γ-Hydroxybutyrate poisoning from toy beads

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A 2-year-old boy and a 10-year-old girl presented to the emergency department with a decreased level of consciousness. The girl had had persistent vomiting and a seizure. Urine metabolic screening tests were positive for γ-hydroxybutyrate (GHB). Samples from toy beads ingested by both children contained 1,4-butanediol, which is metabolised to GHB in humans. Regulatory authorities were notified, leading to an international recall of the toy beads. **(MJA 2008; 188: 54-55)**

Clinical records

Patient 1

A 2-year-old boy presented to the emergency department (ED) with a decreased level of consciousness. Earlier, he had been playing with his siblings in the backyard. He had been unsteady on his feet an hour before and then became difficult to rouse. There was no history of trauma, ingestion of medicines or plants or intercurrent illness. He had been well previously and was the youngest of 10 siblings.

On arrival at the ED, his Glasgow Coma Score (GCS) fluctuated between 7 and 12, with no focal neurological deficit. Pupils were 2 mm, equal and reactive. A pustular vesicle on his right cheek was the only other significant finding. He was afebrile and had no neck stiffness. An electrocardiogram showed sinus bradycardia at 60 beats/min. He was hypotensive, with blood pressure of 59/39 mmHg. Blood glucose level was 5.2 mmol/L. Without a history of ingestion, we initially considered a postictal state or encephalitis.

Laboratory investigations, including full blood count, electrolytes, and renal and liver function tests, were all within normal limits. Computed tomography of the brain showed no intracranial abnormality. Lumbar puncture was not attempted because of the child's fluctuating level of consciousness. He was investigated and treated with cefotaxime and acyclovir for suspected intracranial infection. Urine was sent for toxicology and metabolic screening.

Seven hours after presentation, remarkable clinical improvement was noted, and he became fully alert and cooperative. At this point he vomited and also passed a substantial number of coloured beads in his stool. The family were further questioned about a history of ingestion; the boy's mother divulged that he had been playing with Bindeez brand toy beads (Moose Enterprise, Melbourne, Vic) (Box).

With no obvious diagnosis, he was admitted to hospital for observation and further investigation. An electroencephalogram showed no abnormalities. The urine toxicology screen returned with a negative result for illicit drugs. The urine metabolic screen became available on Day 5 and was positive for γ-hydroxybutyrate (GHB). The source of GHB in this patient was thought to be either exogenous (that is, poisoning) or an inborn error of metabolism. The latter was excluded when a repeat metabolic screen from urine taken on Day 3 returned with a negative result for GHB.

In searching for an exogenous source of GHB, toy beads from the boy's home, similar to those ingested, were sent for analysis and subsequently found to contain 1,4-butanediol (1,4-BD). The patient recovered completely and was discharged on Day 7 with no residual sequelae of his poisoning.

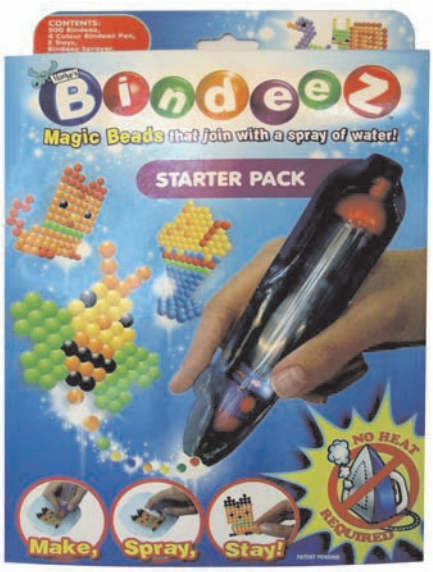
Patient 2

A 10-year-old girl presented to the ED after a 4-minute generalised seizure. She had been unrousable by family an hour earlier. She had then vomited up to 100 Bindeez beads and then had the seizure. She had been well earlier in the day, and there was no history of intercurrent illness or trauma. The patient had a further seven episodes of vomiting and was persistently drowsy. She had a background of Asperger's syndrome and attention deficit hyperactivity disorder, for which she took extended-release methylphenidate.

On arrival at the ED, she was drowsy, with a GCS of 14 and no focal neurological signs. Her heart rate was 70 beats/min, she was normotensive and physical examination was otherwise normal.

On advice from the New South Wales Poisons Information Centre, a urine sample was collected, and beads from the patient's home, similar to those ingested, were sent for analysis. Five hours after ingestion, she became alert and communicated appropriately. She was admitted to hospital for overnight observation and discharged the following day with no further complications. The urine metabolic screen was positive for GHB, and the beads were found to contain 1,4-BD.

Bindeez bead set



"Make, spray and they stay! Bindeez are magic beads that you use to create colourful and fun designs. Just lay out your design in the special Bindeez tray, then spray them with water and your artwork will magically set in place!" (from an advertisement for the toy). ◆

Public health response

After confirmation of GHB poisoning in Patient 1 from 1,4-BD detected in Bindeez toy beads, the NSW Poisons Information Centre was notified. The Centre and the NSW Biochemical Genetics Service alerted the NSW Office of Fair Trading about the product. They in turn contacted the company marketing the product to investigate the formulation of the toy beads. When the manufacturer in Hong Kong was contacted, it supplied a list of ingredients in the production of the toy beads; this list did not include 1,4-BD, but did mention the agent 1,5-pentanediol.

