

ORIGINAL ARTICLE

To Evaluate the Pernicious Histological Changes of the Thickness of Purkinje Cell Layer After Lithium Carbonate Ingestion

FARAH MALIK¹, TAZEEN KOHARI², AFTAB AHMAD³

¹Assistant Professor of Anatomy, Liaquat college of Medicine and Dentistry Karachi

²Associate Professor of Anatomy, Islam Medical and Medical College, Pasrur, Sialkot

³Associate Professor of Anatomy, M. Islam Medical and Dental College, Gujranwala

Correspondance to Dr. Tazeen Kohari, E-mail: tazeenk67@gmail.com. Phone: 0323-2967849

ABSTRACT

Background: The human cerebellum consists of two lobes and each cerebellar hemisphere consists of Gray and white matter. The gray matter has outermost layer called Molecular cell layer, the middle layer composed of Purkinje cell and innermost is Granular cell layer. In the Molecular layer are Stellate, Basket and Dendrites of Purkinje cells. The middle layer presented the characteristic pyramidal shaped Purkinje cells.

Aim: To evaluate and record morphological data of the thickness of purkinje cells layer in normal Control group A and in group B rodents which were given lithium carbonate so as to prove the lethal property of the anti-depressive drug lithium carbonate on the histology of Purinje cells layer of cerebellar cortex.

Method: Ten albino rats were given lithium carbonate for a period of six weeks and then micrometry was carried out for both groups.

Results: The data which was obtained in both groups was analyzed and it was concluded that the Clinicians and population should be aware of the deleterious effects of lithium carbonate.

Conclusion: Our study defined the consequences and the sequele of using Lithium carbonate by patients suffering from psychosis as Lithium can cause toxicity even at therapeutic doses.

Keywords: Micrometry, deleterious, rhombencephalon

INTRODUCTION

Disorders of mood are anxiety, depression, aggression and bipolar disorder. Lithium is the drug of choice in mood and bipolar affective disorder.¹ John Cade, a psychiatrist from Australia, used it for treatment of bipolar disorder. The drug gained a focal standard in psychiatry²

Clinicians prescribing Lithium to patients for long term have found adverse affects of the drug³ on the brain and Cerebellar dysfunction was frequently reported⁴.

The cerebellum or rhomb encephalon is part of hind brain and its gray matter consists of three layers, the outer is the Molecular cell layer, Purkinje cells layer, Granular cell layer. The Purkinje cells layer is one cell layer thick Purkinje cell bodies are shaped like flask these purkinje cells have extensions called dendrites and an axon which receives impulses from Granule cells⁵.

Neurotoxicity with metals are frequently reported by patients ingesting Lithium carbonate⁶.

The present Observational research was conducted to study the histological distortion of the thickness of Purkinje cell layer due to the

Lithium carbonate at a dose of 25⁷ mg/kg/ twice daily in saline solution intraperitoneally for four weeks. They were acclitized to the surroundings of the Animal House on a balanced diet and were put under observation for one week prior to the experiment.

After three weeks animals were sacrificed, brain was removed and the cerebellum was separated from the rest of the brain and fixed in formaldehyde⁸ for 24 hours.

The sections of cerebellar tissue were passed through ascending grades of alcohol and then they were cleared by xylene⁹ and infiltrated by paraffin. The four micron thick sections of tissue were obtained on glass slides were collected for staining with haematoxylin and eosin¹⁰.

The changes of the thickness of Purkinje cells 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 SPSS 2007 version-16. A statistical difference between means and experimental data was carried out by student 'T' test.

Statistical Analysis: Analysis of thickness of Purkinje cells layer was carried out and the results of Micrometry in of major group-B (Lithium carbonate treated) showed a highly significant decrease cell count in the thickness of Purkinje cell layer at four weeks' time interval as compared to the major group-A (control)

RESULTS

Group-A: Histological examination of haematoxylin and eosin stained sections of Purkinje cells layer (PCL) showed pyriform shaped purkinje cells in purkinje cells layer which is almost one cell thick and are situated between the outer Molecular layer and the Inner Granule cell layer. A significantly highly increased thickness ($P < .001$) of PCL was observed in Major group A $15.8 \pm 0.36 \mu\text{m}$ (Table 1) as

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compared to Group B animals which are the Lithium treated group. Histology showed distortion of the Purkinje cells layer of cerebellum in Group B rodents

In Group B animals a highly significantly ($P < .001$) decreased thickness of Purkinje cells layer was recorded at $10.6\mu\text{m} \pm 0.68$ (Table 2)

Group-B: A highly significantly increased of Purkinje cell layer with a P Value $< .001^{***}$ of group A animals (lab diet) as compared to group B animals. (Table 2)

Group -B: A highly significantly ($P < .001^{***}$) decreased in the mean values of the Purkinje cells layer was observed in group B (Lithium carbonate) (Table 2).

Table 1 .Thickness of Purkinje cells layer in microns in Group A and Group B.

Groups	n	4 th Week	
		Mean	SEM
A Normal Diet	4	$15.8 \pm 0.36\mu\text{m}$	0.36
B Normal Diet + Lithium Carbonate (20 mg/kg/OD)	4	$10.6.6 \pm 0.68\mu\text{m}$	0.68

Table 2

Groups	Weeks	P value
A	4 th Week	$P < .001^{***}$
B	4 th Week	$P < .001^{***}$

DISCUSSION

Cerebellum is the largest part of hind brain and it consists of thin gray matter which has three layers from deep to superficial is the Granule cell layer, middle is the Purkinje cell layer, and the outer most is the Molecular cell layer. The outer layer is also called Synaptic layer (molecular layer), an intermediate discharge layer (Purkinje layer) and a receptive layer layer (the granular layer)¹⁰. The Purkinje cell layer consists of flask shaped purkinje cells. Human Purkinje cells are 50-100 μm longitudinally and thickness of this layer is one cell layer thick¹¹.

The nervous tissue is easily injured by use of metals such as Lithium and there is deficient documented histological data of the distorted changes of Purkinje cell layer due to the anti-anxiety drug Lithium carbonate and such was proved in our research. These toxic effects were also observed by Baird-Gunning J¹² who in their research had shown the damaging effects of lithium on central nervous system as they have discussed in their research. Drugs like Lithium cause detrimental and lethal damage to central nervous system¹³.

The same findings of the degeneration of Purkinje cell layer was also discovered by deCates et al¹⁴, that may be due to the fact that lithium causes Nuclear Pyknosis, Chromatin clumping and long term inhibition of neurotransmission due to reduced glutamate activity by decreasing dopamine activity. These changes result in cavitation of neural tissue and decreased purkinje layer thickness¹⁴.

Our data is in accordance with the above researches and showed highly significant atrophy of cerebellar Purkinje cell layer. The same results of Lithium causing decrease release of neurotransmitters in brain tissue were reported by Nabil M et al¹⁵ my observations are in agreement with Nabil and it has been agreed that disruption of Purkinje cells showed decreased thickness of purkinje cell layer

causes decreased excitatory and inhibitory purkinje cell output leading to Cerebellar dysfunction.

CONCLUSION

This experimental research brings forth the result that the use of Lithium salts should be administered with caution in patients with neurodegenerative diseases.

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