Original Article

Anatomy

Depletion of Body and Cerebellar Weights after Chronic Lithium Carbonate Ingestion in Albino Rats

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ABSTRACT

Objective: The effect of Lithium on the body and brain are well known but enough literature is not available on the effects of Lithium on body and Organ weights. So this study was undertaken to see the effect of Lithium on body and cerebellar weights.

Study Design: An experimental study.

Place and Duration of Study: This study was conducted at the Anatomy Department BMSI, JPMC, Karachi. **Duration of study**: April 2012 to June 2012.

Materials and Methods: Thirty male albino rats of 200-250 grams were selected and divided into two major groups A and B. Each major group consisted of 15 animals each groups was further divided into three sub-groups according to the time period of the study which was 2 weeks, 6 weeks and 12 weeks. Group A served as control group which was given lab diet and B was the Lithium treated group. Lithium carbonate was given at a dose of 20mg/kg/day for 2, 6 and 12 weeks. Body weights were recorded at the start and of each time period, but cerebellar, Organ weights were recorded at the end of 2^{nd}, 6^{th} and 12^{th} weeks. The body weights and Organ weights are recorded on digital electronic weighing scale.

Results: Group B showed a progressive decrease of body and cerebellar weights as the time period of study advanced. But relative cerebellar weights of group B increased with increasing time period of study. **Conclusion:** The present study concluded that Lithium carbonate causes a significant decrease of body and cerebellar weights.

Key Words: cerebellum, Lithium carbonate. Relative Weights, Lipid Peroxidation

INTRODUCTION

Lithium received its name from Greek word "Lithos"[1], which means stone, with symbol "Li" [2]. Lithium is the gold standard, mood stabilizer [3]. Lithium salts are useful in treatment of bipolar and unipolar [4] depressions. Lithium carbonate is often referred to as an anti-maniac drug but in many parts of the world, it is considered as the mood stabilizing agent because of its role in preventing mood swings with bipolar affective disorder.[5] It is used for other disorders, such as cycloid psychosis, major depression, cluster headache [6], and schizophrenia. [7] In 1970, the Food and Drug Administration of USA approved lithium as preventive or prophylactic treatment for depressive illness. [8] A cohort study [9] conducted in United Kingdom for the usage of lithium as a mood stabilizer determined that increment in prescribing lithium for women was 33% and 24.1% for men in the year 1995 to 2009.

Lithium is highly effective in the treatment of bipolar disorders and has multiple effects on embryonic development, glycogen synthesis, hematopoiesis, and other biological processes. A variety of enzymes have been proposed as potential targets of lithium action, including inositol monophosphatase, a family of second messenger, and the protein kinase glycogen synthase kinase-3. It was found that GSK-3 inhibition increased translocation of nuclear factor of activated T-cells, ¾ (NFAT C3/4) transcription factors to the nucleus leading to increased Fas ligand (FASL) levels and Fas activation which causes cell death (apoptosis), and it is worth noting that levels of lithium-induced apoptosis was highest in cerebellum.[10] Since chronic lithium administration in rats is known to cause decreased body weight. [11] Lithium effects have been investigated in detail in the brain, intestine, liver and thyroid functions.[12]

In the light of above facts this study had been designed to evaluate the detrimental effect of lithium carbonate on body and cerebellar weight.

MATERIALS AND METHODS

This study was conducted in the department of anatomy, Basic Medical sciences Institute (BMSI), Jinnah Postgraduate Medical Center (JPMC), Karachi. For this study 30 male Albino rats of 200-250 grams of weights were selected for study. They were kept under observation for 7 days prior to commencement of study. The animals were randomized into two experimental groups each comprising of 15 rats. Each major group was divided into three sub-groups that were A1, A2 and A3, B1, B2 and B3 according to the time period of the study that is 2 weeks, 6 weeks and 12 weeks. Group A served as control and group B received Lithium Carbonate, taken from Adamjee Pharmaceuticals, at a dose of 20 mg/kg/day in powder form mixed in flour pellets.[13,14,15] The standard laboratory Chow was available ad libitum. The rodents were weighed at the

start and at the end of each time period. The relative organ weight was taken as the ratio of absolute organ to final body weight and the results were recorded. The albino rats were decapitated. Than the brain was taken out and the cerebellum was separated from the rest of the brain, absolute organ weights were recording on digital weighing balance. Data collected was analyzing using students "t" test. Results were expressed as mean, SEM P<0.05 was considered statistically significant. All calculation was done by utilizing computer software SPSS 16.

RESULTS

The final body weights of group B animals were significantly decreased P<0.001 with increasing time period as compared to control group A.

Table No.1: Mean* body weight (gm) in different groups of Albino rats at start and at the end of experimental procedure.

Comparative statistical analysis of differences in mean body weight of different groups at the end of 2nd weeks

Group	Initial			Final			Major Groups P-value	P-value
	Mean	S.D	SEM	Mean	S.D	SEM		
A (ND)	213.8	3.8	1.72	221.5	3.8	1.71	B v/s A	<0.001
B (Li)	215.4	13.4	5.98	204.1	19.3	8.64		

Mean* ± SEM P-value <0.001 Highly Significant***

The above data showed that the mean final body weight of group B animal decreased significantly (P<0.05) than the initial body weight at the end of 2nd weeks. Comparative analysis of group B shows a highly significant (P-value <0.001) decrease in body weight as compared to that of A.

