Acute High Dose Lithium-Induced Exacerbation of Obsessive Compulsive Symptoms

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ABSTRACT

Obsessive compulsive disorder (OCD) is a chronic neuropsychiatric disorder whose pathophysiology is linked to serotonergic dysfunction. More recently, the role of glutamate has also been posited. Lithium is used as an adjunctive for the treatment of OCD which is found to enhance serotonergic transmission. We present a case of OCD who was on stable dose of sertraline developed exacerbation of obsessive compulsive symptoms with acute high dose of lithium but improved after dose reduction.

Key words: Glutamate, lithium, obsessive compulsive disorder

INTRODUCTION

Obsessive compulsive disorder (OCD) is thought to be one of the most intractable and disabling mental disorders in the community.[1] It is well known that OCD responds to drugs which increase the serotonergic (5-HT) transmission at the synapse. Other neurotransmitters such as dopamine, noradrenaline and glutamate also have role in the causation. Recent literatures have shown that glutamatergic hyperactivity at N-methyl-D-aspartate (NMDA) receptor level is involved in the patho-physiology of OCD.[2] Lithium, as an adjunctive for management of OCD, is based on its putative effect on enhancing 5-HT transmission. But acute high dose lithium administration also increases glutamate transmission[3] which may be hypothesized to exacerbate obsessive compulsive (OC) symptoms. Here, we are reporting a case of OCD on stable dose of sertraline for 3 weeks, who developed exacerbation of OC symptoms with acute high dose of lithium but improved after dose reduction.

Access this article online	
Quick Response Code:	Website: www.toxicologyinternational.com
	DOI: 10.4103/0971-6580.139816

CASE REPORT

An 18-years-old Indian male with no past psychiatric or medical history presented with a history of repetitive distressing thoughts of dirt and contamination with repetitive washing behavior for one and half years. He was diagnosed as OCD, mixed obsessional thoughts, and acts as per International Classification of Diseases (ICD-10).[4] Yale-Brown Obsessive Compulsive scale (Y-BOCS) was administered at the time of admission which indicated severe (obsessions = 13; compulsions = 15; total = 28) and started on sertraline 25 mg/day and hiked to 150 mg/day over 4 weeks. Patient showed minimal improvement after 4 weeks (obsessions = 12; compulsions = 15; total = 27). He started developing side-effects like headache, thus sertraline was not hiked further and lithium 900 mg was added as augmenting agent. Patient started reporting exacerbation of repetitive thoughts (obsessions = 15; compulsions = 18; total = 33 indicating extreme) and fine tremors on fourth day after starting lithium. Serum lithium level was done at 900 mg/day (Serum lithium-1.2 mmol/L) and hence lithium was tapered to 600 mg/day and serum lithium level decreased to 0.65 mmol/L. There was improvement in Y-BOCS score within a week after reducing the dose of lithium (obsessions = 11; compulsion = 14; total = 25 indicating severe) and the dose was maintained on the same dose. Four weeks later, there was further improvement on

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Y-BOCS (obsessions = 9; compulsions = 12; total = 21 indicating moderate) score. Patient was discharged on sertraline (150 mg/day) and lithium (600 mg/day).

DISCUSSION

Till date, numerous hypotheses have contributed to the pathophysiology of OCD, including abnormalities in glutamate neurotransmission. Neuro-imaging studies have demonstrated increased cerebral blood flow, metabolism and activation in the cortico-striato-thalamo-cortical (CSTC) circuitry of individuals with OCD. The excitatory glutamatergic projections from the cerebral cortex, thalamus, and hippocampus target the striatum but the striatal neurons are GABAergic and projects to globus pallidus and substantia nigra that ultimately inhibits glutamatergic neurons of anterior thalamus. These thalamic neurons project back to cingulate and orbitofrontal cortex which forms a negative feedback loop to balance glutamate in these cortical regions.[2] Thus, an increased glutamatergic activity in the cortico-striatal projections may result in a disinhibited thalamus and thereby creating a self-perpetuating circuit between the thalamus and orbito-frontal cortex that may drive OC symptoms.[5]

Dixon *et al*.[3] have shown that acute lithium administration at therapeutic concentration may release glutamate in rhesus monkey and mouse cerebral cortex slices. Lithium at supratherapeutic concentrations may exert its excitotoxicity by elevating synaptic glutamate.[6] We hypothesize that there was increase in glutamatergic neuro-transmission within the CSTC circuitry due to acute high dose lithium administration that might have caused exacerbation of OC symptoms which reduced after decreasing the dose. To our knowledge, there are no reports of lithium-induced OCD exacerbation.

CONCLUSION

Lithium, despite being used as an adjunctive in the treatment of OCD may exacerbate symptoms of OCD which may be due to enhanced glutamatergic neurotransmission at the CSTC circuitry on acute high dose administration.

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How to cite this article: Umesh S, Sinha VK. Acute high dose lithium-induced exacerbation of obsessive compulsive symptoms. Toxicol Int 2014;21:222-3.
Source of Support: Nil. **Conflict of Interest:** None declared.