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A Case Study on Topiramate Induced RenalCalculi

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ABSTRACT
Topiramate is frequently used for the treatment of epilepsy and migraines. It has been liked to the emergence of metabolic disorders like acidosis and hypokalaemia. 10% of people in Europe have kidney stones and this tendency has never been examined analytically. 1-2% of all kidney stones are caused by drug-induced renal calculi. 1-2% of all renal calculi are caused by drugs. There are two categories of medicines that are reportedly capable of causing calculi. The first one contains medications that are poorly soluble excrete a lot of urine, and encourage crystallisation in the urine among that Atazanavir and protease inhibitors used to treat patients with human immunodeficiency virus (HIV) as well as sulphadiazine used to treat cerebral toxoplasmosis are the mostcommon causes among them.

I. INTRODUCTION:

Topiramate is frequently used for the treatment of epilepsy, the prevention of migraines and weight-loss aid. The usage of this medication has been linked to the emergence of metabolic disorders like acidosis, hypokalaemia, hyperuricemia, and kidney stone disease. This tendency, which has been discussed in a number of studies since 1996, has never been examined analytically[1]. Around 10% of people in Europe have kidney stones. It has urinary problems and metabolic illness. The first steps in the diagnostic process for urolithiasis patients include kidney stone analysis and the identification of risk factors for kidney stone production[2]. 1-2% of all renal calculi are caused by drugs. Soon after being introduced to humans in the early 1940s, sulphonamides were the first medications to develop renal calculi and acute renal failure episodes[3]. Topiramate, a recently introduced antiepileptic medicine, is administered in combination with other drugs to treat partial or refractory seizures. More than 40% of patients who taken part in clinical studies reported seizure frequency reduced by 50% or more indicating that topiramate reality provide an adequate benefit in these conditions. There are also includes of other illnesses, such as trigeminal neuralgia and bipolar disorder, being successfully treated[4]. The first steps in the diagnostic process for urolithiasis patients include kidney stone analysis and the identification of risk factors for kidney stone production.

Topiramate use has been linked to the development of metabolic acidosis, hypokalaemia, and renal stone disease[1]. Family history of kidney stones, inadequate fluid consumption, specific diets, certain pharmacotherapies, specific diseases, an increase in stone-forming compounds, and a reduction in stone-inhibiting substances all pose risks for kidney stone development. In identifying risk factors, laboratory medicine is crucial. Numerous laboratory blood and urine tests are advised by European urolithiasis guidelines for individuals with kidney stones of known and unknown composition in order to evaluate their metabolic health. Each form of kidney stone has a clear algorithm with treatment decision points identified to prevent recurrence[2]. There are two categories of medicines that are reportedly capable of causing calculi. The first one contains medications that are poorly soluble, excrete a lot of urine, and encourage crystallisation in the urine. Atazanavir and other protease inhibitors used to treat patients with human immunodeficiency virus (HIV) as well as sulphadiazine used to treat cerebral toxoplasmosis are the most common causes among them[3]. In addition, there are reports of efficacy for other disorders such as bipolar disorder and trigeminal neuralgia[4]. we should be aware of topiramate induced metabolic side effects, which include metabolic acidosis and kidney stones. We recommend testing blood acid base balance, urinary pH and citrates in patients taking topiramate and suffering from kidney stones[5].

II. CASE DESCRIPTION:

A 38 year old female patient came to cardiac outpatient department for master health checkup on April 2023. She was already a known case of epilepsy and without consultation from Physician. She has been taking T.Topirol 50mg for 2 years. The master health check up report shows 2.5mm upper pole, 3mm & 2.5mm lower pole Calculiin the left kidney:

The vital signs report were found to be normal.

BP	**Pulse**	**Spo2**	**Temp**	**Height**	**Weight**	**BMI**
120/70mmHg	83 b/m	97%	98.2◦F	156cm	77kg	32 kg/m^2

ADR "Topiramate Induced Renal Calculi".

Mechanism

It is well known that topiramate inhibits carbonic anhydrase, an enzyme involved in many physiological functions,including the kidneys' ability to maintain acid-base balance.

The renal tubules' reabsorption of bicarbonate is facilitated by carbonic anhydrase. Bicarbonate reabsorption is restricted by this enzyme's inhibition.

Impact on Acid-Base Balance: Topiramate interferes with the regular acidification of urine in the kidney's distal tubules by blocking carbonic anhydrase. Urinary citrate concentration may drop as a result of the inadequateacidification.

Reduced Citrate Levels: One of the main inhibitors of kidney stone formation is citrate. It creates a binding with the calcium in the urine to stop crystals from forming, which can result in the creation of stones. Decreased amounts of citrate in the urine increase the possibility of calcium phosphate stone development. The inhibition of crystallization by citrate is weakened, which leads to the precipitation of crystals of calcium phosphate.

Higher Risk of Stone Formation: Kidney stone formation is more likely when lower citrate levels and altered urine composition from poor acidification are combined. Low urine citrate levels are especially linked to calciumphosphate stones.

