Tidsskriftet Tidsskrift for Den norske legeforening

A teenage girl who took a large quantity of tablets with suicidal intent

EDUCATIONAL CASE REPORT

ESPEN W. SKJEFLO

espenwskjeflo@gmail.com
Division of Medicine
Nordland Hospital, Bodø
and
Faculty of Health Sciences
University of Tromsø – The Arctic University of Norway
Espen W. Skjeflo PhD, specialty registrar in internal medicine and postdoctoral fellow.
The author has completed the ICMJE form and declares no conflicts of interest.

STIG H. NYMO

Division of Medicine
Nordland Hospital, Bodø
and
Faculty of Health Sciences
University of Tromsø – The Arctic University of Norway
Stig H. Nymo PhD, specialty registrar in emergency medicine, and associate professor.
The author has completed the ICMJE form and declares no conflicts of interest.

SILJE M. DJUPEN

Division of Surgery
Nordland Hospital, Bodø
Silje M. Djupen, specialty registrar in anaesthesiology.
The author has completed the ICMJE form and declares no conflicts of interest.

RØNNAUG HAMMERVOLD

Division of Surgery
Nordland Hospital, Bodø
Rønnaug Hammervold, specialist in anaesthesiology and PhD research fellow.
The author has completed the ICMJE form and declares no conflicts of interest.

EIRIK H. OFSTAD

Division of Medicine
Nordland Hospital, Bodø
and
Faculty of Health Sciences
University of Tromsø – The Arctic University of Norway
Eirik H. Ofstad PhD, specialist in internal medicine and specialist in emergency medicine, senior consultant in the Emergency Department and associate professor.
The author has completed the ICMJE form and declares no conflicts of interest.

A young woman with a history of several serious intoxications was admitted to the Emergency Department with another suspected life-threatening intoxication. A rare phenomenon would prove to be life-saving.

The patient was a young woman who on several occasions had been hospitalised for intoxication and given general anaesthesia for endotracheal intubation and gastric lavage as an emergency indication. Following one such episode about a year before the event in question, the patient developed a severe subglotic stenosis after extubation. It was not possible to determine whether the stenosis was congenital or due to frequent intubation. The patient had not undergone tracheostomy. The stenosis was successfully treated with laser resection, which resulted in a higher threshold for subsequent intubation since pressure from the inflation cuff on the tube is associated with recurrence (1).

Immediately prior to the admission in question, in the space of one hour, the patient had broken open a medicine cabinet, cut herself with a razorblade and ingested up to 64 sustained-release tablets of 50 mg quetiapine, 90 sustained-release tablets of 300 mg bupropion, 30 sustained-release tablets of 150 mg bupropion, 56 tablets of 10 mg aripiprazole and 150 mL aripiprazole oral solution (1 mg/mL) as well as an unknown quantity of paracetamol tablets. She arrived at the Emergency Department about one hour after ingestion. At that time she was seemingly awake and alert and had a GCS (Glasgow coma scale) score of 15, but was uncooperative and did not want gastric lavage or any other treatment.

Clinical examination revealed superficial cuts to the skin, but otherwise findings were relatively unremarkable. Her blood pressure was 144/81 mmHg, pulse was regular at 121 bpm, pulse oximetry (SpO_2) was 97 % on room air, respiratory rate was 18 breaths per minute, and aural temperature was 36.4°C. Her pulse fell to 77 bpm during conversation. Blood tests were normal apart from serum paracetamol at 239 µmol/L (therapeutic range 30–130) and venous blood gas analysis results which were pH 7.38 (reference range 7.35–7.45), $PvCO_2$ 4.61 kPa (5.2–6.5), bicarbonate 20.5 mmol/L (21–27), base excess –4.6 (0 ±3) and lactate 3.0 mmol/L (< 2.5). ECG revealed normal axis, sinus rhythm, heart rate 90 bpm (50–100) and PQ interval 151 ms (120–210) with narrow QRS complexes of 93 ms (< 120). Corrected QT interval was 384 ms (380–470), and ST segments were unremarkable.

After the initial examination, the Norwegian Poison Information Centre and the Norwegian Health Library were consulted. Her relatives were also asked to look for hidden tablets in the home in case the amount ingested was less than reported, but none were found. The quetiapine dose of 3.2 g equated to a moderate overdose, for which observation in hospital was indicated according to the recommendations (2). The patient had also taken up to 710 mg aripiprazole. There is limited information on poisoning with aripiprazole, but mild poisoning has been described at doses above 180 mg (3). It is also described as a relatively safe antipsychotic (4). The initial measurement of serum paracetamol levels took place one hour after ingestion and too early for use of the treatment nomogram (5), but it indicated possibly rising serum levels. Bupropion ingestion of over 9 g is associated with severe poisoning (6), and the patient had taken up to 32 g in sustained-release form. Therefore, gastric lavage and treatment with activated charcoal were indicated.

