Deliberate self-poisoning with tiagabine: An unusual toxidrome

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Abstract

Tiagabine is an anticonvulsant acting by selective inhibition of neuronal and glial gamma-aminobutyric acid uptake, resulting in increased gamma-aminobutyric acid-mediated inhibition in the brain. Few reports in the literature describe the clinical course of severe tiagabine intoxication. A 44-year-old woman presented after deliberate self-poisoning with 100 tiagabine 15 mg tablets (1500 mg; 25 mg/kg). Serum tiagabine level was 4600 µg/L (1725 mmol/L) at presentation, 20 times levels associated with therapeutic dosing. Intoxication was manifested by profuse vomiting, coma, myoclonus, generalized rigidity, bradycardia, hypertension, hypersalivation and generalized piloerection within 2 h of ingestion. The patient was intubated and management was supportive. Coma lasted until 10 h post-ingestion, but recovery was complicated by severe agitated delirium lasting 12 h. The patient recovered fully within 26 h of ingestion. Tiagabine deliberate self-poisoning was associated with the rapid onset of coma and an unusual toxidrome. Recovery, although complicated by agitated delirium, was complete within 26 h.

Key words: adverse effect, poisoning, tiagabine, toxicity.

Introduction

Tiagabine is an anticonvulsant used for adjunctive treatment of refractory partial seizures.1,2 It has also been advocated for the treatment of panic disorder, post-traumatic stress disorder and rage.3-5 It acts by selective inhibition of neuronal and glial gamma-aminobutyric acid (GABA) uptake, resulting in an increase in GABA-mediated inhibition in the brain.6 Side-effects reported during therapeutic doses include dizziness, asthenia, tremor and difficulty with concentration.7,8 Non-convulsive and convulsive status epilepticus have been reported at therapeutic doses.9-13 Tiagabine is approved for use in Australia, New Zealand, USA and most of Western Europe. In Australia, tiagabine is formulated in 5, 10 and 15 mg tablets. Recommended maintenance daily doses in adults are 30–50 mg.

Therapeutic tiagabine levels in therapeutic trials were 1–234 µg/L (0.4–88 mmol/L).13 Published reports of tiagabine intoxication are limited. Leach et al.
reported a patient who was comatose for 12 h after ingesting 320 mg tiagabine and a trivial phenytoin dose (400 mg). A serum tiagabine level of 3100 µg/L (1163 mmol/L) was reported. Ostrovskiy et al. reported a patient who developed status epilepticus after ingesting an unknown amount of tiagabine (serum level 1870 µg/L, 701 mmol/L). Sustained myoclonic jerks were noted on continuous EEG monitoring. One week later, the same patient ingested 1000 mg of tiagabine and developed status epilepticus again (serum level 2620 µg/L, 975 mmol/L). Cantrell et al. reported a 46-year-old woman who apparently ingested 72 mg of tiagabine and developed mutism, mydriasis, facial grimacing and flexure posturing that resolved within 12 h. Spiller et al. reported a retrospective series of 57 cases of poisoning sourced from US poison centre data. Neurological symptoms included lethargy, confusion, agitation, seizures, status epilepticus and coma. The onset and duration of symptoms were short (mean 1.3 and 9.1 h, respectively). The lowest dose associated with seizures and coma in an adult was 96 mg.

We present a case of deliberate self-poisoning with tiagabine complicated by an unusual toxidrome and agitated delirium.

**Case report**

A 43-year-old woman (60 kg) was brought to the ED following apparent deliberate self-poisoning. The patient had discussed suicide with her partner that day. She was last seen well at 17.00 hours. Shortly before 19.00 hours, she was found unresponsive. The patient had vomited profusely. She had generalized twitching, and the partner thought she was seizing. The partner reported that his dog had eaten much of the patient’s vomit, then started to have seizures also.

