

Acute intoxication of an adolescent with quetiapine after suicide attempt: A case report

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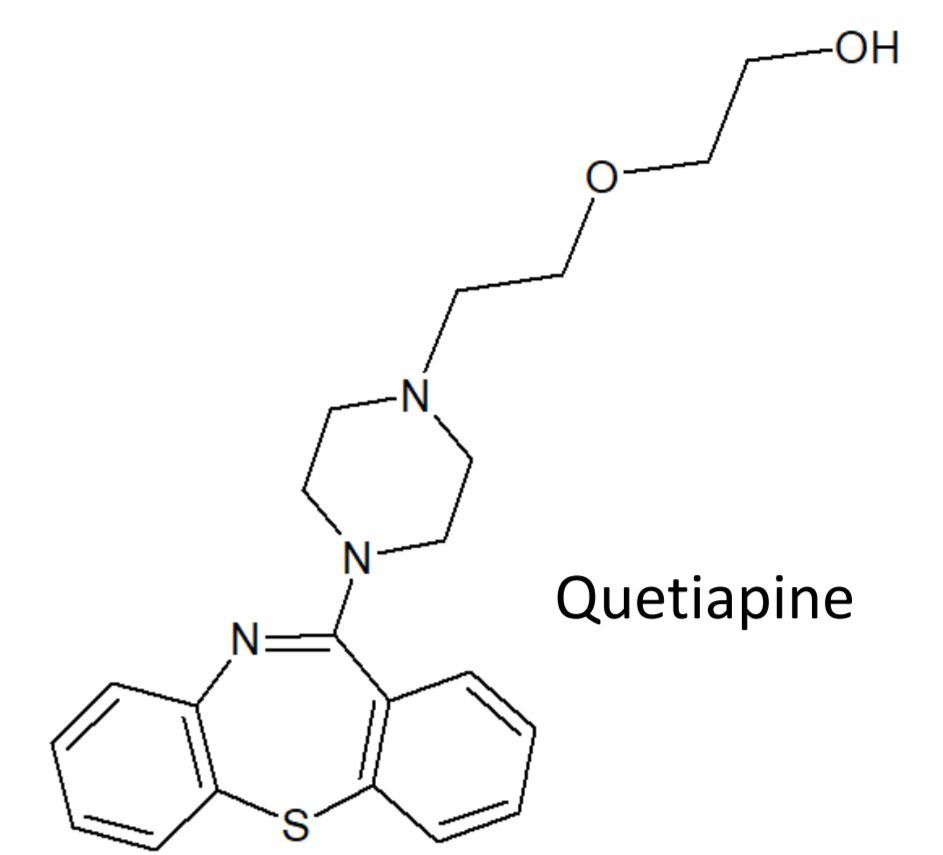
Background

Quetiapine:

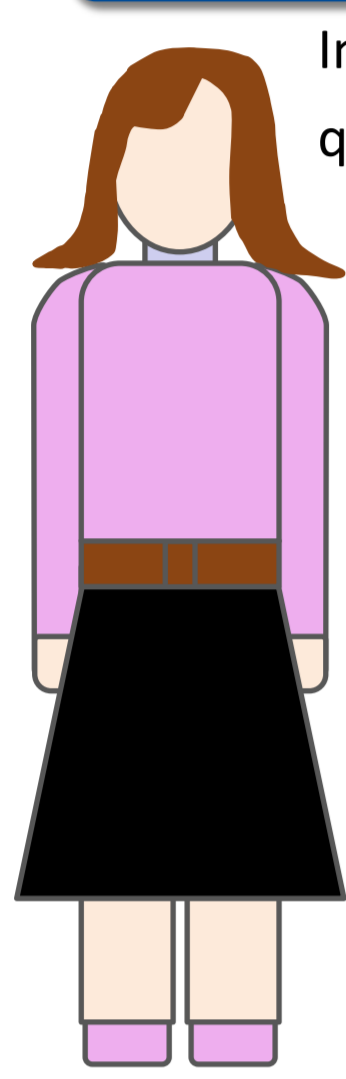
- Atypical/second generation-antipsychotic drug
- Adverse effect profile preferable compared to first generation-antipsychotics, major psychopharmacological product
- Approved for treatment of schizophrenia and major depression
- Often used in suicide attempts
- Therapeutic range in serum 100 – 500 ng/ml^[1]
- Toxic effects from >1000 ng/ml, >1800 ng/ml coma and death possible^[2,3]



