Acute Toxicity From Home-Brewed Gamma Hydroxybutyrate

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Gamma hydroxybutyrate (GHB) has become an increasingly dangerous, illicitly marketed substance with numerous potential health hazards.[1-8] GHB was originally developed as an anesthetic but was withdrawn as a result of unwanted side effects.[4] Marketed for the treatment of narcolepsy and alcohol withdrawal, it was used illicitly as a growth hormone and fat-burning drug by body builders. It has also been used as a date-rape drug.[1,2,9,10] In 1990 the Food and Drug Administration banned the sale of GHB in the United States.

Common street names for gamma hydroxybutyrate include GHB, Liquid E, Liquid X, and Scoop. It is also referred to as gamma hydroxy, 4-hydroxybutyrate, gamma hydroxybutyrate sodium, and sodium oxybate. This drug, reported to stimulate growth hormone release, body building, and weight loss, as well as act as a sleeping potion,[1-5] is also associated with a number of serious neurologic, cardiovascular, respiratory, and gastrointestinal side effects.[10-15] We describe a case of GHB abuse from a home-brewed preparation resulting in toxicity, withdrawal symptoms, and rhabdomyolysis. The withdrawal symptoms included insomnia, anxiety, and tremors, which resolved within 9 days.[13,16] This case is the first reported describing GHB overdose associated with withdrawal symptoms and rhabdomyolysis.

GHB became popular as a drug to help assault women.[1,2,10] Several properties of this drug account for its popularity as an tool in sexual assault. First, although no longer legally accessible, GHB is easily and cheaply manufactured in the home. Second, the drug is colorless, tasteless, and odorless, and it mixes well with all liquid and foods; as a result, it is easy for an unaware person to consume this drug. Third, shortly after consumption of GHB, sedation is rapid, and amnesia is complete.[1] The sedated person will not recall any events that occurred shortly before or during the period of sedation, including rape, physical abuse, or even the person they were with shortly before becoming unconscious. These effects make GHB an ideal agent of assault. A rapist could sexually assault a woman, and the victim would not recall the details of the experience. As a result of the victim's amnesia, the rape might not be reported.

GHB is also popular among body builders. Its popularity increased after GHB was reported to enhance muscle mass.[1] Although the muscle-building properties of GHB have never been proven, GHB remains popular among body builders as an aid to increasing muscle mass.[1,3]

GHB became popular as an aid for weight loss after it was advertised as the active ingredient in Love Potion #8 1/2. This substance was sold in nutrition stores and to the public by mail order under the generic name of GHB. Among the most falsely advertised properties of Love Potion #8 1/2 was that GHB could help a person lose weight by suppressing appetite. Although there is no reported evidence that this claim is true, GHB continues to be used as an appetite suppressant.[4,17]

Case Report

A 27-year-old white man was brought to the emergency department with altered mental status, agitation, hallucinations, and seizures. He became more obtunded but responded to deep pain. Physicians were unable to obtain a history from the patient or his family. The emergency department physician accomplished endotracheal intubation. The patient was given oxygen and intravenous fluids, and cardiac monitoring and pulse oximetry were started. A urinary catheter was inserted, and urine and blood samples were sent for analysis. A total of 4 mg of naloxone hydrochloride and 50 percent dextrose was administered intravenously without effect. The patient's pupils were decreased in size to 3 mm but remained

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equal and reactive, and he was hypertensive (blood pressure 180/100 mmHg). An electrocardiogram showed sinus tachycardia with a rate of 115 beats per minute. The respiratory rate was 16/min with somewhat shallow respirations.

A nasogastric tube was then inserted for gastric lavage followed by oral administration of 50 g of activated charcoal. One hour after arrival the patient became only moderately alert but continued to be severely agitated and have hallucinations and seizure activity. He attempted to remove his endotracheal tube. Information obtained from the immediate family and spouse described the patient as a weight builder who had been using home-brewed GHB for 7 years. His wife stated that her husband consumed 1 tablespoon of GHB four times a day. He had had numerous episodes of impaired psychomotor skills while operating a motor vehicle.

Results of the serum and urine drug screening tests were negative. No serum ethanol was reported. A prominent hilum, without evidence of acute disease, was seen on the portable chest radiograph. Computed tomographic scans of his head with and without contrast were negative. An electrocardiogram showed sinus tachycardia with a heart rate of 113 beats per minute and nonspecific ST segment elevation in precordial leads V_1 and V_2. Arterial blood gas measurements were pH 7.33, pCO_2 26 mmHg, and bicarbonate 22 mEq/L. Serum electrolytes were sodium 142 mEq/L, potassium 4.0 mEq/L, chloride 99 mEq/L, urea nitrogen 52 mg/dL, creatinine 2.0 mg/dL, and serum glucose 71 mg/dL. The anion gap was 26.4 mmol/L. Calculated serum osmolality was 275 mOsm/kg H_2O and measured 297 mOsm/kg H_2O. The white cell count was 14,000 /μL with a normal differential. Hemoglobin was 17.6 mg/dL. Total creatine kinase was 34,500 mg/dL, lactic dehydrogenase 559 U/L, fibrinogen 305 mg/dL, and aspartate aminotransferase 190 U/L. Prothrombin time was 11.2 sec with an international normalized ratio of 0.83. Lumbar puncture was performed, and results were negative. Viral cultures of lumbar puncture grew no organisms.

