Objective: This study is to examine the relationship between the severity of valpromide poisoning and plasma valproic acid concentration.
Methods: A retrospective and observational study of valpromide exposures reported to the Angers Poison Control Center (PCC), France, over a sixteen year period and for which a valproic acid quantitation was performed. The severity was assessed according to the Poisoning Severity Score (PSS).
Results: A total of 163 cases were included, of which 161 were deliberate overdoses. The median age was 41 years and the sex-ratio was 0.73. The median presumed dose intake was 6 g (0.3-63 g). The main signs observed were: somnolence (n = 54), coma (Glasgow Coma Score [GCS] ≤ 8) (n = 43), hyperammonemia (n = 42), hypotension (n = 22), including two cases of circulatory shock, cardiac arrest (n = 6), metabolic acidosis (n = 19), tachycardia <140 bpm (n = 17), vomiting (n = 15), and hyperlactatemia (>5 mmol/L, n = 10). Severe poisoning (PSS3 and 4) accounted for almost one third of cases (n = 51). Among the 5 fatal cases, valproic acid quantitation was performed post-mortem in 4 cases (concentrations of 179 and 335 mg/L in single exposures and 270 and 820 mg/L in multiple exposures). For 32 patients with at least 2 dosages of valproic acid, the maximum concentration was observed at 16 ± 11 hours after ingestion. Severity was correlated with plasma valproic acid concentration ($r = 0.67$, $p < 0.00001$). Median concentrations of patients with PSS1 and PSS3 were significantly different ($p = 0.001$). The risk of severe intoxication (PSS3) was greatly increased when the plasma concentration was greater than 200 mg/L (OR 19 [2.9-239], $p = 0.0002$).
Conclusion: In case of overdose with valpromide, the concentration of valproic acid associated with severe intoxication is much lower than in the case of overdose with valproic acid (200 mg/L versus 850 mg/L) [1].

Reference

[1] Spiller HA, Krenzelok EP, Klein-Schwartz W, et al. Multicenter case series of valproic acid ingestion: serum concentrations and toxicity. J Toxicol Clin Toxicol. 2000;38:755–760.

61. Surgical removal of quetiapine bezoars

Hilda MH Phan and Mark Personne

Swedish Poisons Information Centre, Swedish Medical Products Agency, Stockholm, Sweden

Objective: Quetiapine is an atypical antipsychotic drug. In large overdoses, pharmacobezoar formations (mainly seen with sustained-release preparations) can complicate patient management due to delayed onset of severe symptoms and reduced effectiveness of decontamination procedures [1]. Fatalities have been reported after ingestion of more than 10 g. Three cases of slow-release quetiapine overdose are presented where pharmacobezoar formations occurred and different surgical procedures were deemed necessary.
Case reports: Case 1. A 57-year-old man presented at the hospital after a multidrug overdose including quetiapine 33 g (110 tablets x 300 mg) and unknown amounts of oxazepam, lamotrigine and alcohol. His level of consciousness declined and an abdominal computerised tomography (CT) scan showed a vast amount of tablets in the ventricle and duodenum. Gastroscopy was initiated, but difficulties in removing the sticky conglomerate (the size of a tennis ball) lead to the decision to execute an acute laparotomy with manual removal of the bezoar followed by whole bowel irrigation (WBI). The patient continued to be circulatory stable and was taken off the ventilator the following day. Case 2. A 50-year-old woman ingested quetiapine 18 g (90 tablets x 200 mg) and an unknown amount of methylphenidate and zopiclone. She showed signs of central nervous system depression, nystagmus, tachycardia and twitching of the extremities. A CT scan revealed a lump of tablets resembling a cauliflower. Gastroscopic removal was time-consuming and technically difficult. A broad basket was the best, but not an optimal tool. Aspiration pneumonia ensued but otherwise the course was uneventful. Case 3. A 36-year-old man presented at the hospital shortly after a massive overdose of 80 g (200 tablets x 400 mg). WBI (2 liter/hour) was initiated but proved to be ineffective. A CT scan showed a conglomerate (8 x 5 cm) in the ventricle, 20 tablets in the duodenum and 10 tablets in the jejunum. The bezoar was impossible to remove with gastroscopic methods, and laparoscopic extraction through the abdominal cavity was initiated. Technical difficulties were evident but most of the bezoar could be removed. The post-operative period was uneventful.
Conclusion: Slow-release formulations and the risks of bezoar formation add extra dimensions to patient management after a large overdose. A swift decontamination plan sometimes involving WBI and various surgical procedures can be vital for a good prognosis. Slow-release formulations without the propensity of forming bezoars are to be preferred.

