Case Studies from the Medical Examiner

Intentional Quetiapine Overdose Leads to Patient Death

Spring 2022

Case Studies from the Medical Examiner are a deliverable of the collaborative work of the Adult Inquest Review Committee. The College of Pharmacists of Manitoba, the College of Physicians and Surgeons of Manitoba, and the Chief Medical Examiner's Office work togeter to learn from deaths related to prescription drugs, focusing on opioids and other drugs of misuse. All dates, patient initials, names of pharmacies, and prescribers have been changed and de-identified to protect the identity of the patient and their family.

Introduction

AK is a 63-year-old man who was found dead in his bed at home on May 30, 2017, after not being seen for several days. He had a history of bipolar disorder, depression, heavy cigarette smoking with chronic obstructive pulmonary disease (COPD), atrial fibrillation, high cholesterol, and an untreated seizure disorder (with no seizures for more than 11 years). An autopsy was performed, and the immediate cause of death was determined to be quetiapine toxicity. The manner of death was determined to be suicide.

Discussion

Quetiapine toxicity is associated with levels greater than 1,500 ng/L, which can be life-threatening[1]. This patient's toxicology report showed a quetiapine level of 19,700 ng/L, which is significantly higher than the therapeutic range and 13-fold more than the toxicity level found in literature.

The role of a pharmacist when dispensing quetiapine is to provide counselling that includes the potential risks of the drug and document these conversations appropriately.

Quetiapine is an atypical antipsychotic used for the treatment of schizophrenia, bipolar disorder, and as adjunctive treatment for major depressive disorder. It has also been reported to be used off-label to treat anxiety and sleep disorders[2]. However, its antagonist activity on many receptors contributes to its side effect profile such as dizziness and somnolence due to H1 receptor antagonism, hypotension due to alpha-1 receptor antagonism, and anticholinergic effects from M1 blockade[3]. Quetiapine has also been associated with myocarditis, stroke, and metabolic dysregulation with long-term use.[1,4,5]

In acute quetiapine toxicity, the most common symptoms that patients exhibit are drowsiness, tachycardia, and respiratory depression[6]. Since this patient had COPD, the risk of respiratory events during quetiapine toxicity is elevated due to the obstructed airway from this chronic inflammatory disease[7]. Additionally, quetiapine in high doses can increase the risk of QTc prolongation or life-threatening Torsades de Pointes, especially in patients with risk factors (e.g., older age, concurrent QTc prolonging drugs, hypothyroidism)[1]. Neuroleptic malignant syndrome (NMS) is another life-threatening side effect of antipsychotics that can occur as a result of a sudden drop in dopaminergic transmission. Signs and symptoms of NMS include fever, autonomic instability (e.g., unstable heart rate, blood pressure, sweating, drooling), rigidity, and mental status changes. Any sign or symptom of overdose requires immediate medical attention and quetiapine should be immediately withdrawn.[8,9] Unfortunately, there is currently no available antidote to reverse quetiapine toxicity.[1]

Toxicology Results

The following chart represents the results of the toxicology report.

Drug	Level in blood (ng/mL	Therapeutic Range
Quetiapine*	19700	100 – 1000
Methylphenidate Ritalinic acid (Inactive metabolite)	0 180	5 – 20 80 – 250

*Above therapeutic range.

Relevant DPIN History Prior to Patient's Death

Generic Name	Date Dispensed	Strength (in mg)	Quantity	Days Supply	Prescriber	Pharmacy
Quetiapine	April 3	300	180	90	Dr A.	ABC Pharmacy
Methylphenidate		36	90	80		
Duloxetine		60	180	90		
Levothyroxine		175	90	90		

Recommendations

The role of a pharmacist when dispensing quetiapine is to provide counselling that includes the potential risks of the drug and document these conversations appropriately. Quetiapine is commonly prescribed for its sedating and mood stabilizing properties.[2,10] However, pharmacists must also consider the drug's potential for harm in overdose. According to a paper by Peridy et al, it was shown that 79.8% of quetiapine self-poisonings were voluntary, and within this group, 91.4% had a history of mental illness.[6]

The 2020 Annual National Poison Data System Report also identified quetiapine as being the most common antipsychotic involved in overdose cases, often in combination with other sedating agents.[11] Therefore, pharmacists must critically consider these points when reviewing a patient's medications and carefully assess whether it is appropriate to dispense quetiapine. This can include deprescribing medication that is no longer providing benefit to the patient (e.g., reducing the use of combination sedating agents in older adults with an uncontrolled chronic respiratory condition) or that have been prescribed as a result of prescribing cascade (e.g., discontinue the use of a stimulant that was initiated to override sedating effects of medication), and having contact information available to counseling services in your area or to a crisis line (e.g., Mobile Crisis Line, Klinic Crisis Line, Crisis Services Canada).

It is a pharmacist's primary responsibility to ensure patient safety when dispensing a prescription medication. All members are reminded of their professional obligation to ensure that each prescription is reviewed thoroughly, and potential issues addressed, even if it means there may be a difficult patient encounter. Measures must be taken to address issues with appropriateness of drug therapy, drug interactions, therapeutic duplication, and inappropriate or unsafe dosing. Pharmacists do not have the obligation to dispense medications that they believe may cause patient harm. In such cases, the patient must be referred appropriately according to the Referring a Patient Practice Direction.

References

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