Mean* body weight (gm) in different groups of Albino rats at start and the end of 6th weeks.

Comparative statistical analysis of differences in mean body weight of different groups at the end of 6th weeks

Group	Initial			Final			Major Groups P-value	P-value
	Mean	S.D	SEM	Mean	S.D	SEM		
A (ND)	202.0	8.8	3.92	249.5	9.5	4.25	B v/s A	<0.001
B (Li)	230.4	27.1	12.12	157.2	13.4	5.99		

Mean* ± SEM P-value <0.001 Highly Significant***

The above data showed that the mean final body weight of group B animal decreased significantly (P<0.05) than the initial body weight at the end of 6th weeks.

Comparative analysis of group B shows a highly significant (P-value <0.001) decrease in body weight as compared to that of A.

Mean* body weight (gm) in different groups of Albino rats at start and the end of 12th weeks. Comparative statistical analysis of differences in mean body weight of different groups at the end of 12th weeks

Group	Initial			Final			Major Groups P-value	P-value
	Mean	S.D	SEM	Mean	S.D	SEM		
A (ND)	209.8	9.5	4.26	302.9	3.4	1.51	B v/s A	<0.001
B (Li)	235.2	14.9	6.66	160.02	48.7	21.76		

Mean* ± SEM P-value <0.001 Highly Significant***

The above data showed that the mean final body weight of group B animal decreased significantly (P<0.05) than the initial body weight at the end of 12th weeks. Comparative analysis of group B shows a highly significant (P-value <0.001) decrease in body weight as compared to that of A. The mean final body weights of group B animals was highly significantly decreased (P<0.001), as compared to control group A.

Mean* absolute weights (mg/gm/bwt) of cerebellum in different groups of Albino rats at the end of 2nd, 6th and 12th weeks.

Comparative analysis of differences in mean absolute cerebellar weight of different groups of Albino rats

Group	Absolute weight 2nd week			Absolute weight 6th week			Absolute weight 12th week			Major Groups P-value	P-value
	Mean	S.D	SEM	Mean	S.D	SEM	Mean	S.D	SEM		
A (ND)	251.6	2.07	0.93	293.2	3.70	1.66	336.6	2.41	1.08	B v/s A	<0.001
B (Li)	231.4	2.07	0.93	219.3	2.97	1.33	216.0	8.51	3.81		

Mean* ± SEM P-value <0.001 Highly Significant***

The above data showed that the mean absolute weights of cerebellum of group B animal decreased significantly ($P<0.05$) at the end of 2nd, 6th and 12th weeks. But on major group comparison the absolute weight of cerebellum of group B animals was highly significantly decreased ($P<0.001$), as compared to control group A.

Mean* relative weights (mg/gm/bwt) of cerebellum in different groups of Albino rats at the end of 2nd, 6th and 12th weeks.

Statistical analysis of differences in mean relative cerebellar weight of different groups of Albino rats

Group	Relative weight 2nd week			Relative weight 6th week			Relative weight 12th week			Major Groups P-value	P-value
	Mean	S.D	SEM	Mean	S.D	SEM	Mean	S.D	SEM		
A (ND)	1.13	0.02	0.01	1.17	0.06	0.03	1.11	0.01	0.01	B v/s A	<0.001
B (Li)	1.14	0.10	0.05	1.40	0.11	0.05	1.43	0.35	0.15		

Mean* ± SEM P-value <0.001 Highly Significant***

The above data showed that the mean relative weights of cerebellum of group B animal increased significantly ($P<0.05$) at the end of 2nd, 6th and 12th weeks. On major group comparison the relative weight of cerebellum of group B animals was highly significantly increased ($P<0.001$), as compared to group A.

DISCUSSION

Lithium is an indispensable pharmaceutical component of modern psychiatric therapy.[16] In this study Lithium induced depletion of body and cerebellar weights. These observations are in accordance with Tathagat et al.[17] who also found that Lithium carbonate causes a significant decrease in body and cerebellar weight. This harmful effect of Lithium on decrement of body weight and organ weight was paralleled with increasing time period. The following result was also observed by Bhalla who had recorded a decrement of body and cerebellar weight due to Lithium intoxication. Lithium causes an increase imbalance in antioxidant enzymes which are superoxide dismutase (SOD), Catalase (CAT) and glutathione synthetase (GST), [18] there by leading to excessive generation of free radicals hence resulting in enhanced oxidative stress.[19] Increased oxidative stress leads to cell damage and cell death [20] which results in a decline in body and organ weights.

It was also observed in this study that the relative weight of the cerebellum of the group B animals increased as the body weight decreased with increasing time period of the study. The same was observed on comparison of relative weight of group B when compared with control group A.

CONCLUSION

The present study suggest that chronic Lithium carbonate ingestion causes a highly significant decrease of body and cerebellar weights and increase in relative weights

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