Clinical Toxicology, 35(6), 591–594 (1997)

# A Sudden Awakening from a Near Coma After Combined Intake of Gamma-Hydroxybutyric Acid (GHB) and Ethanol

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## ABSTRACT

**Objective: A case of a sudden awakening from a near coma after combined intake of gamma-hydroxybutyric acid (GHB) (125 μg/mL), ethanol (134 mg/dL), and cannabinoids is described. Methods: GHB was determined by gas chromatography–mass spectrometry after acetonitrile precipitation and derivation with *N*-methyl-*N*-trimethylsilyltrifluoroacetamide, using valproic acid as the internal standard. Conclusion: The described case illustrates the consequences of GHB overdose. GHB overdose should be considered in every case of unexplained sudden coma, i.e., without any evidence of head injury, intake of coma-inducing drugs, or increasing intracranial pressure. GHB overdose will be missed by routine toxicological screening.**

## INTRODUCTION

Gamma-hydroxybutyric acid (GHB) is an endogenous metabolite of γ-aminobutyric acid present in both neural and nonneural mammalian tissues.[1,2] It has been hypothesized to have a role as a neurotransmitter.[2,3] Administered GHB profoundly effects the cerebral dopaminergic system by a mechanism which remains to be elucidated.[2]

The molecule seems to have both exciting and depressing effects. There is evidence that it induces epileptiform activity resembling petit mal epilepsy.[4,5] In recent years, the sodium salt has been sold illicitly as a steroid alternative for body-building (due to the induction of growth hormone release)[6] and as a tryptophan replacement for weight control and sedation.[7] It is used in the dance music scene as an alternative to ecstasy and speed. GHB is also known on the street as "Easy Lay" and authorities fear it

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may be taking the place of flunitrazepam, the tranquilizer that made headlines in 1995 as the "date-rape drug." GHB was described in the early nineties in the US, and it is now becoming popular in Europe as well.[8] GHB has been used clinically since 1960 as an anesthetic and hypnotic agent.[9] It has also been proposed in the treatment of alcohol[10] and opiate withdrawal syndrome.[11,12] GHB is an effective and well-tolerated treatment for narcolepsy.[13]

We describe a case of GHB intoxication in a young woman characterized by a sudden awakening from a near coma.

## Case Report

A 23-year-old female was brought to the emergency department (ED) by private car because she suddenly lost consciousness after consuming a considerable amount of ethanol and smoking a few joints during a house party with African music. According to her two companions, she had also drunk a small amount of GHB about 20 minutes before the collapse. The GHB solution was sold at that party. On clinical examination, the patient was near comatose having a Glasgow Coma Score of 6 (E1, V1, M4; E=eye movements, V=verbal reactions, M=motor reactions). All other clinical examinations were normal except for the slow heart (56 bpm) and respiratory rate (8/min). Despite the rather low Glasgow Coma Score, no therapeutic interventions were undertaken. Routine biochemistry was normal except for the low serum potassium (3.22 mmol/L). Routine toxicological screening of a serum sample consisting of immunoassay analysis of benzodiazepines, tricyclic antidepressants, salicylates, acetaminophen, and barbiturates was negative; blood alcohol was 134 mg/dL. A urine sample for the detection of illegal drugs could not be obtained. After about 45 minutes of unaltered near coma, the patient suddenly woke up as if she had snapped out of a dream. She said she felt nauseated and dizzy and vomited a few times. She was disoriented in time and had problems writing her name. After another 15 minutes, the patient categorically refused further testing or observation and walked out of the ED. The GHB concentration in the serum sample taken upon admission was 125 $\mu$g/mL.

## METHODS

### Reagents

The sodium salt of GHB (standard) was obtained from Aldrich Chemical (St. Louis, MO) and valproic acid (internal standard,[14] IS) from Sigma (St. Louis, MO). Acetonitrile (HPLC grade) was purchased from Lab Scan Ltd. (Dublin, Ireland). *N*-methyl-*N*-trimethylsilyltrifluoroacetamide (MSTFA) obtained from Alltech (Deerfield, IL) was used for derivation.