Reference

[1] Rauber-Lüthy C, Hofer KE, Bodmer M, et al. Gastric pharmacobezoars in quetiapine extended-release overdose: a case series. Clin Toxicol (Phila). 2013;51:937–940.

62. Regional variability in intentional exposures to prescription medications in France and Italy

Samantha J Leroy[a], Zachary R Margolin[a], James J Lagrotteria[a], Geoff Severtson[a], Bruno Mégarbane[b], Antoine Villa[b], Fabrizio Sesana[c], Janetta L Iwanicki[a] and Richard C Dart[a]

[a]Rocky Mountain Poison & Drug Center, Denver, United States; [b]Centre Antipoison et de Toxicovigilance de Paris, Paris, France; [c]Poison Control Centre of Milan, Milan, Italy

Objective: To assess regional differences in rates of intentional exposures involving benzodiazepines, GABA analogs, prescription opioids, and Z-drugs within France and Italy.
Methods: Data from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System Global Toxicosurveillance Network (GTNet) were used. Rates of intentional exposures per 100,000 population were calculated by Nomenclature of Territorial Units for Statistics (NUTS) regions using data collected from participating poison centres in Italy (Milan) and France (Paris). The Milan Poison Centre receives approximately 67.5% of the total human exposure calls to Italian centres. The Paris Poison Centre reports coverage of 18% of the national population. Intentional exposures include exposures where the patient was attempting to gain a euphoric effect (abuse), attempting self-harm (suicide), or intentionally improperly used a medication for reasons other than to gain a euphoric effect or for self-harm (misuse). Data collected on exposures involving select prescription opioids, benzodiazepines, GABA analogues, and Z-drugs from first quarter of 2012 through fourth quarter of 2016 were analyzed. Exposures where postal code information could be linked to a NUTS level-3 region were used

Table 1. Regional variability in intentional exposures to prescription medications in France and Italy, showing regions with the highest rate of intentional exposures per 100,000 population by country and drug group in descending order.

Country	Benzodiazepines n (rate per 100,000 population)	GABA analogs n (rate per 100,000 population)	Prescription opioids n (rate per 100,000 population)	Z-drugs n (rate per 100,000 population)
France	Paris	Meurthe-et-Moselle	Paris	Haute-Marne
	n = 202 (9.3)	n = 9 (1.2)	n = 150 (6.9)	n = 11 (6.2)
	Meurthe-et-Moselle	Nièvre	Meurthe-et-Moselle	Paris
	n = 65 (8.9)	n = 2 (1.0)	n = 47 (6.4)	n = 128 (5.9)
	Haute-Marne	Vosges	Vosges	Meurthe-et-Moselle
	n = 15 (8.5)	n = 2 (0.5)	n = 20 (5.4)	n = 32 (4.4)
Italy	Varese	Varese	Varese	Varese
	n = 426 (47.9)	n = 40 (4.5)	n = 39 (4.4)	n = 35 (3.9)
	Enna	Perugia	Livorno	Enna
	n = 58 (34.5)	n = 21 (3.2)	n = 13 (3.9)	n = 5 (3)
	Rovigo	Cremona	Grosseto	Ascoli Piceno
	n = 77 (32.3)	n = 10 (2.8)	n = 8 (3.6)	n = 6 (2.9)

in the numerator. Population estimates by region from Eurostat [1] were used as the denominator.

Results: In France, Paris had the highest rate of intentional exposures involving benzodiazepines and exposures involving prescription opioids per 100,000 population (Table 1). Meurthe-et-Moselle had the highest rate of intentional exposures involving GABA analogs, and Haute-Marne had the highest rate per population for Z-drugs. In Italy, Varese had the highest rate of intentional exposures for all drug groups.

