Original Article

Assessment of the Noxious Effects of Lithium Carbonate on Granular Cell Layer of Rat Cerebellum

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ABSTRACT

Objective: To evaluate and document the effects of ingestion of i.e. of 34 mg/kg body weight/OD of lithium carbonate on Cerebellar Granular cell layer.

Study Design: Prospective Experimental research

Place and Duration of Study: This study was conducted at the Basic medical sciences institute Jinnah post graduate medical Centre Karachi, from June, 2012 till August, 2012.

Materials and Methods: This present study is designed to observe the microscopic changes of Granular cell layer in rat cerebellum. For this experimental study 20 animals weighing 170-175 grams were selected, they were divided into two groups, each comprising of 10 animals. Control group-A were given lab diet and water for a time period of 12 weeks while the rats in group-B received Lithium Carbonate dissolved in distill water given orally by tube 34 mg/kg body[7] weight/OD for 12 weeks respectively.

Results: Our study documented decreased granular cell layer thickness in group B animals, after they had ingested Lithium carbonate for 12 weeks as compared to the Group A animals on lab diet.

Conclusion: The changes of the thickness of cerebellar Granular cell layer was found to be highly significantly decreased in group B animals treated with Lithium than group A rodents which were placed only on lab diet. Lithium carbonate caused apoptosis and injury to Cerebellar Granular layer.

Key Words: Noxious, Granular layer, Mitochondrial Clumping

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INTRODUCTION

The popular treatment for the last 70 years for bipolar disorder is the Lithium a soft alkali metal[1] and medicinal literature has proved that metal accumulation in brain causes permanent brain damage[2], leading to neurological sequele[3]

The cerebellum controls posture and movement, it has two cerebellar hemispheres. The cerebellar cortex consists of three layers, Molecular layer, and middle Purinje cell layer and innermost is the Granular cell layer.[4.] Accumulation of Dietary metals causes' irreversible neuronal damage[5] to Cerebellum Soft alkali metals like Lithium cause irreversible brain[6] decomposition.

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This research was completed at the animal house of Basic medical sciences institute (BMSI) JPMC Karachi.

MATERIALS AND METHODS

The Albino rats were obtained from Charles River Breeding Laboratories, Brooklyn, Massachusetts, USA, and were cross bred at Animal House of Basic Medical Sciences Institute, JPMC, and Karachi. The animals were on a balanced diet and were observed for one week prior to the experiment.

Twenty animals weighing 170-175 grams were divided into two group. The control group A (n=10) and group-B (n=10) animals were selected. The rats in control group-A were given lab diet and water for a time period of 12 weeks while the rats in group-B received Lithium Carbonate dissolved in distill water given orally by tube 34 mg/kg body[7] weight/OD for 12 weeks respectively

At the end of 12 weeks the animals were sacrificed, brain was removed; the cerebellum was separated from the rest of the brain and fixed in Formal aldehyde [8] for 24 hours.

The cerebellum was dehydrated by passing through ascending grades of alcohol cleared by xylene and infiltrated by paraffin. The fixed tissue blocks were sectioned and obtained on glass slides five micron thick sections were collected for staining with haematoxylin and eosin[9].

The changes of the Granular cell layer thickness were observed and documented under light microscope. Observations were recorded for the thickness of inner most cerebellar layer in each group according to time interval. The Granular cell layer thickness was observed under 40 x objectives in selected fields of the tissue. The data was subjected to statistical analysis by using software SPSS (Statistical Program for Social Sciences) 2007 version-16. A statistical difference between means and experimental data was carried out by student 'T' test.

Table No.1: Comparison of the mean values of cerebellar Granular cell layer thickness µm among Groups-A and B albino rats according to time interval

Major Groups	No. of Subjects	12^{th} Week		P Value
		Mean	SEM	12 Weeks
A Normal Diet	10	181.5	0.18	
B Normal Diet + Lithium Carbonate	10	84.1	0.50	0.001

Statistical Analysis
P values of Group A and Group B

Major Group	12^{TH} Week	12^{TH} Week
A vs. B	P<0.001****	P<0.001****
Key: **** Highly significant		

Statistical analysis of cerebellar Granular cell layer thickness in major group-B (Lithium carbonate treated) shows a highly significant decrease in the thickness of Granular cell layer at 12 weeks' time interval as compared to the major group-A (control).

RESULTS

Group-A and B (At 12 weeks): On histological examination of H&E stained section of the gray matter showed multiple basophilic cerebellar Granule cells in normal architecture of the Granular cell layer in Group A animals. The sections of innermost layer in Lithium Carbonate treated Group B showed empty spaces due to Granule cell death, Apoptosis and Spongiosus leading to decreased Granular layer thickness in sections of cerebellar cortex was observed.

A highly significant (P<0.001) increased in the mean values of the thickness of Granular layer in Group A on Lab diet (181.5±2.06) µm was observed as compared to group B animals (84.1±0.50 µm)

A highly significantly (P<0.001) decreased in the mean values of the thickness of Granular layer was observed in group B (84.1±0.50 µm) when compared with A (181.5±2.06 µm).

DISCUSSION

Toxic subsances like Methyl mercury and Ethanol are found to cause cerebellar toxicity[10], the same neurodegenerative changes were found in cerebellum after Lithium ingestion[11]

The cerebellar cortex consists of inner most Granule layer which comprises about ninety percent of Granule cells[12]

As clinical and medical sciences is deficient of the literature on the adverse effects of Lithium carbonate on Granular layer of Cerebellum for the same reason we carried out the present study. We in our study found out that there was a highly significantly decreased thickness of Granular layer in Group B animals as compared to Group A rodents

The same detrimental effects of Lithium on Neuronal tissue were found by Joseph, Badyal and Gulrez[13]. The Neuro toxic effects of Lithium ingestion may be due to the fact that Lithium causes clumping of neurons and degeneration of cerebellar cortical layers as observed by Dethy[14.] (et al 1997). This may be due to that Lithium causes release of reactive oxygen species which causes Mitochondrial clumping leading to Nuclear and Granule neuronal death evident by increase in the distance of neurons and decrement of cortex which results in decreased thickness of Cerebellar Granular cell layer.

These results of cerebellar and toxicity loss of Cerebellar cortex after Lithium intake were also documented by A.valle (2021)[15]. They in their study found that lithium causes inhibition of glycogen kinase synthetase this results in a reduced mitochondrial fission and a decrement of mitochondrial fission leads to the disruption of the electron transport chain causes neuronal cell death[16] and resulting in loss of cortical tissue.

Our study is in accordance with the above facts of Lithium ingestion causes decreased thickness of Cerebellar Granular cortical layer**.**

CONCLUSION

This study cautions Neuropsychiatrists in prescribing Lithium to the masses.

Author's Contribution:

Concept & Design of Study:	Tazeen Kohari
Drafting:	Tazeen Kohari, Meshaal Azhar
Data Analysis:	Faryal Azhar, Usama Faruqui
Revisiting Critically:	Tazeen Kohari
Final Approval of version:	Tazeen Kohari

Conflict of Interest: The study has no conflict of interest to declare by any author.

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