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RHINOLITH ASSOCIATED WITH LONG-TERM TOPIRAMATE THERAPY IN ALCOHOL WITHDRAWAL PATIENTS

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ABSTRACT

Topiramate, a commonly used drug in the management of seizures & migraine headache, can increase the risk of calcium phosphate kidney stones. However, specific side effects are nausea, anorexia, parasthesia, memory problems etc. We report a case of 54 year old male patient with alcohol withdrawal syndrome treated with bupropion, disulfiram, topiramate, chlordiazepoxide. After one year of treatment, the patient developed nephrolithiasis& rhinolith on right side which was confirmed by USG & CT scan respectively. As all other drugs except topiramate do not have any tendency to form stones, the most probable drug may be topiramate. ENT specialists should be aware of this possible complication to undertake early interventions.

Keywords: Topiramate, Alcohol withdrawal syndrome, Disulfiram, Rhinolith, Bupropion

INTRODUCTION

Topiramate (Topamax) which is an anticonvulsant (antiepilepsy) drug (first approved by the US FDA, Food and Drug Administration, in 1996).[1] It is usually used to control seizures in epileptic patients either as monotherapy or with other antiepileptic medications. It acts through various mechanisms, including blocking sodium channels in neurons (like phenytoin) & modulating chemical receptors in brain.[2] Topiramate is used to treat epilepsy seen both in children and adults. It is indicated for the treatment of Lennox-Gastaut syndrome in children, also most frequently prescribed for the prevention of migraines also. Psychiatrists prescribed topiramate to treat bipolar disorders.[3] This drug has been investigated for use in treating alcoholism,[4,5] methamphetamine addiction[6] and obesity,[7,8] as it reduces binge eating.[9,10] The main adverse effects of this drug are parasthesia, URTI(upper respiratory tract infection), diarrhea, nausea, anorexia & memory problems. The inhibition of carbonic anhydrase by topiramate is rarely being strong enough to cause metabolic acidosis of clinical importance.[11] The U.S. Food and Drug Administration (FDA) has notified prescribers that long term use of topiramate can cause acute myopia and secondary angle closure glaucoma in a small group of people. Researchers found that chronic topiramate therapy (about one year), caused systemic metabolic acidosis (excessive acid in the blood) which make the kidney unable to excrete acid. There is also increased the urine pH and lowered urine citrate with topiramate use which is an important inhibitor of kidney-stone formation. The propensity to form calcium phosphate stones in the kidney is increased due to the above mentioned reason.[12]

Bupropion is an atypical antidepressant and used as an aid for smoking cessation.[13] Mechanisms behind its pharmacological action is thought to be norepinephrine-dopamine reuptake inhibition. It binds selectively to the dopamine transporter, but its behavioral effects is due to its inhibition of norepinephrine reuptake.[14,15] It is also a nicotinic

acetylcholine receptor antagonist.[13,16] Bupropion is used for clinical depression[17], social anxiety disorder. [18] Bupropion reduces the severity of nicotine cravings and withdrawal symptoms, for obesity[19], attention-deficit hyperactivity disorder (ADHD)[20] , in methamphetamine dependence.[21.] Most important side effects which seen with the ingestion of this drug are seizure, hypertension, myocardial infarctions etc. There is no report established for formation of stones with bupropion till date.

In the 1920s disulfiram was discovered and as it produces an acute sensitivity to alcohol, used for the treatment of chronic alcoholism.[22] It inhibits the acetaldehyde dehydrogenase & blocks the alcohol metabolism in the body and producing an unpleasant reaction with alcohol. The most commonly seen side effects with disulfiram in the absence of alcohol are drowsiness, headache, and a metallic or garlic taste in the mouth.[23] Disulfiram also causes neurotoxicity in the form of extrapyramidal and other symptoms.[24]

CASE REPORT

We report a case of 54 year old male presented to the outpatient department of psychiatry, IMS & SUM Hospital, Bhubaneswar with chief complaints of tremor in hand, restlessness, increase in sweating, palpitation, and insomnia with irrelevant talk for last 2days. Then the patient was admitted to the psychiatric indoor of our hospital with a diagnosis of alcohol withdrawal syndrome. There was no history of diabetes mellitus, hypertension, epilepsy in the past. The patient was apparently alright 2 days back. To start with he developed the above mentioned symptoms after discontinuation of alcohol which he was taking since last 20 years in a regular basis (> 300ml/day foreign liquor). There was also history of smoking (4-5 cigarettes/day).