- Antipsychotic effects: Antagonism at dopaminergic D₂ and serotonergic 5-HT_{2A} receptors
- Adverse effects: Antagonism at adrenergic α₁, muscarinic M₁ and histaminergic H₁ receptors
- Symptoms of overdose: Somnolence, sinus tachycardia, hypotension, CNS & respiratory depression



Case report



15 year-old

Anamnesis:

- Depression
- Prior suicide attempts with alcohol
- Foetal alcohol syndrome
- Automutilation
- No current treatment with psychiatric drugs

Intake of ~120 crushed quetiapine tablets in water

Patient found, first responders detect Glasgow Coma Score (GCS) of 8, transport to ICU

Arrival at ICU: Comatose, GCS of 3 prompting immediate intubation, tachycardia (110 bpm), cranial CT unremarkable

Patient transferred, intubation due to GCS of 6

Diary with suicide plan including quetiapine tablet doses and a timetable found on site

Patient was released from ICU and transferred to psychiatric care

0 h

5.5 h

12 h

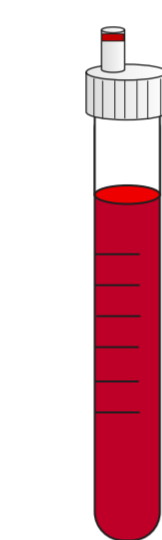
24 h

26 h

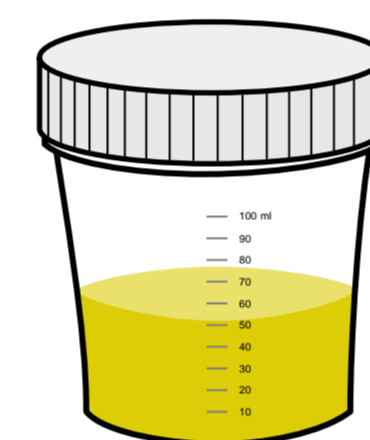
30 h

5 d

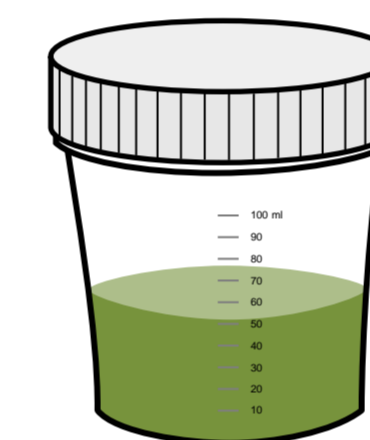
First blood sample



Urine sample collected, Mahsan immunoassay in hospital positive for tricyclic antidepressants and THC



