A 31-year-old male presented to the Emergency Department (ED) wanting to cease his frequent GHB (Gamma-HydroxyButyric acid) use two hours after his last dose. He admitted to GHB ingestion up to seven times per day (40ml/day total). He denied using other illicit drugs, medications or alcohol.

His had a heart rate of 105bpm, blood pressure 132/78mmHg, respiratory rate 16/minute and temperature of 37°C. Although he was lucid, psychomotor agitation, tremor and diaphoresis were present. He was treated with droperidol (10mg IM) and olanzapine (20mg orally) within 2 hours of presentation. He received 60mg of oral diazepam over the next 9hrs, but became more confused and agitated. In view of his increasing delirium and inadequate response to benzodiazepines, the toxicology service was consulted. To control increasing agitation, he was intubated and commenced on propofol and midazolam infusions.

Attempts at weaning sedation over the following 48 hours were unsuccessful due to reappearance of physiological signs of a severe withdrawal state. Nasogastric baclofen 5mg BD was introduced on day 3 and gradually titrated up to 20mg TDS. Extubation attempts failed on day 6 due to worsening agitation despite high doses of diazepam (total of 115mg via NG tube). On day nine, phenobarbitone was added to the diazepam and baclofen (loading dose 10mg/kg IV followed by ongoing administration of 100mg IV TDS).

Further complications included a right lower lobe pneumonia treated with IV piperacillin and tazobactam. He received a tracheostomy on day 9, and sedation was weaned with discontinuation of diazepam and phenobarbitone on day 18. He was discharged on day 19 on baclofen 20mg TDS, with a weaning regimen over the following few weeks.

The patient had not recommenced GHB use at 2-week post discharge.

Discussion

GHB intoxication is a common recreational drug presentation to Australian EDs, (35% of in one study) (1). Clinical effects include altered conscious state (profound sedation with intermittent agitation), vomiting bradycardia, miosis, and myoclonic jerks.

However, GHB withdrawal is an uncommon presentation to Australasian EDs. Long-term use of GHB leads to addiction and development of tolerance and physical dependence. (2) The withdrawal syndrome appears to manifest in those who self-administer multiple times per day, every 2-3 hours, over many months. The clinical features of GHB (and its analogues) withdrawal are similar to those seen with ethanol withdrawal (3), and include initial anxiety, insomnia and tremor rapidly progressing to uncontrolled delirium, agitation and seizures. Withdrawal manifests within 1-6 hours from last dose, escalates rapidly, is often prolonged (1 to 2 weeks) and frequently requires high dependency care (4). Unlike severe alcohol withdrawal the autonomic instability appears less severe but tachycardia is a common early manifestation.

Benzodiazepines have traditionally been used as first line agents to treat GHB withdrawal but most patients in GHB withdrawal have an extremely high tolerance to the sedating effects of benzodiazepines and require early administration of repeated high doses following abrupt GHB cessation. This may be due to differing pharmacodynamic properties; benzodiazepines act via "indirect" agonism of GABA-A receptors, while GHB and its analogues act mainly as GABA-B receptor agonists. (5). Therefore, adjunct therapies other than benzodiazepines to manage withdrawal may be needed.

Other agents such as baclofen (GABA-B receptor agonist), phenobarbitone (a long acting "direct" GABA- A receptor agonist) and propofol have been successfully used in conjunction with benzodiazepines to manage severe GHB withdrawal (2). Dexmedetomidine (an alpha 2 agonist) has been used in the intensive care setting for sedation, however, may not decrease the overall length of stay and works at a different receptor to GHB (6).

In conclusion, GHB withdrawal is an uncommon ED presentation, but can progress rapidly and may be prolonged and severe. Early recognition of the potential for progressive neuropsychiatric manifestations and physiological dysfunction, initiation of rapidly escalating doses of benzodiazepines (in addition to other GABA receptor agonists) and early consultation with a clinical toxicologist are cornerstones of management.

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