During transfer to hospital by ambulance, the patient had generalized twitching movements. An oropharyngeal airway could not be placed owing to pronounced masseter spasm. Glasgow coma scale (GCS) was three. At presentation, the patient’s GCS was 5 (E1, V1, M3). She was bradycardic (40–60) and hypertensive (205/60 mmHg). Her respiratory rate was 15, oxygen saturation 80% on oxygen by mask at 15 L/min, and tympanic temperature 35.5°C. Pupils were 5 mm and reactive. The patient had generalized neuromuscular rigidity and intermittent large myoclonic movements. Marked hypersalivation was present, requiring constant airway suctioning. There was no evidence of lip, oral, mucosal or pharyngeal burns. The patient exhibited generalized piloerection, most notable on the arms and legs.

The patient was intubated and ventilated following rapid sequence induction with midazolam, fentanyl and suxamethonium. Gastric lavage was performed, and 50 g activated charcoal was administered via nasogastric tube. The patient was not paralysed but sedated by propofol infusion.

The patient was thought to have access to lithium, paroxetine, topiramate, diazepam, ethanol, glyphosate and a metal-cleaning product containing sulphamic acid and thiourea. The patient had a history of deliberate self-poisoning using her sister’s topiramate, and a recent inpatient admission with acute lithium intoxication.

The 12-lead ECG showed bradycardia with normal pulse rate, QRS and QT conduction intervals. Serum lithium level was 0.8 mmol/L (0.5–1.0 mmol/L). The serum lactate was normal (1.2 mmol/L). Serum pseudocholinesterase level was within the normal range (7670 IU/L; reference range 5000–12 900 IU/L).

The patient was admitted to the intensive care unit. No further overt seizures were noted, but intermittent myoclonic movements of the limbs were seen. The diagnosis was not clear, but nicotinic, topiramate and clozapine intoxication were entertained. An atypical syndrome of central serotonergic toxicity was also considered.

Eight hours after intubation, the patient awoke and inadvertently extubated herself. She had a severe agitated delirium that lasted a further 12 h. This agitation resembled a central anticholinergic delirium or hallucinogenic intoxication, with extreme vigilance, paranoia and possible visual hallucinations. She appeared frightened, frequently cried out and tried to jump out of bed when not sedated. Physical examination at this time showed persistent mydriasis but normal mucous membranes, vital signs, bowel sounds, deep tendon reflexes and tone. Her arousal was managed with titrated doses of midazolam (total 92 mg) and olanzapine 10 mg. Approximately 26 h after presentation, the patient’s mental status returned to normal and she admitted taking 100 of her sister’s tiagabine 15 mg tablets (1500 mg; 25 mg/kg). She denied any co-ingestion. Serum tiagabine level at presentation was 4600 µg/L (1725 mmol/L).

**Laboratory analysis**

Serum concentrations were measured using high-performance liquid chromatography by comparison of the peak heights of the tiagabine with an internal standard from an extracted standard curve.
Discussion

This patient ingested an entire bottle of tiagabine, a common scenario in deliberate self-poisoning. The resulting clinical presentation was notable for profuse vomiting, coma, myoclonus, generalized rigidity, sinus bradycardia, hypertension, excessive salivation, mydriasis and generalized piloerection within 2 h of ingestion, followed by agitated delirium during the recovery phase. No definite tonic-clonic seizures were witnessed, but continuous EEG monitoring was not performed. Seizures might have occurred in the prehospital phase. It is possible the delirium represented a state of non-convulsive status epilepticus, but it did not seem to respond readily to midazolam. Total duration of symptoms was 26 h.

This is the largest ingestion of tiagabine reported and the serum tiagabine level of 4600 µg/L (1725 mmol/L) is the highest reported in the literature to date. This case illustrates more fully the spectrum of symptoms and signs associated with tiagabine intoxication. Given the potential for tiagabine to be prescribed for panic disorder, post-traumatic stress disorder and rage, tiagabine intoxication is likely to become a more common presentation to the ED.

Author contributions

RAF and HK performed literature review and drafted report; LPH provided quantitative analysis and drafted analysis report; FFSD drafted report.

Competing interests

No competing interests or conflict of interest identified.

References