Gastric lavage, stomach content and a "tablet bezoar" were preserved



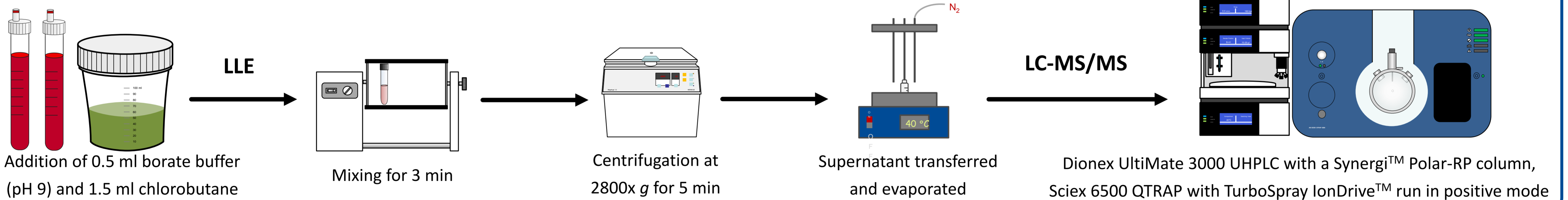
Second blood sample



Methods

- LLE of blood and gastric content with deuterated quetiapine as internal standard
- Chromatic separation on a Dionex UltiMate 3000 UHPLC with a Synergi™ Polar-RP column
- Sciex 6500 QTRAP equipped with a TurboSpray IonDrive™ ion source run in positive mode

- Mobile phase used was A1 (deionized water, 0.01% 10 M ammonium formate, 0.1% formic acid) and B1 (Methanol, 0.1% formic acid).



Analytical results

First blood sample: 5.5 h after intake

- Quetiapine: 4100 ng/ml
- Norquetiapine: 2000 ng/ml

Second blood sample: 26 h after intake

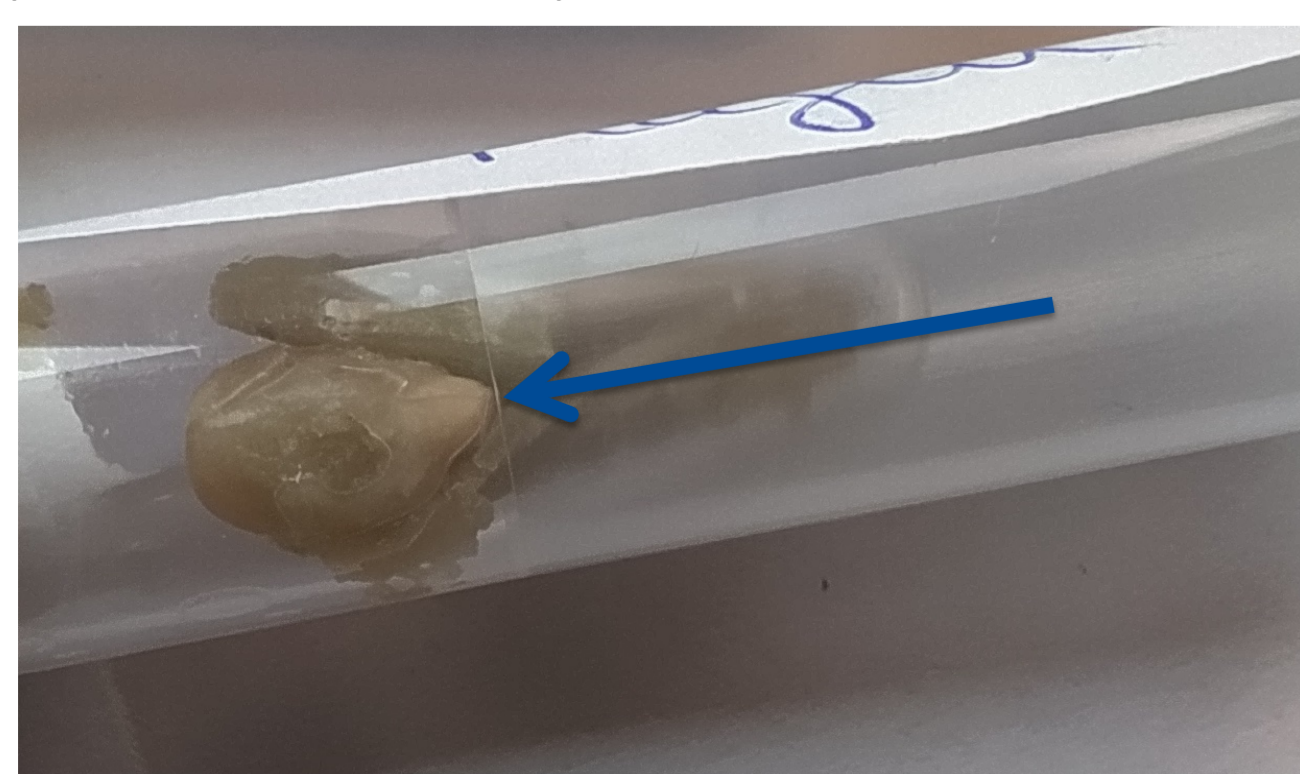
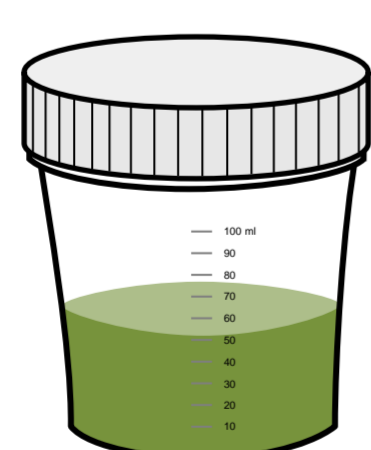
- Quetiapine: 220 ng/ml
- Norquetiapine: 630 ng/ml

