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SCIENCE

Lithium carbonate toxicity in sprague dawley rats

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ABSTRACT

Lithium carbonate is commonly used in the treatment of bipolar disorder and in delaying the progression of amyotrophic lateral sclerosis. However a narrow therapeutic window and safety concerns limits its clinical utility. The present study was carried out on forty eight sprague dawley (SD) rats divided in to group I, II, III and IV (each having six male and six female rats) for the period of 30 days to study the effects of lithium carbonate on haemato-biochemical parameters and organ weight. The group I served as control while group II, III and IV were gavaged with lithium carbonate @ 10, 40 and 80 mg/kg bodyweight respectively. Exposures of lithium carbonate resulted in decrease in relative organ weights of spleen, thymus, prostate and uterus and significantly altered the hemato-biochemical parameters as compared to control.

Key words: Organ weight, Hemato-biochemical changes, Lithium carbonate, sprague dawley rats

INTRODUCTION

Lithium carbonate is well-recognized dietary and environmental toxicant. Nevertheless it is used to treat manic states and bipolar disorder in humans. Elemental lithium is a component of metal alloys; lithium hydride is used as a nuclear reactor coolant. Lithium hydroxide is used in alkaline storage batteries; lithium carbonate and lithium borate are used in the ceramic industry; and lithium chloride and fluoride are used in welding and brazing fluxes. There is little information on the effects of lithium on the organ weights and hemato-biochemical parameters. We hence designed this study to evaluate the effects of lithium carbonate on the organ weights and hemato-biochemical parameters in SD rats.

MATERIAL AND METHODS:

Animals were maintained in accordance with CPCSEA guideline and experiment was approved by the Institutional Animal Ethics Committee. SD rats of 5-6 weeks age were used for experiment and were housed in polypropylene cages with 2 animals per cage. Animal room temperature was maintained between 18-25°C with 12 h light/dark cycle. Animals were provided certified lab animal diet and RO water ad libitum. An acclimation period of five days was allowed before start of experiment.

The subacute toxicity study of lithium carbonate was evaluated on 48 SD rats divided into 4 different groups each consisting of 6 male and 6 female rats. The group I served as a control and was given only deionised water orally for 30 days. The group II, III and IV were orally dosed with lithium carbonate @ 10, 40 and 80 mg/kg body weight respectively for 30 days. Body weight, and feed consumption of all the rats were measured initially on day 1 and then on 8th, 15th, 22nd and 29th day of experiment. Rats were observed twice a day until sacrifice for presence of any clinical signs. At the end of experiment all the rats were fasted overnight and subjected to blood collection via retro-orbital sinus and then sacrificed. The detailed postmortem examination of each rat from different groups was performed and gross changes were recorded. The internal organs viz. liver, kidney, intestine, lung, spleen, heart and testis were collected, weighed and preserved in 10% neutral buffered formalin for further histopathological examination.

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RESULTS

Among different groups of male and female rats the significant decrease in relative organ weight was observed in group IV towards the end of experiment. The male and female rats of group IV showed increase in relative brain weight and decrease in relative thymus weight. Male rats of group IV showed decrease in relative spleen and prostate weight and increase in relative adrenal weight. Female rats of group IV showed decrease in relative uterus weight (Table 1). Animals from group IV also developed polydipsia and polyuria during the experiment.

For hematological and biochemical estimation, blood was collected from retro-orbital sinus before necropsy. Oral administration of lithium carbonate in group IV female resulted in significant reduction in RBC value, hemoglobin, hematocrit value and MCV (at $p<0.05$) with marked increase in WBC. Significant increase in clotting time, serum total protein and increase in blood glucose level in female rats was also observed (Table 2).

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Table 1 : Different groups with dose rate

Organ	Gr. I (0.0 mg/kg b.wt.)		Gr. II (10.0 mg/kg b.wt.)		Gr. III (40.0 mg/kg b.wt.)		Gr. IV (80.0 mg/kg b.wt.)	
	Male	Female	Male	Female	Male	Female	Male	Female
Brain	0.557 ± 0.052	0.780±0.029	0.587 ± 0.109	0.860±0.051	0.598±0.0569	0.830±0.031	0.754* ±0.106	0.966*±0.134
Spleen	0.212 ± 0.016	0.290±0.100	0.210±0.018	0.231±0.120	0.222±0.022	0.216±0.082	0.140*±0.035	0.212±0.094
Adrenals	0.015 ± 0.003	0.031±0.004	0.021±0.007	0.033±0.005	0.019±0.004	0.036±0.002	0.027*±0.006	0.032±0.005
Prostate	0.148±0.034	-	0.142±0.046	-	0.174±0.051	-	0.090*±0.017	-
Uterus	-	0.204±0.043	-	0.221±0.049	-	0.231±0.054	-	0.147*±0.028
Thymus	0.161±0.034	0.214±0.021	0.172±0.029	0.216±0.026	0.155±0.036	0.202±0.037	0.105*±0.046	0.196*±0.043