III. DISCUSSION:

It is important for healthcare providers to monitor patients taking topiramate for these potential renal-related complications and manage them accordingly. Regular monitoring of electrolyte levels, urine pH and kidney function can help identify any abnormalities and guide appropriate interventions. Valentina G et al., compared the study it was discovered that the annual incidence of symptomatic kidney stones was 2.1%. With the exception of the short research conducted in Mexico, a country with a relatively high prevalence of renal stones, all of the trials were uncontrolled. The annual incidence of kidney stones in this trial was 14% in control patients and 19% in topiramate-treated subjects. Adults using topiramate had a considerably higher susceptibility for kidney stone development. Imaging tests can occasionally detect kidney stones in persons who are asymptomatic[1].

It's important to note that the study you mentioned is a case study involving a single patient, which limits the generalizability of the findings. If you or someone you know is taking topiramate and experiencing kidney stones or any related symptoms, it is essential to consult a healthcare professional for proper evaluation, diagnosis and management. Tomas Salek et al,. the study compared with the primary cause of metabolic acidosis as well as its relation to kidney stone production were verified after the patient stopped taking topiramate and their acid-base state returned to normal. Topiramate has been previously mentioned as having the ability to cause calcium phosphate kidney stones through a variety of pathways, which is consistent with the stone type in our patient. The medication causes acidity in the renal tubules. Proximal and distal tubular disorders are coupled. The normal urine profile of topiramate medication includes low urine citrate excretion, urine pH > 6, and elevated urine HCO3 ion. Given that obesity is a risk factor for kidney stone development, her weight may have also contributed to the creation of the stones[2].

IV. CONCLUSION:

A effective drug that is primarily used to treat partial or refractory seizure disorders is topiramate. Because this medication inhibits carbonic anhydrase, long-term usage in patients may result in a substantial metabolic acidosis. Moreover, long-term topiramate use may cause a distal tubular acidification deficiency, which raises the possibility of calcium phosphate nephrolithiasis. Serious side effects are uncommon with topiramate, and it is usually well tolerated. However, the current evaluation suggests that using it may increase

the risk of renal stones,hypokalaemia, hyperuricaemia, and metabolic acidosis.

REFERENCE:

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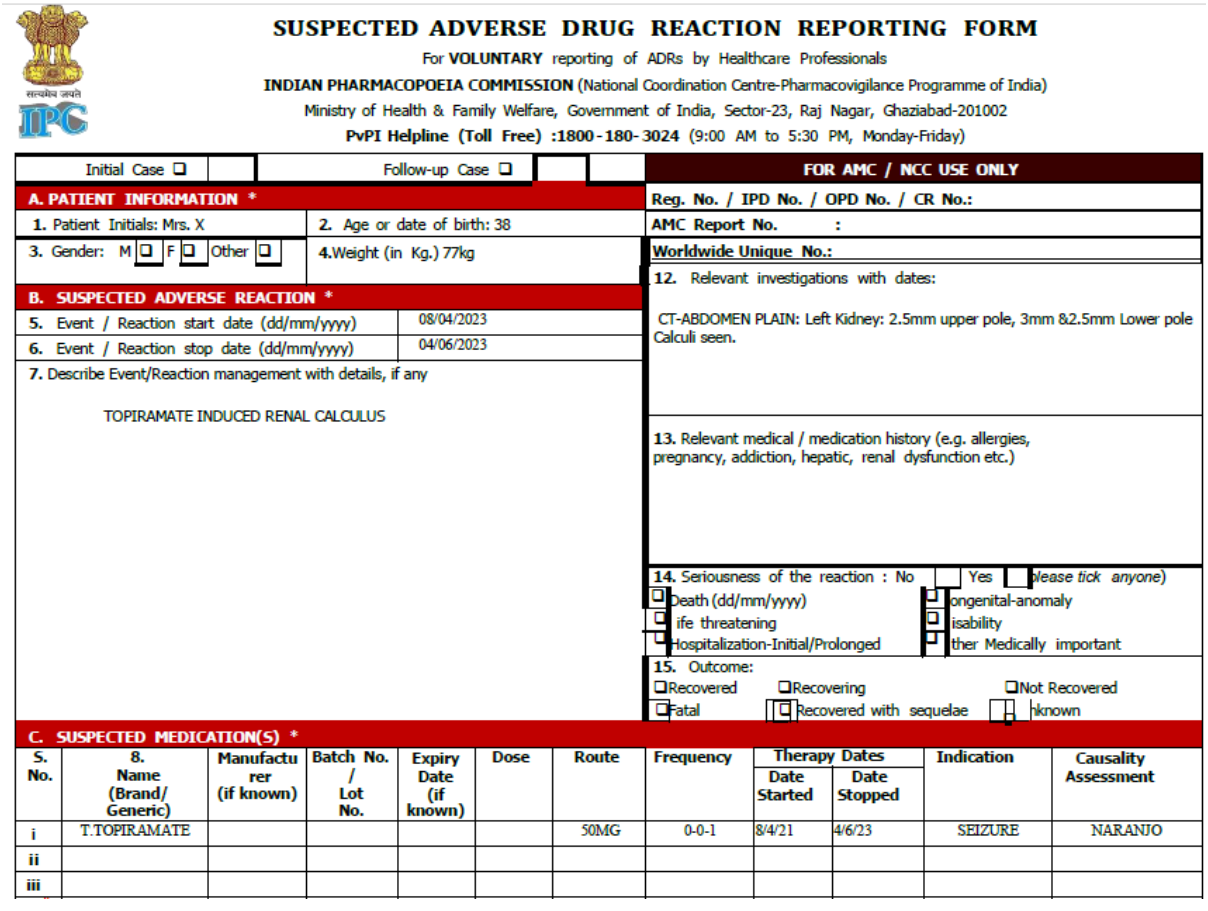

