# Toxicology

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This blog focuses on a case of quetiapine poisoning, and details the initial assessment, appropriate investigations, and management of quetiapine toxicity and is based on an interview discussion with Emergency Physicians, Dr Angela Chiew and Dr James Edwards.

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## Introduction

In this blog we hear from Dr Angela Chiew, an Emergency Physician and Toxicologist at Prince of Wales Hospital. This blog focuses on a case of quetiapine poisoning, and details the initial assessment, appropriate investigations, and management of quetiapine toxicity.

## Case

A 28 year old male with a history of drug-induced psychosis presents two hours after ingesting 50 X 200 mg tablets of modified-release quetiapine with alcohol. On presentation to the emergency department, he has a heart rate of 120 beats per minute, blood pressure of 125/85, reduced Glasgow Coma Scale (GCS) score of 11, confusion and dilated pupils.

**James Edwards: What is most concerning about this patient's presentation? Is there anything we should particularly note from the history?**

**Angela Chiew:** What is most concerning about this case is the large dose of quetiapine the patient has ingested.

The timeframe was 2 hours ago, which gives an indication that we can act early and administer gastrointestinal (GIT) decontamination with activated charcoal. He has taken a total of 10 g of quetiapine, and toxicity may be delayed. What you are seeing now is not the peak toxicity, as it is a modified-release medication that is released over many hours.

**James Edwards: You mentioned that modified-release medication may cause prolonged sedation. Are you concerned that the GCS may reduce over the coming hours, and this may require further intervention, such as intubation?**

**Angela Chiew:** The issue with the dose raises the question of whether it may be beneficial to intervene early.

In a patient who has taken a large dose of modified-release quetiapine, it may be best to anticipate delayed effects and intervene early. Intervention may include endotracheal intubation, and GIT decontamination with activated charcoal to avoid the development of significant toxicity. The patient has a low GCS at presentation and this will only get worse.

**James Edwards: What is your general assessment of the patient?**

**Angela Chiew:** All toxicology patients require a risk assessment. Often this cannot be obtained from the patient and is dependent on collateral history from ambulance paramedics, family and sometimes eHealth resources (e.g. to determine which prescriptions have been filled and what medications he has been prescribed in the past).

In the risk assessment, you need to determine what has potentially been ingested. In this case we already know. Ambulance paramedics or family may be able to provide you with empty packets. You also need to determine the time of ingestion. These are both important aspects.

Furthermore, you need to determine whether there are signs and symptoms of drug toxicity and whether they are consistent with the suspected drug overdose. Sometimes, you need to return to the history and determine what other medications may have may have been ingested. What other medications has the patient been on? What medications do other people who live with the patient take?

When assessing signs and symptoms of toxicity, you must also consider how long ago the patient ingested the drug.

The risk assessment can also be considered alongside any relevant bedside investigations, if appropriate.

This patient has taken a large dose of quetiapine 2 hours ago. It was a modified-release preparation, so he is not yet at peak toxicity, and he will become progressively drowsier. He may develop delayed signs of severe quetiapine toxicity. In this case, the risk assessment is a large overdose, early in the course of the poisoning (given the time since ingestion).

You must then think about what does this drug specifically cause in poisoning? Quetiapine has 3 main effects:

- **anticholinergic toxidrome - he already has dilated pupils, confusion, delirium and tachycardia; he may also develop urinary retention, which is commonly missed**
- **seizures - rarely**
- **hypotension - in larger doses, such as in this case, hypotension, can be one of the pitfalls of quetiapine poisoning**

**To summarise:** we are concerned that this is a large ingestion and he will develop more severe toxicity over the coming hours. It may be best to intervene early because his GCS is already 11 and will drop further. You have time to prepare to intubate him and administer GIT decontamination with activated charcoal.

**James Edwards: What are you looking for on examination?**

**Angela Chiew:** At lower doses of quetiapine, you are looking for signs of early toxicity. The anticholinergic toxidrome, as previously mentioned, causes dilated pupils, delirium and decreased level of consciousness. It is important to look for urinary retention. Often patients who have ingested lower doses are agitated and cannot tell you they are in urinary retention. Inserting a urinary catheter may reduce the patient's agitation.

Assessing level of consciousness involves asking yourself whether the patient if ventilating adequately. Often it is said that the patient is 'protecting their own airway' or 'ventilating fine'; however, if the patient is on high-flow oxygen, it can mask the presence of hypoventilation. The PaCO2 may be climbing while their oxygen saturation appears to be adequate.

A blood gas analysis can help guide whether patients who have overdosed on sedative agents (e.g. quetiapine, benzodiazepines, opioids) are ventilating adequately. It provides a PaCO2 (or PvCO2) and if this is high, the patient is not adequately ventilated, and you may need to intervene.