Following unsuccessful attempts to perform gastric lavage in the patient without general anaesthesia, in consultation with local secondary on-call doctors and a secondary on-call doctor at the Poison Information Centre it was decided to perform intubation for gastric lavage under general anaesthesia. There were no technical complications with the procedure, but no tablets were recovered, only small pink particles in a total of 2.5 L administered and aspirated fluid. Treatment with intravenous acetylcysteine infusion was initiated for paracetamol poisoning (15 g over 1 hour, followed by 5 g over 4 hours and then 10 g over 16 hours), and the patient was transferred to the intensive care unit for observation in case of development of tachycardia, QT interval abnormalities, electrolyte imbalances, seizures or hyperthermia.

To avoid prolonged intubation and the risk of recurrence of tracheal stenosis, the patient was not administered activated charcoal. Charcoal administered under general anaesthesia may be aspirated if the patient is extubated early, which would have led to an increased intubation time of at least 24 hours. The patient had ingested over 240 tablets in a short space of time. This requires a considerable effort, and we had to consider whether this was actually possible in the stated timeframe. The patient was also oriented on arrival and in the subsequent hour in the Emergency Department when it might be expected that serum levels of the individual drugs would have increased. However, she did

have elevated serum paracetamol levels on arrival. Pink particles could be consistent with sustained-release quetiapine, and the patient had a history of taking large amounts of tablets several times.

In the intensive care unit, the patient had normal sinus rhythm with a heart rate of 50–90 bpm and blood pressure of 120/55 mmHg. Her blood pressure fell slightly following treatment with propofol (3.5 mg/kg/min intravenously) and remifentanil (0.15 µg/kg/min intravenously), leading to initiation of treatment with low-dose noradrenaline (0.04 µg/kg/min intravenously). The patient had good hourly diuresis and a temperature of 36.3–36.8°C. The second measurement of serum paracetamol, performed about four hours after ingestion, found levels of 133 µmol/L, and the acetylcysteine infusion was stopped. Blood gas analysis now revealed pH 7.37, $PvCO_2$ 5.0, bicarbonate 21 mmol/L, base excess –3, lactate 1.7 mmol/L, sodium 141 mmol/L (136–146), potassium 4.4 mmol/L (3.5–5.0), chloride 109 mmol/L (97–107), calcium 1.29 mmol/L (1.20–1.35) and glucose 6.5 mmol/L (4.0–6.0). Her ECG was unchanged.

Approximately five hours after ingestion, we again consulted the Poison Information Centre and agreed to extubate the patient if she had not become tachycardic six to eight hours after ingestion. This was the outcome of weighing up continued sedation of the patient with observation for life-threatening intoxication against the risk of recurrence of tracheal stenosis.

The patient was extubated after approximately eight hours, at which point her pulse increased rapidly to 150 bpm and her temperature to 37.4°C. She developed severe motor restlessness, as well as visual and auditory hallucinations, headache, nausea and dizziness. She alternated between being lucid in conversation and whispering to people in the room, and between lashing out physically, being extremely anxious and somnolent. Treatment with midazolam (1 mg intravenously) was tried, and a few seconds later the patient had a transient generalised tonic-clonic seizure with cessation of breathing for 40 seconds. The patient then had a few smaller, transient seizures and trembling, and vomited shiny mucus twice.

Her condition was initially interpreted to be delirium, but we did not want to administer psychotropic medications due to possible continued intoxication. Seizures are also not a typical finding in delirium, and when we reviewed the situation approximately eleven hours after ingestion, overdose of bupropion was considered likely.

Blood samples were now taken to measure serum levels of bupropion and quetiapine. The third and last measurement of serum paracetamol was < 70 µmol/L. Three hours after the first seizure and thirteen hours after ingestion, the patient vomited whole tablets, clearly recognisable as modified-release bupropion (7). Following a short period of observation and discussion, the patient was reintubated and gastroscopy was performed. Several clumps of tablets were found, particularly in the fundus of the stomach. Over 50 tablets were removed after several passes with a polyp snare (Roth Net) (Figure 1). Activated charcoal was administered via a gastric tube at this point.

Figure 1 Monitor shows pharmacobezoar in the snare as well as some standalone tablets.

