

Topiramate induced lithium toxicity

Abstract

We are reporting and documenting a suspected case of Lithium toxicity following administration of Topiramate. This report discussed our experience with a 47-year-old patient, who has been inpatient for the past one year and diagnosed with Schizoaffective Disorder Bipolar Type 1, for the past 20 years according to the criteria of DSM-5. He manifested symptoms of Lithium toxicity following administration of Topiramate. He was also diagnosed with compulsive urge of drinking fluids for the past five years and a compulsive urge of food intake for the past 8 months. He rapidly gained 40 pounds within a period of 8 months. We have been managing his water intake by daily weight monitoring and water restriction. Excessive compulsive eating behavior and weight gain management was attempted by the Topiramate. The patient was already being treated with Lithium Carbonate for mania, labile mood and aggressive behavior for the past one year. Comprehensive metabolic panel, Lithium levels, thyroid panel, HbA1C and Complete Blood chemistry were within normal reference ranges before initiating treatment with Topiramate. The patient developed symptoms of lithium toxicity on the fourth day of the treatment. He appeared delirious, confused, disoriented with time, place and person. He had slurring of speech, bilateral coarse tremors in his hands, shallow and rapid breathing. He complained of nausea, vomiting and an inability to eat. We transferred the patient to local ER and ordered stat CMP and Lithium levels. At the ER, the patient was diagnosed and treated for renal insufficiency due to Lithium toxicity. It also demonstrates the toxic interaction of medications with narrow therapeutic index, such as Lithium. Informed consent was obtained from patient and guardian.

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Opinion

Numerous studies have described that mechanism of action of Topiramate has wide spectrum pharmacological properties. He has been used as mood stabilizers in bipolar and schizoaffective disorder, anorexia bulimia, epilepsy, migraine, essential tremors and cluster headache. It is also effective in treatment resistant bipolar disorder by augmentation of effects of lithium. It has been reported in recent literature that topiramate also use in binge eating disorder (BED) and for weight loss.¹ Topiramate reduces the frequency of the voltage sensitive sodium channels and play a key role in treatment of epilepsy. Topiramate potentiates the effects of inhibitory effects of Gama amino butyric acid-A in the brain. Topiramate has been also found, enhance the effects of Gaba stimulated chloride influx in cerebral which also increase frequency of activation of Gaba-A receptor in brain and exhibits an anticonvulsants action. Topiramate is also known to have inhibitory action on excitatory pathways of AMPA and glutamate receptors and contributes as an anticonvulsant agent. TPM also inhibits high voltage activated calcium channels and decrease their neurotransmitter release and inhibit calcium dependent second messenger system. TPM also has inhibitory action at carbonic anhydrate at proximal tubular level. TPM has been considered weak CA- inhibitor and this property has no therapeutic values in treatment of epilepsy and other conditions. This action determines some of its side effects such as hyponatremia, metabolic acidosis and increase risk of nephrolithiasis.²

A 47-year-old African American man was admitted to the psychiatric state hospital from group home. He became increasingly aggressive, violent and threatening toward other residents and staff. He became noncompliance with his treatment prior to relapse. Upon admission, the patient was hyper-verbal, presented with pressured

speech, flight of ideas. He manifested aggressive, threatening behavior and insomnia for the past seven days. He was started on mood stabilizer lithium carbonate and psychotropic medication, paliperidone to ameliorate his symptoms of mania and psychosis. Comprehensive metabolic panel, thyroid panel, complete blood chemistry and HbA1C were within normal reference ranges. He responded rapidly to above combination and stabilized. His Schizoaffective bipolar type 1 was in remission. We routinely monitored lithium levels, CMP, thyroid panel. During hospitalization, patient developed compulsive urge to drink excessive amount of fluids which has been managing by daily weight monitoring and water restriction. For the past eight months patient developed compulsive urge to eat excessive amount of food with rapid gain of 40 lbs. Despite various trials of behavioral modifications and therapies, we were unable to control above behavior. There was urgent need of pharmacological intervention in order to prevent further weight gain, comorbidities and metabolic syndrome. He was started on TPM, another mood stabilizer. Patient's labs values of lithium levels, HBAIC. Thyroid panels, CMP and CBC all were within normal reference ranges prior administrating Topiramate. His kidneys were functioning at normal levels. Fourth day of treatment patient appeared disoriented, increasingly confused, and delirious. He had slurring of speech, tremors in his both hands and unsteady gait. He presented with rapid and shallow breathing. He was complaining of nausea, vomiting, inability to eat and increased urinary frequency. Lithium toxicity was suspected. Topiramate and lithium carbonate was stopped immediately. We ordered stat labs CMP, lithium level, thyroid panel and CBC. Lithium levels were in toxic range, creatinine and blood urea nitrogen (BUN) were above the normal reference ranges. He was transferred to ER where he was diagnosed and treated for renal insufficiency secondary to lithium toxicity. Patient showed significant improvement with conservative and supportive treatment including rehydration and correction of electrolytes imbalance. Our

