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Syndrome of Irreversible Lithium – Effectuated Neurotoxicity (Silent Syndrome)

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Abstract

SILENT syndrome (Syndrome of Irreversible Lithium-Effectuated Neurotoxicity) is a rare permanent neurological sequelae of lithium toxicity that develops in patients without any previous history of neurological impairment. Most classically it causes a fine, 8–12 Hz postural tremor considered to be an “enhanced” physiological tremor. Cognitive impairment, ataxia, dyskinesia and incoordination may also occur. Despite the availability of newer drugs, lithium remains the most effective treatment for bipolar disorder. But treatmentwith lithium is complicated by its narrow therapeutic index and its effects on renal function, both of which increasesthe risk of toxicity. Hence, careful attention to its administration is needed. Chronic toxic effects of lithium result when the intake exceeds elimination.

Keywords: silent syndrome, lithium toxicity,bipolar disorder.

Introduction

Lithium was approved by FDA for its use in both acute and maintenance treatment of Bipolar disorder 1 and Major Depressive disorder in 1974.Apart from its psychiatric use, it is indicated in management of several neurological disorders like cluster headache.Toxic effects of lithium are frequently encountered in clinical practice due to its narrow therapeutic index.Lithium toxicity occurs not only during acute intoxication but also in patients who are on long term treatment. Fortunately, these side effects are reversible in most of the patients upon discontinuation of the drug. Rarely, neurological disturbances particularly cerebellar dysfunction develop, which are usually persistent causing disability.

Case Report

Ms.P, 22yrs female, had come to us in 2009 with features of Mania and was diagnosed to have Bipolar Disorder 1. She was started on T.Lithium carbonate 300mg TDS and T.Risperidone 2mg BD. She was maintaining well on the above regimen and came for regular follow up. In 2016, patient developed altered mental status and disorientation for which she was admitted in emergency room for acute care. She did not have fever or muscle rigidity during admission. Her creatine phosphokinase level was normal. Her serum lithium level at the time of admission was 4.2mEq/L. Lithium was stopped and she underwent hemodialysis.

Her symptoms improved and around 12 weeks patient recovered from encephalopathy but displayed coarse tremors and ataxic gait. On neuropsychiatric evaluation, patient had gross axial tremor (predominantly in the head and trunk), an ataxic broad-based gait, nystagmus, dysarthria, and limb incoordination. Her neurological examination shows bilateral cerebellar signs more on left than right side, all the reflexes were absent, muscle power was 4+ in all four limbs. Her Mini mental state examination (MMSE) score were 30/30. Her lithium levels were undetectable.The brain magnetic resonance image was normal. Blood tests showed no electrolytic abnormalities and no sign of acute infection. CSF analysis was normal.Peripheral nerve conduction study showed-sensorimotor axonal neuropathy of both lower and upper limbs more in lower limbs.A diagnosis of SILENT syndrome (Syndrome of Irreversible Lithium-Effectuated Neurotoxicity) was made and she was started on T. Sodium Valproate 750mg/day, physiotherapy and balance training were initiated.

Discussion

Despite the availability of newer drugs, lithium remains the most effective treatment for bipolar disorder. Lithium initially distributes in extracellular fluid then gradually redistributes to other areas including brain over 24 hrs after absorption. Hence toxic manifestations of lithium are classified into acute and chronic.

SILENT syndrome (Syndrome of Irreversible Lithium-Effectuated Neurotoxicity) is a rare permanent neurological sequelae of lithium toxicity that develops in patients without any previous history of neurological impairment and persists for at least two months even after the stoppage of the drug.Many neurological disturbances due to lithium have been studied . Most classicallyit causes a fine, 8–12 Hz postural tremor considered tobe an “enhanced” physiological tremor.

Cognitive impairmentand incoordination may also occur even in therapeutic window, but are usually tolerable and not disabling. Acute intoxication manifests asfever with encephalopathy that often corresponds to high serum lithium levels which usually improves once plasma level decreases. Cerebellar symptoms become apparent after the resolution of acute encephalopathic state due to slow release of lithium from the intracellular compartments, where patients present with ataxia, tremors, dyskinesia and incoordination. Usually serum lithium levels are normal during this stage thus demonstrating that blood levels do not correlate directly with intracellular level.

Several factors that contribute to the development of permanent neurological sequelae have been studied which includes : serum lithium levels at the time of acute intoxication state and its rapid correction, fever, use of adjunctive medications like antipsychotics and presence of co morbid medical illnesses.

Conclusion

Despite being a wonderful drug, treatment with lithium is complicated by its narrow therapeutic index and its effects on renal function, both of which increase the risk of toxicity. Hence, careful attention to administration is needed. Chronic toxic effects of lithiumoccur because intake exceeds elimination. This is most commonly due to lithiuminducednephrogenic diabetes insipidus or intercurrent illnesses. Lithium poisoning has a low mortalityrate; however, chronic lithiumpoisoning may need a long hospital stay due to neurological impairment and leads disability. Hence monitoring of lithium is important to prevent toxicity and disability.

References

1. Jonathan Baird-Gunning, Tom Lea-Henry, Lotte C. G. Hoegberg,SophieGosselin, and Darren M. Roberts, et al. Lithium Poisoning ,Journal of Intensive Care Medicine 2016, 1-15,DOI: 10.1177/0885066616651582.

2. SarabSodhi, Samantha Lee and Antoinette Spevetzet al, “But the lithium level is normal!” SILENT Syndrome: A rare diagnosis of irreversible lithium toxicity to consider in cases of irreversible neurotoxicity, Trauma Emerg Care, 2016, Volume 1(2): 33-33, doi: 10.15761/ TEC.1000111.

3. Fábio H.G. Porto , Marco A.A. Leite , Leonardo F. Fontenelle , Rogério P. Marrocos , Natália F. Szczerback , Marcos R.G. de Freitas et al, The Syndrome of Irreversible Lithium-Effectuated Neurotoxicity (SILENT): One-year follow-up of a single case, Journal of the Neurological Sciences 277 (2009) 172–173.

4. Niethammer M, Ford B. Permanent lithium-induced cerebellar toxicity: three cases and review of literature. MovDisord 2007:570–3.

5. Adityanjee, Munshi KR, Thampy A. The syndrome of irreversible lithiumeffectuated neurotoxicity. ClinNeuropharmacol 2005;28:38–49.

6. Morgan JC, Sethi KD. Drug-induced tremors. Lancet Neurol 2005;4:866–76.

7. Pullinger S, Tyrer P. Acute lithium-induced tremor. Br J Psychiatry 1983;143:40–1

8. Chen KP, Shen WW, Lu ML. Implication of serum concentration monitoring in patients with lithium intoxication. Psychiatry ClinNeurosci 2004 Feb;58:25–9.

9. Jaeger A. Lithium. Medicine 2007;35:535–6.

10. Sadosty AT, Groleau GA, Atcherson MM. The use of lithium levels in the emergency department. J Emerg Med 1999;17:887–91.