EFFECT OF LITHIUM CARBONATE ON RENAL AND EXTRA-RENAL FUNCTIONS OF RATS

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SUMMARY

Effect of high doses of lithium carbonate (40 mg/Kg. i. p. and p. o.) and lithium chloride (40 mg/Kg. i. p.) on renal and extra-renal functions were studied in normal male Charles Foster Strain of rats. Insignificant effect on urine output, creatinine clearance, sodium, potassium and lithium excretion was observed with these salts. Antidiuretic hormone levels were also not effected. However lithium clearance was significantly raised in both groups with lithium carbonate and with lithium chloride treated rats. Lithium carbonate and lithium chloride had failed to produce nephrogenic polyuric syndrome in this strain of rats.

Lithium carbonate has been widely used in clinical practice for treatment of manic depressive psychosis. Plasma levels of lithium above 1 or 2 meq/litre may cause a nephrogenic syndrome like diabetes insipidus (Forrest et al., 1974). lithium chloride has been used extensively in experimental studies to evaluate its pharmacological profile. As the pharmacokinetic disposition of lithium carbonate and chloride are different, it was of interest to study the effect of lithium carbonate and chloride on renal and extrarenal functions in rats.

MATERIALS AND METHODS

Male Charles Foster strain of rats (200±20 g.) were kept in individual metabolic cages at room temperature (24°C) and maintained on standard pellet diet (Hind Lever Ltd., India) and tap water ad libitum.

Lithium carbonate suspension was given orally or i.p. at the dose of 40 mg/kg. Lithium chloride was given in same dose i. p. Urine out put was recorded in paraffin coated polyethylene cages. Rats were given p.o. or i.p. doses thrice and three such groups were used for the experiments. Rats were sacrificed 4 hour after the fourth dose of lithium salts.

Blood was collected in heparinized tubes and posterior pituitary was dissected from pitutary gland and extract was prepared as described by Daniels et al. (1967). Pressor activity was estimated on urethanized (25% solution 0.6 ml/100g. B. W.) and priscoline (10 mg/ kg. i. v.) treated rats (Dekanski, 1952). Kidneys of either side were dissected out removing perirenal fascia from its pedicle and around. Both kidneys were removed and wet weights were determined on an analytical balance.

Blood and urinary creatinine were determined by Jaffe’s reaction. Plasma and urinary lithium, sodium and potassium were measured by flame photometer.

RESULT:

Effect of Lithium carbonate on renal functions

Urine out put, creatinine clearance, lithium clearance, sodium and potassium excretion are shown in table I in control and in lithium carbonate treated rats by i.p. and p.o. routes (40 mg/kg) urine out put was insignificantly increased compared with the control values but the difference was not statistically significant. Creatinine clearance, urinary sodium and potassium excretion did not change to significant levels on lithium
### TABLE 1. Effect of Lithium carbonate (40 mg/Kg p. o. and i. p.) on renal functions.

|                              | Control   | i. p.     | Oral      |
|------------------------------|-----------|-----------|-----------|
| Urine output ml/min          | 4.06±0.76 | 4.9±0.46  | 4.13±1.05 |
| Urine output ml/min g KW     | 6.6±0.82  | 8.2±0.76  | 6.9±1.4   |
| G. F. R. ml/min              | 461±54    | 462±16    | 466±87    |
| G. F. R. ml/min g KW         | 766±80    | 728±77    | 866±106   |
| Lithium clearance ml/min     | 0.020±0.01| 0.148±0.09| 0.122±0.05|
| Lithium clearance ml/min g KW| 0.034±0.01| 0.306±0.15| 0.205±0.08*|
| Sodium excretion meq/min     | 16.3±3.2  | 23±6.0    | 20±5.0*   |
| Sodium excretion meq/min g KW| 26.6±3.8  | 38.9±10.9 | 34.7±10.7 |
| Potassium excretion meq/min  | 17.6±5.5  | 15.0±3.6  | 14.4±3.7  |
| Potassium excretion meq/min g KW| 28.3±8.0 | 25.3±6.7  | 24.9±7.0  |

KW = Kidney weight
* = P<0.001

Effect of Lithium carbonate administration. Lithium clearance in the control rats was 0.020±0.10 ml/min. However, on lithium carbonate exposure values increased to 0.184±0.09 ml/min in i. p. group while slightly lower value 0.122±0.05 ml/min in oral group, the difference is statistically significant (p <0.001).

