

Documented Lipid Peroxidative Intoxication of Cerebellar Molecular Cell Layer after chronic Lithium Carbonate Ingestion

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ABSTRACT

Background: Cerebellar cortex consists of three layers. The outer molecular, middle Purkinje cell layer, inner granule cell layer. Lithium the alkali metal has deleterious effects on nervous tissue and this study proved the injurious effects of lithium on molecular cell layer of cerebellum.

Aim: To observe and report the damaging histological and morphological change of the decrement in the thickness of cerebellar molecular layer by Lithium.

Methods: This study was designed to observe the microscopic changes of thickness of molecular layer in rat cerebellum. For this experimental study 12 animals were used, they were divided into two groups, each comprising of 6 animals.

Results: Group-A received normal lab diet and water ad libitum while group B received injectable lithium carbonate 20 mg/kg/ for 4 weeks respectively. Micrometry was done and changes of the thickness of molecular cell layer were recorded and documented.

Conclusion: The pernicious effects of Lithium Carbonate on molecular cerebellar cortex were visualized and evaluated. Highly significantly decreased changes of thickness of molecular cell layer were documented in rat cerebellum.

Keywords: Lipid peroxidation, Molecular cell layer atrophy, decomposition

INTRODUCTION

Neurological and psychiatrically related disease like depression and anxiety have proved that Lithium was successfully used for 70 years¹, Today it is used in Bipolar disorder but groups of clinicians have reported Neurotoxicity² due to use of Lithium.

Cerebellum is easily damaged by metals³ like Aluminum, Lithium etc and it has been observed by Manto and Perrotta that Lithium salts lead to permanent Cerebellar Ataxia.⁴

Cerebellum plays an important part in non-motor and in motor systems⁵ and its cortex contains Golgi, Granule, and Purkinje and Stellate cells⁶ in three layers which are molecular, Piriform and Granule layers⁶.

The objective of the study was to observe and report the damaging histological and morphological change of the decrement in the thickness of cerebellar molecular layer by Lithium.

MATERIALS AND METHODS

This study was carried out in the Anatomy department of BMSI Basic medical sciences institute JPMC Karachi. For this study twelve Albino rats weighing 155-160 grams were selected and divided into two groups. Group A Contained six animals on Lab diet for four weeks, Group B was given injection IM Lithium carbonate 20⁷ mg /kg for four weeks. For research these animals were retrieved from Charles River Breeding Laboratories, Brooklyn, Massachusetts, USA. After cross breeding they were kept at Animal House of Basic Medical Sciences Institute, JPMC

Karachi. The animals were kept in Animal House on a balanced diet. They were put under observation for one week prior to the experiment.

On day 28 the animals were sacrificed, brain was removed and the cerebellum was separated from the rest of the brain and fixed in formaldehyde⁹ for 24 hours.

The cerebellar tissue 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 four micron thick sections were collected for staining with haematoxylin and eosin⁹.

The changes of the thickness of molecular cell layer were observed under light microscope. Observations were recorded. The micrometry was made at 40 x objectives in selected fields of the tissue. The data was subjected to statistical analysis by using software SPSS version-16.

A statistical difference between means and experimental data was carried out by student 'T' test.

Statistical Analysis: Statistical analysis of cerebellar granules cells count of major group-B (Lithium carbonate treated) shows a highly significant decrease cell count at 2 and 6 weeks time interval as compared to the major group-A (control)

RESULTS

Group A: On histology and micrometry of H&E stained section of the thickness of Molecular cell layer was found to be 225± 24. Microns 13 in Group A albinos who were on Lab diet. This indicates a highly significantly increased thickness with a P Value <.001*** of group A animals (lab diet) as compared to group B animals.

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Group B: A highly significantly ($P < 0.001^{***}$) decreased in the mean values of the Molecular layer was observed in group B (Lithium carbonate). The molecular cell layer thickness was 109 ± 3.04 microns recorded which was highly significantly decreased when compared with A.

Table 1 .Thickness of molecular cell layer in microns in Group A and Group B.

Groups	n	4 th Week	
		Mean	SEM
A Normal Diet	4	225.9 μ m	24.13 μ m
B Normal Diet + Lithium Carbonate	4	109.4 μ m	3.04 μ m

Table 2

Groups	Weeks	P value
A	4 th Week	$P < 0.001^{***}$
B	4 th Week	$P < 0.001^{***}$

DISCUSSION

Metals like Lithium carbonate are found to cause Spongiosus in neural tissue ¹⁰the same is agreed by Li ¹¹(et al 2018)peri neuronal spaces in the cerebellum as a result of intake of this drug. My research is in agreement with their findings. As Lithium caused atrophy of Molecular cell layer: This may be due to the fact that lithium causes oxidative stress leading to lipid per oxidation of cell membrane¹² and this resulted in cerebellar gray matter atrophy. The above mentioned facts are also accepted by Yousefani(et al 2020)¹³ and they in their study found that lithium use caused Oxidative stress^{14,15} which leads to lipid cell membrane¹⁶ distortion causing neuronal cell death and cellular atrophy resulting in decreased molecular cell layer thickness

CONCLUSION

My study proved the fact that metals like Lithium induced atrophy of Cerebellar Molecular layer.

Conflict of interest: Nil

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