucose (Glycogenolysis / Gluconeogenesis). In the present experiment, however, it appears that there is a paucity of glucagon secretion (due to its storage). So, we can expect more storage of glycogen and less glucose formation. But the result is contrary to what is being expected. Therefore, in the present context, it may be quite possible that insulin is probably playing a greater role than glucagon. Insulin, which is secreted from the beta cells of the islets, converts glucose into glycogen according to the pathway shown below :

Probably, lithium in a high dose (9 m.eq. / kg body weight) affects the function of insulin which, in turn, is unable to convert more glycogen from glucose (*i.e.* glycogenesis is somewhat retarded). As a result, amount of blood glucose increases but the tissue store of glycogen depletes.

Understanding of these problem will be clarified if, in future, we study the cellular



complex of lithium - treated islets with the help of more specific staining methods. Possibly, a parallel study on quantitative determination of insulin will also be fruitful.

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