**Effect of Lithium carbonate on extra renal functions**

Lithium carbonate (40 mg/Kg), i.p. or p. o. had no effect on the pituitary antidiuretic hormone level Table 3a.

### TABLE 2. Effect of ‘Lithium chloride’ (40 mg/Kg i. p.) on renal functions.

|                              | Control   | i. p.     |
|------------------------------|-----------|-----------|
| Urine output ml/min          | 1.7±0.36  | 1.3±0.33  |
| Urine output ml/min g K. W.  | 2.7±0.74  | 2.3±0.61  |
| Creatinine ml/min            | 629±144   | 505±103   |
| Creatinine ml/min g K. W.    | 1136±146  | 906±185   |
| Lithium clearance ml/min     | 0.015±0.002| 0.103±0.027*|
| Lithium clearance ml/min g K. W.| 0.029±0.005| 0.185±0.027**|
| Sodium excretion meq/min     | 32.1±9.4  | 30.7±5.3  |
| Sodium excretion meq/min g K. W.| 33±14.6  | 35.4±10.1 |
| Potassium excretion meq/min  | 7.1±1.4   | 6.9±0.0   |
| Potassium excretion meq/min g K. W.| 12.9±2.3 | 12.3±0.27 |

K. W. = Kidney Weight.
* = P<0.02
** = P<0.01
significant levels. Lithium chloride in fact slightly decreased the urine output instead of increasing as was observed with the lithium carbonate. Lithium clearance did show statistically significant change (p<0.02) on Lithium chloride administration to rats.

Effect of Lithium chloride on extra-renal function

Lithium chloride (40mg/kg.) i.p. has failed to produce any significant change in pituitary antidiuretic hormone levels in the rats, Table 3b.

TABLE 3(a). Effect of Lithium carbonate on ADH levels of rat.

| Sl. No. | Control | ip | Oral |
|--------|---------|----|------|
| 1.     | 95      | 92 | 94   |
| 2.     | 95      | 92 | 94   |
| 3.     | 128     | 140| 140  |

Mean±S. E. 106±11 109±16 109±15

TABLE 3(b). Effect of lithium chloride on ADH levels of rat.

| Sl. No. | Control | ip |
|--------|---------|----|
| 1.     | 92      | 89 |
| 2.     | 59      | 112|
| 3.     | 123     | 101|

Mean±S. E. 91±20 101±8

ADH mU/100 g of body weight.

DISCUSSION

Administration of high doses of lithium carbonate and chloride (40 mg/Kg/day) in male Charles Foster strain of rats have failed to produce the marked polyuric diabetes insipidus like syndrome as reported by Dousa, (1974); Stenchristensen (1976) and Schou (1958). In our model lithium clearance is statistically significant on administration of these two salts of lithium. I. P. clearance is higher than p. o. clearance. It is thus clear that i. p. absorption of lithium carbonate is better than lithium carbonate p. o. Rats failed to produce polyuria may be due to the higher doses used in this study. Higher doses are non diuretic as compared to lower dose of lithium chloride used in other studies (Dousa, 1974; Trop Pederson, 1973; Stenchristensen, 1976).

Jenner and Macniel (1975) have shown that lithium chloride on chronic exposure cause increase in urinary ADH activity and thus antidiuresis in rats. In our results lithium chloride caused slight reduction in urine volume. It may be due to the augmentation of peripheral antidiuretic activity. Pituitary ADH did not show change which further confirms the observations and the slight reduction may be due to its peripheral effects. Stenchristensen (1976) has reported that there is slow development of polyuria in rats which may be due to increased rate of secretion of the ADH. In our experimental rats, non-development of polyuric syndrome may be due to the increased activity of the ADH, which needs further elucidation by measuring plasma ADH levels.

Recently Walker et al. (1981) have shown that patient maintained on lithium therapy and patient with affective disorders prior to lithium therapy, chronic renal damage did not differ significantly in the two groups of patient. Glomerular filtration rate was not effected as is the case in this study of rats.

It is thus concluded that two type of salts in Charles Foster strain of rats are resistant to develop polyuric syn-
drome on lithium chloride and carbonate administration in higher doses.

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