Gastric content: 24 h after intake

- Quetiapine: 120 000 ng/ml
- Norquetiapine: 20 000 ng/ml

Tablet bezoar:

- Seed of *Helianthus annuus* (Common sunflower)



Discussion

The patient showed typical symptoms of quetiapine intoxication, including coma, tachycardia and respiratory depression. In contrast to other quetiapine poisoning reports, hypotension requiring treatment only occurred as a minor symptom after the second intubation. The ingestion of extended release-quetiapine explains the progressive worsening of the symptoms from the initial assessment by the first responders to the assessment at the ICU. The false-positive result of the urine immunoassay screening for tricyclic antidepressants can be explained by a known cross-reaction of quetiapine with the employed Mahsan test. Once the tablet emulsion was removed from the patients stomach, the serum levels of quetiapine and norquetiapine decreased and the status of the patient improved. The ingestion of extended release-formulation quetiapine has been connected to the formation of tablet bezoars, however the suspected tablet bezoar was found to be a sunflower seed. It is possible that the formulation of the ingested quetiapine tablets is not prone to cause the formation of a bezoar, or that the process of crushing the tablets has dispersed the tablet matrix responsible for bezoar formation, thereby preventing its clustering into a bezoar.

Conclusion

In the case presented here, the detected **levels of quetiapine in serum** are well in agreement with the values for quetiapine overdoses found in literature, as well as with the symptoms experienced by the patient. Likewise, individuals have survived quetiapine serum levels higher than 1800 ng/ml solely with supportive treatment^[2,3]. The observed **CNS depression requiring intubation** can be explained due to antagonism of quetiapine at histaminergic H₁ receptors. Similarly, **tachycardia** can be explained by the antagonism of quetiapine at adrenergic α₁ and muscarinic M₁ receptors. Since an immunoassay screening was performed only after 12 h since suspected intake, the process of identifying the intoxicating agent was unnecessarily prolonged. As an outlook for easier detection of quetiapine intoxications, both an immediate urine screening for drugs of abuse including CNS depressants and closer on-site inspection allow for more timely identification. While positive immunoassay results should always be confirmed with analytically more specific methods, even a false-positive result of an immunoassay can be a clue if the substances commonly causing cross-reactions are known.

References

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- [2] Peridy E, Hamel JF, Rolland AL, Gohier B, Boels D. Quetiapine Poisoning and Factors Influencing Severity. *J Clin Psychopharmacol*. 2019 Jul/Aug;39(4):312-317.
- [3] Müller C, Reuter H, Dohmen C. Intoxication after extreme oral overdose of quetiapine to attempt suicide: pharmacological concerns of side effects. *Case Rep Med*. 2009;2009:371698. 3.

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