

SPECIAL ARTICLE: First of Two Parts

ACUTE GAMMA HYDROXYBUTYRATE TOXICITY

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Gamma hydroxybutyrate (GHB) is a naturally occurring substance in the brain with a structure very similar to the major central nervous system inhibitory neurotransmitter, gamma-aminobutyric acid (GABA).¹ It was synthesized initially in the 1960s for use as a GABA analogue capable of crossing the blood brain barrier. Being a central nervous system depressant, it was temporarily used as a general anesthetic. This use was curtailed secondary to recognition of the side effects of petit and grand mal seizures, myoclonus, and vomiting.² Based on a study showing that GHB administration led to increased release of growth hormone,³ the drug was marketed in the 1980s as an alleged growth hormone stimulator, and was sold in health food stores.⁴ In addition, the euphoria-inducing property of GHB led to recreational abuse. Increasing reports of serious adverse effects from GHB misuse quickly led to making the sale and manufacture of GHB illegal. On March 13, 2000, GHB was made a schedule I drug by the DEA.⁵ Legal use of GHB in the United States remains only for research on narcolepsy, a condition which appears to be effectively treated with GHB.⁶

Despite the schedule I classification, abuse of GHB continues. GHB can be obtained illicitly and also made from home manufacturing kits.⁷ It has become a popular drug used at raves, and a drug implicated in "date rape" owing to its property of rapid coma induction.⁸ Two precursors to GHB, namely gamma-butyrolactone (GBL), and 1,4-butanediol (1,4-BD) have been marketed as alternatives to GHB.⁹ The FDA has asked for a voluntary recall of products containing GBL, some of which are solvents.¹⁰

GHB and its precursors are typically sold as liquids or white powders and are administered orally. GHB is referred to by various slang names, and a multitude of products contain the precursors GBL and 1,4-BD. Below is a partial list of some of them.¹¹

Drug: GHB

Synonyms: sodium oxybate, sodium oxybutyrate, gamma hydrate
 Slang: GBH, grievous bodily harm, Georgia home boy, easy lay, liquid ecstasy, salty water

Drug: GBL

Synonyms: 2(3H)-furanone dihydro, butyrolactone, 4-butyrolactone, dihydro-2(3H)-furanone
 Products: Renewtrient, Revivarant, Blue Nitro, Remforce

Drug: 1,4-BD

Synonyms: 1,4-tetramethylene glycol, tetramethylene glycol, 1,4-tetramethylene
 Products: Enliven, Thunder Nectar, Pine Needle Extract, Serenity

GHB is rapidly absorbed after oral administration and the onset of systemic effects occurs within minutes.² GHB is a structural analogue of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). It readily crosses the blood brain barrier and may lead to general anesthesia and respiratory depression.¹ However, the exact mechanism by which GHB exerts its effects remains unclear. GBL is rapidly converted in vivo by peripheral lactonases to GHB. 1,4-BD is converted by alcohol dehydrogenase to gamma hydroxybutyraldehyde and then by aldehyde dehydrogenase to GHB.⁹ GHB is metabolized to carbon dioxide and water via the Krebs' cycle with no active metabolites.¹

GHB and its precursors are abused recreationally for their disinhibitive, euphoric, and purported aphrodisiac effects. However, used in excess, significant toxicity may occur. Chin et al. described the clinical characteristics and course of GHB overdose. Of GHB ingestions presenting to the emergency department, profound decreased level of consciousness is typical. In addition, mild hypothermia, asymptomatic bradycardia, mild acute respiratory acidosis, and emesis are frequent. Coingestion of ethanol and other drugs is common and may contribute to the occasional hypotension that is observed. Rapid, spontaneous, recovery of consciousness is typical, often within 5 hours of ingestion. Although the comatose state induced by GHB is nonspecific, the rapid recovery of consciousness from a severely comatose state is considered the hallmark of GHB toxicity.⁸ Although recovery is typical, death has occurred with the coadministration of other drugs.¹² As predicted from the in vivo metabolism of GBL, and 1,4-BD to GHB, the clinical presentation of toxicity of these agents has been identical to that of GHB.⁹

Both tolerance and physical dependence may occur with prolonged, and frequent use of GHB. Withdrawal from GHB and its precursors has been described. The withdrawal symptoms are very similar to those seen in ethanol withdrawal. Symptoms and signs include tremor, agitation, diaphoresis, hallucinations and tachycardia.⁴ Unlike with ethanol, convulsions have not been reported with GHB withdrawal.