Key: * = Significant ($p < 0.05$)

TABLE 2: Hemato-biochemical changes in female rats after lithium carbonate administration:

	G I		G II		G III		G IV	
	Male	Female	Male	Female	Male	Female	Male	Female
WBCx 103/ul	9.373± 2.2744	7.482±2.5799	8.800±1.6663	7.635±3.0726	8.822±1.2794	7.617±2.1613	7.750±2.7556	8.133±1.4996
RBCx 106/ul	8.250±0.5296	8.097±0.4068	7.982±0.5107	7.535±0.2604	7.720±0.2288	7.860±0.1811	9.648±0.9850	7.337±0.5574
HGB g/dl	15.733±0.7685	15.383± 0.8424	15.133±0.7633	14.517±0.8280	14.650±0.3782	15.367±0.7146	18.033±1.8779	13.417±1.1890
HCT%	47.150±2.8515	45.45±2.3382	45.067±3.1399	43.117±2.8301	43.600±1.4792	44.650±2.3990	52.033±4.4693	37.733±3.8614
MCVfl	57.250±2.6151	56.183±1.6154	56.483±1.8798	57.200±2.2262	56.517±2.0952	56.800±2.0572	53.983±1.0815	51.383±2.2418
PTSec.	8.95±2.4550	8.3667±0.4131	8.467±0.5465	8.283±0.5456	8.483±0.3251	8.300±0.2280	24.450±28.6100	16.717±5.0042
Total Protein g/dl	6.742±0.1444	7.348±0.2199	6.793±0.2674	7.095±0.3012	6.422±0.2915	7.165± 0.2870	6.440±0.3326	5.980±0.2297
Glucose mg/dl	75.333±11.1295	84.833±8.1097	88.667±10.5388	95.667±9.1141	90.333±7.8401	91.667±15.3319	112.333±40.6776	91.833±22.4537

WBC: White Blood Cells, RBC: Red Blood Cells, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean Corpuscular Volume, PT: Prothrombin Time. Data are presented in mean ± S.E. Statistical significance was evaluated by ANOVA (analysis of variance), followed by Dunnett's t-test. Difference in mean values was considered statistically significant (*) at $p < 0.05$.

DISCUSSION

We observed that administering lithium carbonate orally for 30 days at 80 mg/kg/day resulted in reduction in organ weights due to severe adverse effects on body weight gain in both sexes of SD rats.[1,2,4] Brain weight generally remains static even in the case of severe body weight loss, but to our surprise we observed increase in brain weight 80 mg/kg/day lithium carbonate treated group. Oral lithium carbonate administration resulted in increase in water intake and urine output. This could be due to inability to concentrate urine by dilated tubules of kidney. Polyuria was compensated by increased water intake (polydipsia) in all animals in the high dose group.[3,5,8]

Decrease in RBC count, hemoglobin content, hematocrit value and MCV is indicative of macrocytic hypochromic type of anemia which might have affected the body condition of animals due to hypoxia.[3] Increase in WBC count is indicative of condition developed to remove waste products generated due to lithium induced damaged[3] to tissues. Significant increase in prothrombin time (clotting time) is indicative of ability of lithium to prevent / delay clotting of blood.[3]

Significant reduction in total protein is related to kidney damage and could also be due to reduced body weight after lithium administration.[3] Serum glucose increase was observed in animals from group IV may be indicative of altered glucose metabolism due to adverse effect of lithium administration on host metabolism pattern resulting in reduction in glucose utilization by animals.[6, 7]

Significant decrease in relative weight of prostate, uterus, spleen and thymus was evident in animals due to lithium administration.[2] Reduction in prostate weight could be due to the complete blockage of prostate secretion after lithium administration. Due to lithium, reduction in sperm concentration / density in cauda epididymis and secretion of seminal vesicle were completely blocked.[2,9]

CONCLUSION

The overall findings gave impression that lithium carbonate induced polyuria which might have affected hemato-biochemical parameters and organ weights in the current study.

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