### Instrumentation

Gas chromatography–mass spectrometry (GCMS) analyses were performed on a Hewlett-Packard 5890 gas chromatograph coupled to a Hewlett-Packard 5970 mass-selective detector (MSD). Separation was achieved with a Hewlett-Packard ULTRA 1 bonded phase capillary column (12 m $\times$ 0.20 mm) with a 0.33-$\mu$m film thickness, connected to the MSD through a direct capillary interface. Splitless injection was performed using a capillary silanized glass insert. The inlet pressure of the carrier gas (He) was 0.2 kg cm$^{-2}$ and the flow rate was 1 mL/min. Injector and interface temperatures were 250°C and 290°C, respectively. The oven was initially held at 50°C for 0.6 minutes, then programmed at 10°C/min to a temperature of 100°C, then programmed 50°C/min to a final temperature of 250°C, and held for 1 minute. The MSD was used in the electron impact (at 70 eV) selected ion monitoring mode, programmed to detect the characteristic ion species at m/z 233 (GHB specific ion after derivation) and 201 (IS specific ion after derivation).

### Procedure

Twenty $\mu$L of serum was mixed with 20 $\mu$L of IS and 40 $\mu$L of acetonitrile.[14] The mixture was vortexed and centrifuged (8000 rpm, 5 minutes). Twenty $\mu$L of the supernatant was evaporated to dryness with $N_2$ at room temperature. MSTFA 20 $\mu$L was added and the sample was derivatized for 10 minutes at 90°C. Derivatized extract 1 $\mu$L was injected in the GCMS. Quantitation was based on peak area, relative to valproic acid. The chromatogram of the patient's sample is shown in Figure 1.

The assay had a detection limit of 2 $\mu$g/mL and was linear up to 200 $\mu$g/mL. The correlation coefficient of the calibration curve was 0.999.