Quantitative testing in both the serum and urine exists for GHB. Recently, methods have been developed that can differentiate between the presence of GHB and GBL.¹³ However, few laboratories perform GHB testing and currently no rapid test exists that would be immediately available to the treating emergency physician. Laboratory testing is most appropriate in situations such as possible date rape, or other forensic cases, in which confirmation of exposure may be critical. After ingestion, GHB is detectable in the serum for approximately eight hours, and for slightly longer in the urine.¹³

Treatment of GHB toxicity is supportive with airway protection being of primary importance. Because patients acutely intoxicated with GHB are expected to have a relatively rapid return to consciousness, and have little reported aspiration, some experienced with GHB toxicity describe withholding endotracheal intubation if a clear history of GHB ingestion exists.⁸ However, as history is often unreliable, and coingestants may be present, a conservative approach would certainly favor intubating the comatose patient. Hypotension should be treated with intravenous fluid and symptomatic bradycardia should be treated with atropine. Withdrawal has been successfully treated with large doses of benzodiazepines and phenobarbital.⁴

Emergency physicians should be knowledgeable about GHB and the precursors GBL, and 1,4-BD. The patient who presents to the Emergency Department with toxicity from these agents is likely have a nonspecific comatose state, and management should be focused on airway control. Rapid recovery from unconsciousness is considered the hallmark of GHB toxicity.

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MEETING REMINDER:

American Academy of Emergency Medicine
Annual Scientific Meeting
February 22 - 25, 2001
Orlando, Florida For Detail: www.aaem.org

The Call for Academic Departments of Emergency Medicine Throughout the University of California

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Introduction

The ten University of California (UC)-affiliated teaching hospitals suffer from a collective lack of influence in the academic hierarchy of their five parent medical schools. This is in stark contrast to the vital position of emergency medicine (EM) in California healthcare, and to the nationwide trend of prominence of emergency academics. Nationwide, there are 57 academic Departments of EM, including the Universities of Michigan and Pennsylvania, Johns Hopkins, Vanderbilt and Ohio State. UC must recognize the central importance of EM to the state's medical students. Academic department status will enable UC emergency departments (EDs) to fulfill their destiny as premier sites of clinical care, teaching and research.

Current Scope of Influence of the Specialty of Emergency Medicine

The five University hospitals and their five affiliated county and city facilities see more than 600,000 patients per year, (personal communication from medical directors) and comprise 6% of the California ED census. However, the import goes far beyond patient volume. All five campuses have affiliated Level I trauma centers, which care for 18,000 critically injured patients per year. The UC campuses at San Diego, Irvine, Los Angeles, San Francisco, and Davis support seven accredited emergency medicine residencies. Four of the five university hospitals support EM residencies. These programs now train more than 200 EM residents, two-thirds of the state's complement.

EM programs provide clinical rotations for medical students at all affiliated hospitals, to assure that all UC students receive instruction in this vital field. More than 6% of UC medical students train in EM (compared to 4% nationwide). This is testimony to the quality education that UC medical students receive.

The ten hospitals engage in substantial EM research. This research effort has been hampered by lack of faculty resources, grant funding, and time to pursue independent investigation. Nevertheless, EM faculty publish in some of the most prestigious journals, including *JAMA*, *NEJM*, and the *Annals of Emergency Medicine*.

The ten UC-affiliated EDs lead such important initiatives as the reduction of child and elder abuse, domestic and gun violence, and injury prevention. They also work to define the statewide response to earthquakes and bio/chemical terrorism. They are active in surveillance for established and emerging infectious diseases such as AIDS, tuberculosis and influenza. They provide radio control and education to more than 1000 paramedics, who deliver patients to UC, community and public hospitals. They staff the state's poison centers, which field hundreds of thousands of calls yearly.