patient developed lithium toxicity due to Pharmacokinetic interaction of TPM with lithium by affecting renal excretion. Patient had been on lithium for the past one year without any significant adverse effects. Topiramate may increase lithium level by increase excretion of Sodium. The potential mechanisms of Topiramate-induced lithium toxicity appear to be both pharmacokinetic (competition for renal excretion) and pharmacodynamic (weight loss induced decrease in sodium lithium counter transport activity). Topiramate also reportedly increases plasma Lithium levels by 140% as well increase plasma Lithium clearance by 36% and decreases AUC by 12%. These both effects are due to Topiramate's inhibitory action on Carbonic anhydrase in proximal tubule of kidneys and consequently effects Lithium renal clearance. Topiramate can increase plasma lithium level significantly by 5-fold.³ This may be result of its inhibitory action on the carbonic anhydrase in proximal tubules of kidneys. This results in a decrease excretion of Lithium² (Tables 1-3).

Table 1 Lab values with lithium carbonate prior trial of topiramate for compulsive urge of excessive food intake/binge eating disorder(BED) Na+(135-145mEq/L) Potassium (3.5-5.0mEq/L) lithium therapeutic value (0.4-1.3meq/l) bun (8.0-22.0) creatinine/bun ratio (10.0-22.0) creatinine (0.50-1.20)

Lithium levels 0.47
Na.Values 141
Creatinine 1.1
Blood urea Nitrogen 15
Creatinine/BUN Ratio 17
Weight no increase
Potassium 3.8

Table 2 Labs values with topiramate added with lithium carbonate. tpm for compulsive urge of excessive food intake/binge eating disorder(bed) Na+(135-145meq/l) potassium (3.5-5.0meq/l) lithium therapeutic value (0.4-1.3meq/l) bun (8.0-22.0) creatinine/bun ratio (10.0-22.0) creatinine (0.50-1.20)

Lithium levels 1.46
Na.Values 131
Creatinine 3.4
Blood urea Nitrogen 47
Creatinine/BUN Ratio 23
Weight dec. 6lbs
Potassium 2.9

Table 3 Lithium level and labs after reintroduction of lithium carbonate to the treatment. topiramate was never reintroduced to the treatment after episode of lithium toxicity. Na+(135-145meq/l) potassium (3.5-5.0meq/l) lithium therapeutic value (0.4-1.3meq/l) bun (8.0-22.0) creatinine/bun ratio (10.0-22.0) creatinine (0.50-1.20)

Lithium levels 0.79
Na.Values 141
Creatinine 1.1
Blood urea Nitrogen 15
Creatinine/Burn Ratio 17
Weight no gain
Potassium 3.8

Weight gain and binge eating disorder is an ongoing problem with psychotropic medications. Management is hectic and time consuming. After failure of behavioral and life style modifications we have no choice but to utilize pharmacological intervention. Topiramate is a useful mood stabilizer in addition to ongoing treatment for weight loss. There is no psychotropic medication available with efficacy may reduce weight. As healthcare providers, we do not recommend Topiramate as weight reducing medication but we also need to prevent patient from developing coronary heart disease, diabetes, hypertension and metabolic syndrome consequence of drastic weight gain due to psychotropic medications. Unfortunately, our patient developed lithium toxicity due to pharmacokinetic interaction between Topiramate and lithium. Our patient made a rapid recovery with conservative treatment including rehydration and correction of electrolyte imbalance. Our case report also underscores the importance of psychopharmacology, psychiatrist should be aware of interaction of medication between psychotropic medications particularly drugs with narrow therapeutic index such as lithium.

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None.

Conflict of interest

The author declares no conflict of interest.

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