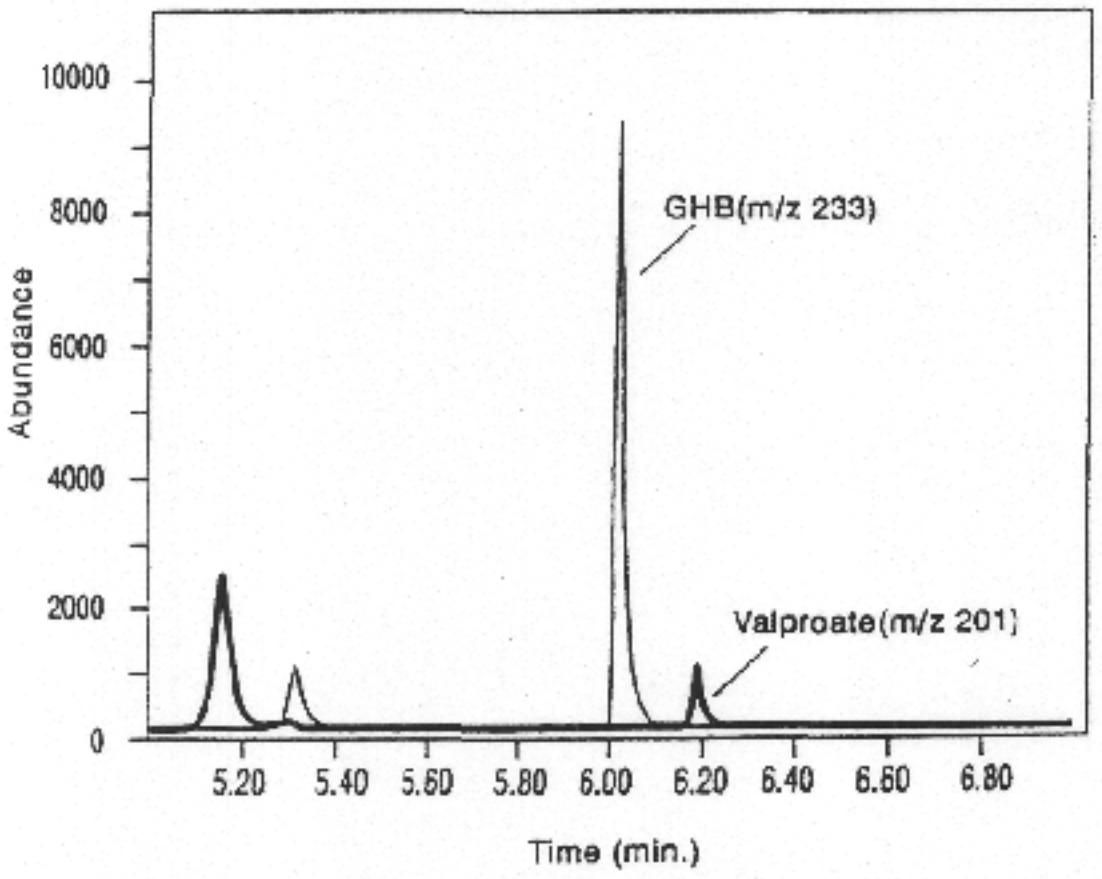


**Figure 1.** Chromatogram of the patient's sample.

## RESULTS AND DISCUSSION

The method we used to determine GHB is simple, rapid, and reliable. The assay was linear over the clinically relevant concentration range. Most described methods use a benzene extraction method after conversion of GHB to its lactonic acid gamma-butyrolactone (GBL).[15,16] Unfortunately, this method is very time consuming because the organic phase must be evaporated to dryness at room temperature due to the volatile character of GHB and GBL. Moreover, this method detects GBL and one cannot be sure whether the patient has taken GBL or GHB.

In the patient, a rather high serum GHB concentration of 125 μg/mL was found. In one study,[17] serum levels between 24 and 88 μg/mL were found when an oral dose of GHB of 25 mg/kg body weight was prescribed in patients treated for the alcohol withdrawal syndrome. In the study dealing with the correlation between serum GHB concentration and clinical features,[18] the symptom observed in patients with GHB levels between 52 and 156 mg/L is unconsciousness with occasional eye opening and spontaneous movement, which corresponds well with our findings.

Several poisonings with GHB have been described but in only a few reports has a GHB concentration been determined. Acute poisonings are characterized by unexplained seizures and/or coma.[19,20] A simultaneous intake of alcohol worsens the symptoms and increases the risk of aspiration pneumonia when vomiting occurs.[6,20] A fatal case of the combined use of heroin and GHB has been reported.[21] A case of GHB abuse associated with a Wernicke-Korsakoff syndrome has been published recently.[22] A driver was found apparently asleep behind the steering wheel of his car with a running engine after GHB intake.[23] Overdoses occur because the amount of GHB required for euphoria is very close to the amount required to cause seizures and coma. Moreover, GHB can be easily synthesized in underground, uncontrolled laboratories. The GHB concentration in the sold GHB drinks are untitred and can vary widely. Forty mL may contain a dose as small as 3 g or one as potentially toxic as 20 g.[24]

The presented case illustrates the typically sudden and reversible character of a GHB-induced coma. Most cases of GHB-induced coma are diagnosed on a presumptive basis only and there are only few reports in the literature correlating levels with symptoms. The low serum potassium concentration found in our patient seems to be a frequent observation after intake of the sodium salt of GHB, although not found in all cases.[25]

GHB intoxication will be missed in a routine toxicological screening as it can only be detected by a specific procedure. To our knowledge, no studies have been done to determine the incidence of GHB poisoning, but we suspect that it is rather low. At this time, we see no reason to screen systematically for GHB in poisoned patients. The method described above can be used to determine GHB if there are specific anamnestic indications or in cases of unexplained coma with negative routine toxicological results.

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