After gastroscopy, the patient was in continuous sinus rhythm (90 bpm), and her temperature and blood pressure returned to normal with no need for vasopressors. She remained sedated and intubated for a total of two days. EEG on day 1 showed no signs of epileptiform activity. Abdominal CT revealed areas of high attenuation in the stomach and duodenum, which could represent sparse residues or disintegrating tablets. Another dose of charcoal was administered, but there were no more signs or symptoms of intoxication. Blood sample analysis results for quetiapine taken eleven hours after ingestion came back showing serum levels of 423 nmol/L (100–800). The patient also had transient hypokalaemia with lowest potassium levels of 3.0 mmol/L, as well as myoglobin elevated to 267 µg/L (< 50) and CK elevated to 3,608 U/L (35–210).

On day 2, the patient was awakened and extubated. She was calm and in a relatively good condition, but slightly hoarse. Following laryngoscopic assessment by the otolaryngologist, two doses of hydrocortisone (100 mg intravenously) were administered for soft tissue swelling, which resolved well without any further action. The patient was observed on the ward, with no signs of deterioration of the stenosis or post-intoxication sequelae, until being discharged for psychiatric treatment on day 6. The day after discharge, the result of the blood sample analysis for hydroxybupropion taken 11 hours after ingestion came back. The analysis showed serum levels of 16,061 nmol/L (500–4,000), quantified at the Department of Clinical Pharmacology at St Olav's Hospital, Trondheim University Hospital.

Discussion

A bezoar is an aggregation of foreign material, formed in the gastrointestinal tract (8). It is rare and reported in 0.07–0.43 % of all endoscopies (8). Bezoars are named according to their contents, and phytobezoars of plant material are most common. Other bezoars are trichobezoars (containing hair) (9), lactobezoars (containing undigested milk protein) and pharmacobezoars (containing medications), as in this case. It is not known exactly how bezoars form, but it is assumed to be due to a combination of insoluble material, delayed gastric emptying and possibly dehydration. Phytobezoars are probably formed from fibre and starch.

Pharmacobezoars can occur with both sustained-release formulations and rapid-acting formulations, with both water-soluble and water-insoluble drugs, when a drug is overdosed and when taken as prescribed (10). The bezoars may form as high as in the oesophagus with a risk of life-threatening corrosive injury (11). Sustained-release products are more likely to aggregate because the tablet film often contains cellulose (8, 10). Modified-release bupropion tablets contain ethylcellulose, and the coating can pass undigested and be recovered in the stools (12, 13). Even without bezoar formation, tablets may have delayed intestinal transit, and intoxication may arise late in the clinical course, particularly with sustained-release formulations, which has been described for paracetamol (14).

In this case report, it was uncertain how many tablets the patient had taken, but the pharmacobezoar contained 50 tablets and thus at least 7.5 g bupropion, and probably much more since most of the tablets taken were 300 mg bupropion. Rapid onset of symptoms and toxic serum levels eleven hours after ingestion indicated that a large quantity of tablets had already transited or that medicinal product had been released from the pharmacobezoar. The gastroscopy was probably life-saving, but it was primarily the patient vomiting tablets thirteen hours after ingestion that raised suspicion of bezoar formation. Gastric emptying may have been delayed by anticholinergic adverse effects of quetiapine, aripiprazole and bupropion, as well as sedation, bedrest and hypotension.

Bupropion poisoning is known to have a protracted course with the risk of seizures and serious aspiration 10–15 hours following ingestion (15). This may be due to the long half-life (approximately 20 hours), but also pharmacobezoar formation with delayed release. Therefore, patients should be carefully monitored for the first 24 hours following a large intake. Bezoar formation is not a new phenomenon, but is sufficiently rare that it is easy to overlook it in the assessment. In cases of potentially lethal overdoses, we should not be satisfied by unproductive gastric lavage, but consider gastroscopy and possibly abdominal CT, which also has good sensitivity for foreign bodies when the clinician's request is precise (16).

Several similar cases of bupropion poisoning have been reported, but with fatal outcomes. One patient was found dead 24–48 hours after ingestion of up to 27 g bupropion with post-mortem findings of a 40-tablet (12 g) pharmacobezoar (17). Bupropion and its metabolites were quantified in available material, but not in blood, making it difficult to compare. In another case, intoxication with 23 g bupropion resulted in a generalised tonic-clonic seizure with hypokalaemia, hypophosphatemia and asystole with a fatal outcome after four days. Blood tests found serum hydroxybupropion levels of 3,212 ng/mL after 18 hours (18). By way of comparison, our patient had levels of 16,061 nmol/L, equivalent to 4,107 ng/mL (19), 11 hours after ingestion.

The authors thank Henrik Sloth for input and explanation as regards the aforementioned gastroscopy, and Dag Jacobsen for reviewing the article and input.

The patient and relatives have given consent for the article to be published.

The article has been peer-reviewed.