Meanwhile, two further samples of Bindeez toy beads were tested at our institution. Both samples tested positive for 1,4-BD. None of the beads tested contained 1,5-pentanediol. With confirmation of similar biochemical analyses from the beads in the second case, the NSW Department of Health and the NSW Office of Fair Trading were further alerted about banning the product. The following day, the NSW Minister for Fair Trading issued an interim ban on the sale of Bindeez products in NSW; other Australian states rapidly followed suit. Further cases of GHB poisoning in Australia came to light during the ensuing days. Staff of the Poisons Information Centre also alerted toxicologists and poisons control centres worldwide where similar products are marketed (eg, Bindeez in the United Kingdom and Aqua Dots in North America) and the potential for GHB poisoning may have existed. With worldwide media coverage and similar cases in North America, an international recall soon followed.

Discussion

GHB is an endogenously occurring neurotransmitter derived from γ-amino butyric acid (GABA).[1] Its known metabolic precursors are 1,4-BD and γ-butyrolactone. A potent sedative and anaesthetic agent, it was initially synthesised in the 1960s.[2] GHB and its precursors have recently found notoriety as recreational and club drugs. In 2000, GHB became a banned substance by the United States Drug Enforcement Agency and classified as Schedule 1 by the US Food and Drug Administration.[2,3]

1,4-BD is a widely available industrial chemical used as a solvent and in the manufacture of some types of plastics and fibres. When ingested, it is metabolised rapidly by alcohol and aldehyde dehydrogenases to GHB.[4,5] Hence, the toxicity and clinical features of 1,4-BD poisoning are similar to those of GHB. While 1,4-BD is not a scheduled drug in Australia, it is a category 1 precursor under the Drug Misuse and Trafficking Regulations 2006, which restrict the supply of 1,4-BD (Pharmaceutical Services, NSW Department of Health, personal communication, 12 Nov 2007).

GHB is an agonist at inhibitory $GABA_B$ receptors and is excitatory at specific GHB receptors. There is a dose–response relationship in GHB toxicity. Low doses result in vomiting, drowsiness, visual disturbance and disinhibition, while higher-dose effects include confusion, coma, bradycardia and myoclonic (seizure-like) movements.[3] Routine urine toxicology screens do not detect GHB in their profile. Specific analysis with gas chromatography–mass spectrometry (GC–MS) or as part of a urine metabolic screen is required. The urine sample from Patient 1 was investigated for possible inherited metabolic diseases, including urinary organic acid analysis by GC–MS.[6] This showed a marked increase in GHB (a metabolite seen in succinic semialdehyde dehydrogenase deficiency) but without any increase in 4,5-dihydroxyhexanoate lactone, as would be expected in the inborn error. This pattern strongly suggested an exogenous source of GHB, which was confirmed by the compound being undetectable in a second urine sample taken 3 days later.

Treatment of GHB poisoning is primarily supportive and may involve airway and ventilatory intervention, and atropine for symptomatic bradycardia[7] Gastrointestinal decontamination with activated charcoal is not indicated, owing to the rapid absorption of this liquid poison. Additionally, there are no specific antidotes that reliably reverse GHB toxicity.[7]

Where patients are suspected of ingesting Bindeez toy beads (containing 1,4-BD), they should be observed in the ED for depressed level of consciousness. Patients who remain asymptomatic after 4 hours are unlikely to have ingested enough beads to cause toxicity and can be safely discharged from hospital. Patients developing symptoms should be managed in a similar way to those with GHB intoxication. Moderately intoxicated patients may be managed and observed in the coma position until awake, while patients with airway compromise or respiratory failure may require intubation and mechanical ventilation until toxicity resolves.

The identification of these cases highlights the important role of poisons centres in toxicovigilance and monitoring of potential clusters of poisoning related to new pharmaceuticals and chemical agents. Rapid electronic communication of these cases to worldwide toxicological networks enables health authorities to make a risk assessment of similar toy products overseas. So far, this has resulted in identification of similar suspected cases of GHB poisoning in children and an international withdrawal of the product. Chinese authorities confirmed that toy beads from the Hong Kong manufacturer contained a substance which metabolised to GHB.[8]

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Competing interests

None identified.

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References

1 Quang LS, Levy HL, Law T, et al. Laboratory diagnosis of 1,4-BD and GHB overdose by routine urine organic acid analysis. *Clin Toxicol (Phila)* 2005; 43: 321-323.
2 Strickland RM, Felgate P, Caldicott DGE. Survival of massive γ-hydroxybutyrate/1,4-butanediol overdose. *Emerg Med Australas* 2005; 17: 281-283.
3 Wong CGT, Chan KFY, Gibson KM, Snead OC III. γ-Hydroxybutyric acid — neurobiology and toxicology of a recreational drug. *Toxicol Rev* 2004; 23: 3-20.
4 Zvosec DL, Smith SW, McCutcheon JR, et al. Adverse events, including death, associated with the use of 1,4-butanediol. *N Engl J Med*, 2001; 344: 87-94.
5 Lora-Tamayo C, Tena T, Rodriguez A, et al. Intoxication due to 1,4-butanediol. *Forensic Sci Int* 2003; 133: 256-259.
6 Tanaka K, West-Dull A, Hine DG, et al. Gas-chromatographic method of analysis for urinary organic acids. II. Description of the procedure, and its application to diagnosis of patients with organic acidurias. *Clin Chem* 1980; 26: 1847-1853.
7 Shannon MW, Quang LS. Gamma-hydroxybutyrate, gamma-butyrolactone, and 1,4-butanediol: a case report and review of the literature. *Pediatr Emerg Care* 2000; 16: 435-440.
8 China says Bindeez has toxic substances. *Sydney Morning Herald* 2007; 11 Nov. http://www.smh.com.au/news/World/China-says-Bindeez-has-toxic-substances/2007/11/11/1194716047932.html (accessed Nov 2007).

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