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For **VOLUNTARY** reporting of ADRs by Healthcare Professionals

INDIAN PHARMACOPOEIA COMMISSION (National Coordination Centre-Pharmacovigilance Programme of India)

Ministry of Health & Family Welfare, Government of India, Sector-23, Raj Nagar, Ghaziabad-201002

PvPI Helpline (Toll Free) :1800-180-3024 (9:00 AM to 5:30 PM, Monday-Friday)

Initial Case ❑ Follow-up Case ❑

FOR AMC / NCC USE ONLY

A. PATIENT INFORMATION *

1. Patient Initials: Mrs. X
2. Age or date of birth: 38
3. Gender: M ❑ F ❑ Other ❑
4. Weight (in Kg.) 77kg

Reg. No. / IPD No. / OPD No. / CR No.:

AMC Report No. :

Worldwide Unique No.:

B. SUSPECTED ADVERSE REACTION *

5. Event / Reaction start date (dd/mm/yyyy) 08/04/2023
6. Event / Reaction stop date (dd/mm/yyyy) 04/06/2023
7. Describe Event/Reaction management with details, if any

TOPIRAMATE INDUCED RENAL CALCULUS

12. Relevant investigations with dates:

CT-ABDOMEN PLAIN: Left Kidney: 2.5mm upper pole, 3mm &2.5mm Lower pole Calculi seen.

13. Relevant medical / medication history (e.g. allergies, pregnancy, addiction, hepatic, renal dysfunction etc.)

14. Seriousness of the reaction : No ❑ Yes ❑ (please tick anyone)

❑ Death (dd/mm/yyyy) ❑ Congenital-anomaly

❑ Life threatening ❑ Disability

❑ Hospitalization-Initial/Prolonged ❑ Other Medically important

15. Outcome:

❑ Recovered ❑ Recovering ❑ Not Recovered

❑ Fatal ❑ Recovered with sequelae ❑ Unknown

C. SUSPECTED MEDICATION(S) *

S. No.	8. Name (Brand/ Generic)	Manufacturer (if known)	Batch No. / Lot No.	Expiry Date (if known)	Dose	Route	Frequency	Therapy Dates		Indication	Causality Assessment
								Date Started	Date Stopped		
i	T.TOPIRAMATE					50MG	0-0-1	8/4/21	4/6/23	SEIZURE	NARANJO
ii											
iii											

iv#											

9. Action taken after reaction (*please tick*)							10. Reaction reappeared after reintroduction ofsuspected medication (*please tick*)			
S. No. as per C	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	Yes	No	Effect unknown	Dose (if re-introduced)
i										
ii										
iii										
iv										

11. Concomitant medical product including self-medication and herbal remedies with therapy dates (Exclude those used to treat reaction)

S. No.	Name (Brand / Generic)	Dose	Route	Frequency (OD, BD, etc.)	Therapy Dates		Indication
					Date Started	Date Stopped	
i	T. Riboflavin	10mg		0-0-1			
ii	T. Nortimar	25mg		0-0-1/2			
iii#							

Additional Information :

D. REPORTER DETAILS *

16. Name & Address : Narmadha.U
Swamy Vivekanandha College of Pharmacy, Tiruchengode, Namakkal.
Pin:637 205 Email:narmadhaudayakumaran30@gmail.com
Contact No: 9597656209
Occupation : Student Signature: U.Narmadha

17. Date of this report (dd/mm/yyyy) :

Signature and Name of Receiving Personnel :

Confidentiality : The patient's identity is held in strict confidence and protected to the fullest extent. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction. Submiss ion of an ADR report does not have any legal implication on the reporter.

Use separate page for more information
* Mandatory Fields for suspected ADR Reporting Form

Naranjo Adverse Drug Reaction Probability Scale

Question	Yes	No	Do Not Know	Score
1. Are there previous *conclusive* reports on this reaction?	+1	0	0	+1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	0
3. Did the adverse reaction improve when the drug was discontinued or a *specific* antagonist was administered?	+1	0	0	+1
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	+2
6. Did the reaction reappear when a placebo was given?	-1	+1	0	+1
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in *any* previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	0
			TOTAL SCORE:	5

SCORE: Definite (≥9)
Probable(5-8)
Possible (1-4) Unlikely (≤0)