REFERENCES

1. Cooper JD. Tracheal Injuries Complicating Prolonged Intubation and Tracheostomy. Thorac Surg Clin 2018; 28: 139–44. [PubMed][CrossRef]

2. Helsebiblioteket. Kvetiapin - behandlingsanbefaling ved forgiftning. https://www.helsebiblioteket.no/forgiftninger/legemidler/kvetiapin-behandlingsanbefaling-ved-forgiftning Accessed 11.1.2022.

3. Helsebiblioteket. Antipsykotika - behandlingsanbefaling ved forgiftning. https://www.helsebiblioteket.no/forgiftninger/legemidler/antipsykotika-behandlingsanbefaling-ved-forgiftning Accessed 11.1.2022.

4. Carstairs SD, Williams SR. Overdose of aripiprazole, a new type of antipsychotic. J Emerg Med 2005; 28: 311–3. [PubMed][CrossRef]

5. Helsebiblioteket. Paracetamol - behandlingsanbefaling ved forgiftning. Kort oversikt. https://www.helsebiblioteket.no/forgiftninger/legemidler/paracetamol-behandlingsanbefaling-ved-forgiftning.kort-oversikt Accessed 11.1.2022.

6. Helsebiblioteket. Bupropion - behandlingsanbefaling ved forgiftning. https://www.helsebiblioteket.no/forgiftninger/legemidler/bupropion-behandlingsanbefaling-ved-forgiftning Accessed 11.1.2022.

7. Felleskatalogen. Wellbutrin Retard «GlaxoSmithKline». https://www.felleskatalogen.no/medisin/wellbutrin-retard-glaxosmithkline-565480 Accessed 11.1.2022.

8. Iwamuro M, Okada H, Matsueda K et al. Review of the diagnosis and management of gastrointestinal bezoars. World J Gastrointest Endosc 2015; 7: 336–45. [PubMed][CrossRef]

9. Ohnesorge S, Skari H, Zochowski K et al. Trikobesoar. Tidsskr Nor Legeforen 2020; 140: 1780–1. [PubMed][CrossRef]

10. Simpson S-E. Pharmacobezoars described and demystified. Clin Toxicol (Phila) 2011; 49: 72–89. [PubMed][CrossRef]

11. Mortensen KE, Munkholm J, Dalhoff KP et al. Oesophageal Obstruction from a Pharmacobezoar Resulting in Death. Basic Clin Pharmacol Toxicol 2017; 120: 213–6. [PubMed][CrossRef]

12. Legemiddelsøk. Wellbutrine Retard. https://www.legemiddelsok.no:443/?searchquery=wellbutrin+retard&f=Han;MtI;Vir;ATC;Var;Mar;Mid;Avr;gen;par;&pane=0 Accessed 11.1.2022.

13. Tungaraza TE, Talapan-Manikoth P, Jenkins R. Curse of the ghost pills: the role of oral controlled-release formulations in the passage of empty intact shells in faeces. Two case reports and a literature review relevant to psychiatry. Ther Adv Drug Saf 2013; 4: 63–71. [PubMed][CrossRef]

14. Salmonson H, Sjöberg G, Brogren J. The standard treatment protocol for paracetamol poisoning may be inadequate following overdose with modified release formulation: a pharmacokinetic and clinical analysis of 53 cases. Clin Toxicol (Phila) 2018; 56: 63–8. [PubMed][CrossRef]

15. Starr P, Klein-Schwartz W, Spiller H et al. Incidence and onset of delayed seizures after overdoses of extended-release bupropion. Am J Emerg Med 2009; 27: 911–5. [PubMed][CrossRef]

16. Gayer G, Petrovitch I, Jeffrey RB. Foreign objects encountered in the abdominal cavity at CT. Radiographics 2011; 31: 409–28. [PubMed][CrossRef]

17. Schmit G, De Boosere E, Vanhaebost J et al. Bupropion Overdose Resulted in a Pharmacobezoar in a Fatal Bupropion (Wellbutrin®) Sustained-release Overdose: Postmortem Distribution of Bupropion and its Major Metabolites. J Forensic Sci 2017; 62: 1674–6. [PubMed][CrossRef]

18. Harris CR, Gualtieri J, Stark G. Fatal bupropion overdose. J Toxicol Clin Toxicol 1997; 35: 321–4. [PubMed][CrossRef]

19. Farmakologiportalen. Omregning fra stoffkonsentrasjoner til massekonsentrasjoner og omvendt. http://www.farmakologiportalen.no/content/9019/Omregning-fra-stoffkonsentrasjoner-til-massekonsentrasjoner-og-omvendt Accessed 11.1.2022.

Publisert: 4 April 2022. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.21.0620
Received 1.9.2021, first revision submitted 11.12.2021, accepted 11.1.2022.