During the period of admission, all the investigations such as all the blood parameters, CT scan of head, USG(ultrasound) abdomen were done which showed the increased LFT(liver function test) values, fatty liver on USG but CT scan & other parameters were within normal limits.

After admission, he got treated with injection lorazepam, injection haloperidol with phenargan, thiamine & multivitamin injection for 4-5 days. After 5 days, the above drugs were changed to its oral formulations along with anticraving drugs such as tab topiramate (100mg/d), tab bupropion (300mg/d), tab chlordiazepoxide (75mg/d), tab disulfiram (250mg/d). Then after 10th day of admission, the patient was discharged from the hospital with the advice of continuing the medicines & to consult after 6months.

He was maintaining the abstinence & discontinued the tab chlordiazopoxide gradually. Again he came after one year of the initial visit with a complaint of heaviness around periorbital area. USG abdomen revealed nephrolithiasis & CT scan revealed antrorhinolith in right side with right maxillary sinus collection. The patient was referred to the ENT department of our hospital for further interventions.

DISCUSSION

A rhinolithh is a calculus present in the nasal cavity which can cause nasal obstruction, epistaxis, headache, sinusitis, epiphora.[25] In our present case the drugs that are prescribed for a long duration are disulfiram, bupropion & topiramate. The most common side effects of disulfiram are drowsiness, headache & a metallic or garlic taste[26] & extrapyramidal side effects.[27] Most controversial side effect of bupropion is seizure.[28,29,30] Other side effects are hypertension28, myocardial infarction[31], delirium, hallucination[32], coma. [30]

An association between topiramate & the development of kidney stones has been described previously in several different case reports.[33] But all these case reports were of kidney stones & we did not come across any case reports on rhinolith with the use of topiramate. Though our patient

was receiving three anticraving drugs, topiramate was thought to be the most likely cause of rhinolith, as there was risk of calcium & phosphate deposition with long term use of topiramate around one year in the kidney. The causality assessment by Naranjo algorithm [34] showed that this adverse drug reaction was "probable" with topiramate.

CONCLUSION

Rhinolith is an uncommon disease. It is the formation of a calculus or stone in the nasal cavity due to calcium, magnesium and phosphate salts deposition in that area. The underlying cause of formation of rhinolith in our present case report was not clear. As more patients receive topiramate now-a-days as anticraving drugs in chronic alcoholism, it is important to alert patients about this kidney stones & rhinolith formation. So precautions to be taken in people with the following conditions like history of kidney stones and liver & kidney diseases. Physicians should also focus on preventing adverse effects & distinguishing serious adverse effects from self limiting adverse effects in order to manage prejudiced & fearful patients with anticraving drugs.

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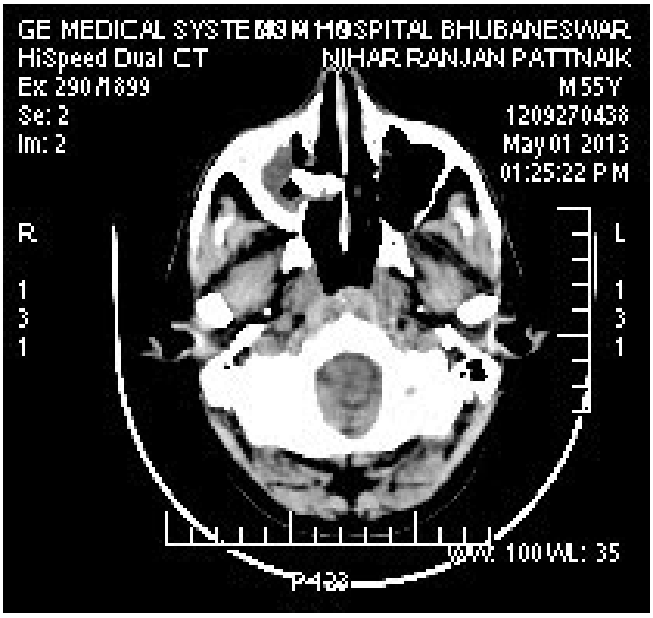

Figure 1: CT Scan showing antrorhinolith in right side with right maxillary sinus collection