Conclusion: There is substantial regional variation in intentional exposures involving prescription medications. Considering regional rates per population is important in developing targeted interventions. Results are limited by population coverage and medications comprising drug groups vary between countries.

Reference

[1] EUROSTAT website. Population on 1 January by age group, sex and NUTS 3 region [cited 2018 Sep 28]. Available from: http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=demo_r_pjangrp3&lang=en

63. Button battery exposures in Australian children: a prospective observational study highlighting the role of poisons information centres

Rose Cairns[a], Jared A Brown[a], Kishen Lachireddy[b], Carol J Wylie[c], Jeff Robinson[d], Andrew H Dawson[a] and Nicholas A Buckley[a]

[a]New South Wales Poisons Information Centre, The Children's Hospital at Westmead, Sydney Pharmacy School, The University of Sydney, Sydney, Australia; [b]Environmental Health Branch, Health Protection NSW, Sydney, Australia; [c]Queensland Poisons Information Centre, Lady Cilento Children's Hospital, Brisbane, Australia; [d]Victorian Poisons Information Centre, Austin Hospital, Melbourne, Australia

Objective: Button battery ingestion is a worldwide problem, with evidence of increasing harm and deaths in recent decades. In the last 5 years, two Australian children have died following ingestion of button batteries. In the 2015 coronial inquest into one case, a number of health system problems were identified, and the coroner recommended that Australian Poisons Information Centres (PICs) are the first point of contact following button battery exposures. Australian PIC experience includes cases of treatment delay due to lack of healthcare professional recognition of risks, and/or lack of local resources. Consequently, New South Wales PIC (NSWPIC) introduced a protocol for button battery exposures, whereby PIC staff call ahead to the hospital a child is to present at. The PIC (i) confirms the hospital's ability to perform an X-ray (if not, callers are diverted to another hospital to minimise delay), and (ii) discusses the risk of severe injury to ensure the child is given priority for X-ray. This study aims to characterise Australian button battery exposures, focusing on exposure circumstances and preventable health system shortcomings.

Methods: A prospective observational study of button battery exposure calls to NSWPIC, November 2015-May 2017, using a follow-up survey to obtain outcome data and additional details. Survey data was combined with nationwide PIC data over the same period.

Results: Australian PICs were consulted on 578 exposures over the 19-month study period, including 506 paediatric cases. The median (IQR) age for the pediatric cases was 23 months (14-36 months). Where the source was identified, batteries came from toys in 26% of cases, with hearing aids, watches, and remote controls being other common sources. Children in outer regional, remote and very remote areas were overrepresented, and 15 cases were referred to a different hospital due to X-ray facilities being unavailable at their nearest hospital. We identified inconsistent triage from a range of first responders, and knowledge gaps regarding button battery dangers amongst some healthcare professionals.

Conclusion: Button battery exposures are a common call to Australian PICs. This study highlights a potential role of education campaigns, professional guidelines, and child-resistant battery compartments in toys and household devices. PICs calling ahead to ensure X-ray availability/diversion to a different hospital likely reduced delays for this time-critical exposure. Data collected by PICs can provide useful information for public health and product safety initiatives. A PIC-led protocol to direct initial medical management of button battery exposures could reduce delays and improve outcomes.

64. Review of enquiries to the UK National Poisons Information Service (NPIS) Birmingham Unit originating from NHS 111, NHS 24 and NHS Direct advice services

Pardeep S Jagpal[a], Hayley A Williams[a], Muhammad EMO Elamin[a], Euan A Sandilands[b], Simon HL Thomas[c], John P Thompson[d] and Sally M Bradberry[a]

[a]National Poisons Information Service (Birmingham Unit), City Hospital, Birmingham, United Kingdom; [b]National Poisons Information Service (Edinburgh Unit), Royal Infirmary, Edinburgh, United Kingdom; [c]National Poisons Information Service (Newcastle Unit), Regional Drug and Therapeutics Centre, Newcastle, United