Approximately 3 hours after arrival, the patient became more alert but continued to be belligerent, severely agitated, and confused. He was admitted to the intensive care unit, sedated, paralyzed, and subsequently intubated secondary to rhabdomyolysis. He continued to be combative, agitated, and uncooperative throughout his stay in the intensive care unit and after extubation on the 5th day. His creatine kinase level decreased to 1300 mg/dL with vigorous intravenous hydration, and by day 7 his temperature, blood pressure, and heart rate remained stable, and results of a physical examination were unremarkable. During his hospitalization he was examined by a consulting psychiatrist, nephrologist, and neurologist. Recommendations were followed. The psychiatrist diagnosed the patient's condition as Axis I (acute brain disorder with delirium secondary to illicit drug use). Axis II was GHB withdrawal.

Arrangements were made to transfer the patient from the intensive care unit to a hospital for addiction management and detoxification. The patient had a good support system at home. His mother was instrumental in making arrangements to assist in placing him in an addiction center for inpatient therapy.

Discussion

GHB is an illegal drug in the United States.[10] It is falsely promoted for strength training, muscle building, weight loss, and inducing sleep. GHB is produced as a white powder, but it is more commonly encountered as an odorless, clear liquid. It has a salty taste that is masked when mixed with a drink. GHB will remain in a person's blood for approximately 4 hours and will remain detectable in the urine until it has been excreted.[4,6,9,13]

Illicit use of GHB often involves oral doses of $^1/_4$ teaspoon to 4 tablespoons. It has been associated with numerous central nervous system effects, and reported complications include convulsions, confusion, seizure-like activity, shortness of breath, and combative and self-injurious behavior followed by coma. Less severe effects include drowsiness, dizziness, hypomania, hallucinations, headache, confusion, nausea, vomiting, diarrhea, uncontrollable shaking, transient amnesia, and incontinence. In all reported cases, symptoms resolved rapidly with drug discontinuation. Acute symptoms usually resolve within 8 hours. Body builders usually ingest 1 to 2 teaspoons (2.5 to 5.0 g) per day.[8,10,17-19]

Because GHB is an illegal drug in the United States, much of the drug sold on the street is home-brewed and laced with accidental contaminants, the most common and dangerous of which

is lye. No antidote to GHB exists. To date there have been no reported deaths in the medical literature directly attributed to GHB. Physical dependence was reported in one source.[15] Gamma hydroxybutyrate is known to act synergistically with alcohol, benzodiazepines, narcotics, and other neuroleptic medications to produce central nervous system and respiratory depression.[6,7] This case is the first report of chronic high-dose abuse with withdrawal syndrome.

In our case, the patient took GHB to increase his muscle mass, and his use of GHB resulted in an acute episode of seizures, rhabdomyolysis, and a profound coma with respiratory depression. Rhabdomyolysis most likely was secondary to his seizure activity. The diagnosis of GHB abuse was supported by the patient's history of ingestion of GHB as reported by his family. The patient also admitted to taking increasing amounts of GHB to achieve euphoria. Comprehensive urine drug testing did not identify other central nervous system depressants.

With supportive treatment, the symptoms of acute GHB toxicity resolved within 8 hours. The patient began to experience withdrawal symptoms within 24 hours, however, and subsequent rhabdomyolysis required sedation with ventilatory support. During the withdrawal period, he experienced tremors, shakes, insomnia, and anxiety and was stabilized by day 7 of intensive care hospitalization.

The mechanism by which GHB produces its clinical effects remains unknown despite extensive investigation. GHB is undetectable by routine toxicology testing and does not appear to alter routine laboratory studies drastically. The lack of rapid distinctive diagnostic markers mean that all other causes of acute unresponsiveness must be ruled out even when a history of GHB is known.[13,19]

Diagnosis of GHB is made after detecting toxic levels of GHB in either serum or urine of a patient suspected to have ingested toxic levels of GHB. The diagnosis is not made based on clinical signs and symptoms, but the clinical signs and symptoms and the history should alert the physician to the possibility of GHB toxicity, for which a drug-specific screening test should be ordered. Treatment of GHB overdose is symptomatic and supportive care. Special interventions include continuous observation, cardiac and pulse oximetry monitoring, airway maintenance, and ventilatory support as needed. Temperature regulation might also be indicated if hypothermia develops. Intravenous access should be maintained. Standard treatment of polysubstance overdose, such as gastric lavage and the administration of activated charcoal, is indicated. If GHB toxicity is strongly suspected, then induction of vomiting should be avoided, because the patient can suddenly experience decreased alertness, which would increase the risk of aspiration. Naloxone hydrochloride, flumazenil (Romazicon), or both should be considered because of possible multiple drug abuse. On recovery the patient's mental status should be assessed and substance abuse counseling arranged. Cases should be reported to local poison control centers so that accurate statistical data can be collected regarding the incidence of GHB toxicity.[7]

Conclusion

GHB is a dangerous drug with potential for abuse among all segments of the population. Its use can be associated with coma and seizure-like activity. Abuse can become more widespread as reports of euphoric effects increase. Although further sale of this drug is prohibited, new cases with acute symptoms continue to be reported.[1,2] Family physicians should be alerted to the potent effects of GHB. Family physicians should also educate their patients about the true dangers of this unusual recreational drug and ask their patients who they suspect or know to be body builders about their use of any dietary or muscle-building supplements. Additionally, they should ask patients about the use of any other substances they might be using to increase muscle mass and warn them about the dangers associated with using GHB.

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