**James Edwards: What other investigations are important?**

**Angela Chiew:** All toxicology patients should have a 12-lead electrocardiograph (ECG). Quetiapine can cause QT-interval prolongation and the risk of developing torsades de pointes (which is very rare). If the patient co-ingested other drugs, the ECG may assist in determining the presence of other drugs (e.g. stimulants such as amphetamines or cocaine can cause ischaemic changes on ECG, or tricyclic antidepressants can cause a wide QRS complex and arrhythmias).

Any unconscious patient must have a blood glucose concentration checked to exclude hypoglycaemia that can be easily treated with glucose supplementation.

A blood gas analysis can also be helpful to demonstrate whether the patient is acidotic or ventilating inadequately. A high blood lactate concentration or severe acidosis may also indicate the presence of another ingested substance.

A serum paracetamol level should be checked in all patients, especially if they are unconscious. Paracetamol is a very accessible drug within the community, with high potential morbidity that can be easily treated with acetylcysteine.

In summary: the minimum investigations for this patient include an ECG, blood glucose concentration, blood gas analysis, and paracetamol level. These investigations can help to determine further management.

**James Edwards: What would you do next?**

**Angela Chiew:** Resuscitation is always the first step, followed by 3 specific management options for toxicology patients (if indicated):

- **GIT decontamination with activated charcoal**
- **enhanced elimination**
- **antidote**

For patients who present late after an immediate-release quetiapine poisoning, it may be too late to decontaminate them; however, this case involves a modified-release preparation and the patient is drowsy. We anticipate that he will develop hypotension that may require inotropic support. There is still an opportunity to intervene and administer GIT decontamination within 4 hours.

A GCS of 11 indicates that he is too drowsy to drink activated charcoal independently; he must be alert to do this. There is a reasonable amount of time to pre-emptively intubate him and place a nasogastric tube. The safest option is to intubate and ventilate him and administer 50 g of activated charcoal via the nasogastric tube.

The modified-release preparation means there will be prolonged, ongoing absorption, or even bezoar formation within the GIT (modified-release tablets tend to clump together). If he has bowel sounds, consider administering a second dose of activated charcoal 25 g in 4 hours time.

eTG: Toxicology and Toxinology recommends administering activated charcoal for GIT decontamination within 2 hours of ingestion (previously it was within 1 hour). This is supported by a study that evaluated gastroscopies in poisoned patients and found that papillate matter/ slurries/ full tablets persisted in the stomach for up to 4 hours after ingestion. Other studies have found that modified-release tablets stay within the GIT for a lot longer than 4 hours.

There is no technique to enhance the elimination of quetiapine.

There is no specific antidote for quetiapine.

**James Edwards: If the patient's systolic blood pressure drops to below 90, how would you manage his hypotension?**

**Angela Chiew:** Hypotension is anticipated in this patient. Start with intravenous fluid. If there is no response after 2 litres, it is recommended to start inotropic support.

Noradrenalin is the vasopressor of first choice Noradrenaline can be commenced peripherally rather than via a central venous line, as the placement of a central venous line can delay urgent management of hypotension. Peripheral administration of noradrenaline can be started peripherally prior to insertion of the central line.

Quetiapine is a potent alpha-adrenoceptor blocker. It is important to avoid adrenaline in this case, as adrenaline has both alpha- and beta-agonist effects. When adrenaline is given for quetiapine poisoning, only the beta-agonist effects are observed and these can worsen hypotension.

**James Edwards: What are your take home points for junior doctors?**

**Angela Chiew:** Urinary retention is often missed and can be an easily reversible cause of patient agitation. Even agents that are not anticholinergic can cause urinary retention (e.g. any sedative that causes drowsiness so the patient cannot communicate).

It is also important not to administer too much oxygen, because hypoventilation is often missed.

A thorough history and risk assessment can be gained from ambulance paramedics and family. Family may need to visit the patient's home to look through their possessions, to assess what the patient has potentially ingested. eHealth resources may also give information about the patient's prescription(s).

**James Edwards: What are some resources available for toxicology patients?**

**Angela Chiew:** eTG: Toxicology and Toxinology was recently updated and expanded in content by an expert group of Clinical toxicologists and Poison information specialists. It now has over 100 specific poisoning topics. Many topics offer specific advice as to when it is appropriate to call a toxicologist and the threshold for calling. For rare overdoses (e.g. theophylline, certain herbicides) it will specify to call a toxicologist as early as possible.

Toxicology and toxinology also details risk assessment and management, including advice on antidotes, and regimens for inotropic support. There is also more specific advice on disposition (e.g. how long to observe a patient with suspected poisoning).

Toxicology and Toxinology is a readily available resource within hospitals in all Australian states, and has up-to date management for many poisonings and exposures.

# Resources

Quetiapine poisoning [published 2019 Aug, Amended Dec 2020]. In: eTG complete [digital]. Melbourne: Therapeutic Guidelines Limited; 2021 Mar. https://tgldcdp.tg.org.au/viewTopic?topicfile=toxicology-quetiapine&guidelineName=Toxicology%20and%20Toxinology&topicNavigation=navigateTopic

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