Case Studies from the Medical Examiner

Zopiclone Toxicity Contributes to Patient Death

Summer 2020

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

SN was a 27-year-old female found dead on the floor of her home on June 22, 2019, with evidence of blunt head trauma. The immediate cause of death was determined to be blunt head trauma with zopiclone toxicity as a contributing factor. SN had a history of chronic back pain and multiple traumatic injuries. Two weeks prior, SN presented to the emergency department with injuries to her face and arm and was unable to recall what happened.

Discussion

SN was consistently requesting and receiving early refills for medications with sedating properties, including cyclobenzaprine, quetiapine, sertraline, and zopiclone, which were always authorized by her primary care provider. Only a few weeks before her death, SN requested a refill of zopiclone 23 days early on a 28-day supply. As per previous requests, the prescriber was contacted to authorize the early release, and the patient was dispensed the medication.

SN had a consistent prescriber and a consistent pharmacy. Reasoning for authorizing early refills were often provided by either the prescriber or the patient, such as an upcoming vacation or a lost/stolen medication supply. While these factors may have served to assuage any initial concerns dispensing pharmacists may have had, pharmacists are reminded of their responsibility to ensure appropriate prescribing before dispensing. This responsibility goes beyond simply confirming that an early refill is authorized. Pharmacists must further ensure the authorization of an early refill is not harmful for the patient.

> **[A pharmacist's] responsibility goes beyond simply confirming that an early refill is authorized. Pharmacists must further ensure the authorization of an early refill is not harmful for the patient.**

Recommendations

Dealing with consistent requests for early refills and inappropriate prescribing practices can be challenging. The following recommendations may be appropriate to implement in your practice.

Communicating with prescribers about concerns such as consistent early refills is paramount to patient safety. While one or two occasional early refill requests may be normal, when these become consistent, it may be a sign of other issues. Even if a prescriber authorizes early refills for each instance, it may be valuable to contact the prescriber about the big-picture issue of early refills rather than only each individual request. When early refills become consistent, a conversation about limited supports or access to supports for the patient to minimize risk associated with their prescription is helpful.

Toxicology Results

The toxicology report shows baclofen and zopiclone present at supratherapeutic levels. Zopiclone, in particular, vastly exceeded the acceptable therapeutic range. Alcohol was also present, and other drugs including quetiapine an sertraline were detected but not quantified.

Drug	Level in blood (ng/mL)	Therapeutic Range (ng/mL)
Baclofen	440	80-400
Zopiclone	88	25 - 65
Ethanol	22	N/A

Six-Month DPIN History Prior to Patient's Death

Generic Name	Date Dispensed	Strength	Quantity	Days Supply	Prescriber	Pharmacy
Baclofen	May 1, 30	20 mg	60	30	Dr. A	EFG Pharmacy
Cyclobenzaprine	June 6 May 15 April 22 March 7, 30 February 13	10 mg	90	30	Dr. A	EFG Pharmacy
Quetiapine	May 4, 30 April 22 March 7, 30 February 13 January 15	100 mg	90	30	Dr. A	EFG Pharmacy
Sertraline	June 6 May 15 April 16 March 7, 30 February 13 January 4, 30	100 mg	30	30	Dr. A	EFG Pharmacy
Zopiclone	June 6 May 4, 15, 30 April 11, 22 March 7 February 13 January 4, 23	7.5 mg	60	30	Dr. A	EFG Pharmacy

Therefore, pharmacists should be aware of available resources in the community

Pharmacists do not have an obligation to dispense a medication they believe may cause patient harm. In such cases, the patient must be referred appropriately according to the Referring a Patient Practice Direction.

If continued attempts to communicate and address concerns with the prescriber are unsuccessful, pharmacists may bring the matter forward to the prescriber's regulatory body (e.g. College of Physicians and Surgeons of Manitoba). As this is a patient safety issue, it is within the mandate of a regulatory college to investigate and intervene as appropriate.

Recommending and implementing controlled dispensing of commonly abused medications (e.g. monthly or weekly dispensing) may be appropriate for patients who are requesting early refills consistently. Controlled dispensing should be initiated gradually and discussed with the patient and prescriber. In these discussions, make your concerns and reasoning known, focusing the conversation on the patient's safety, and the safety of those around them.

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.

Suggested Responses When Patients Request Early Refills

Example of Patient Request/Reason	Possible Pharmacist Response
"The doctor gave me this prescription early so I should be getting it early."	"That's not always the case. There are some concerns I have with the timing of this refill that I'd like to discuss with your prescriber first so we can move forward in the safest way."
"The medication was stolen" or "I lost the medication."	"I'm sorry to hear that. Is there any way we can prevent that from happening in the future? Would it be helpful to have a lock box for your medications, so you can always have a consistent and safe place to store them? Our pharmacy can provide one."
"The other pharmacist always fills my early refills."	"That may be true, but I feel it's important to discuss some concerns I have about early refills because these can pose a danger to your health."
"I'm travelling and need more medication."	"Are you able to receive your next refill on time at a pharmacy near where you're travelling to? I can talk to your doctor about the best way to do that."
Provides repeated requests for early refills as described above. If you feel it's necessary, this may also be a good time to discuss with the prescriber whether the patient appears to be struggling with a substanceuse disorder, and a care plan for moving forward.	"It seems that there are some continuous challenges that often require you to request early refills. I'd like to talk with you and your prescriber about what we can do. Perhaps dispensing smaller quantities of medication at a time may be helpful to prevent these challenges."