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CASE REPORT

Recreational drug Poisoning with Gamma-Butyrolactone and 1,4-Butanediol in Taiwan

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Restriction of gamma-hydroxybutyrate (GHB) in 1990 resulted in a shift toward the use of gamma-butyrolactone (GBL) or 1,4-butanediol (1,4-BD), which remain unregulated in most countries, including Taiwan. Self-reported GBL and 1,4-BD use are less common than GHB use, and the prevalence of GBL or 1,4-BD abuse may be underestimated. The first patient, a 45-year-old male, used GBL to enhance his sexual activity. He developed respiratory system and central nervous system (CNS) suppression; he was intubated and admitted to the intensive care unit. His urine GHB concentration was 289.5 mg/L. The second patient was a 24-year-old male who used 1,4-BD in conjunction with mixed new psychoactive substances to enhance his sexual activity. He also developed CNS suppression, and his urine GHB concentration was 1192.4 mg/L. By reporting these cases, we highlight the recreational use of GHB precursors, such as GBL and 1,4-BD, which is relatively unfamiliar to clinicians. Patients may present with CNS and respiratory depression after the voluntary recreational use of these drugs.

Key words: Gamma hydroxybutyrate, gamma butyrolactone, 1,4-butanediol, recreational drug

INTRODUCTION

Gamma-hydroxybutyrate (GHB) is a metabolite of gamma-aminobutyric acid with a low endogenous concentration.[1] Suppression of the respiratory system and central nervous system (CNS) are the main signs of GHB poisoning. Gamma-butyrolactone (GBL) and 1,4-butanediol (1,4-BD), which are not found endogenously in the body, are rapidly converted to GHB and show similar effects.[1] GHB was first introduced as a general anesthetic, and the restriction of GHB in 1990 resulted in a shift toward the use of GBL or 1,4-BD, which remain unregulated in most countries, including Taiwan.[2,3] In recent years, they have been more commonly used as recreational drugs for their euphoric and aphrodisiac effects, especially in men having sex with men.[4]

As self-reported GBL and 1,4-BD use is less common than GHB use, the prevalence of GBL and 1,4-BD abuse may be underestimated.[3] Furthermore, clinical reports of analytically confirmed GHB use in Taiwan are rare.[5] We present two patients who used a precursor of GHB as a recreational drug.

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CASE REPORTS

Case 1

The patient was a 45-year-old male who weighed 73.3 kg and had a history of hypertension. According to his friend, he ingested 20 ml of ink cleanser that claimed to contain 99.5% GBL [Figure 1] mixed with juice, not alcohol, to enhance his sexual activity. Thirty minutes postingestion, he lost consciousness; he arrived at the emergency department (ED) 3 h postingestion. On arrival, physical examination revealed a Glasgow coma scale (GCS) score of 3, respiratory rate of 9/min, the oxygenation saturation

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level of 93%, heart rate of 86 bpm, blood pressure of 113/62 mmHg, and temperature of 36.4°C. His pupils were 2.0 mm in diameter. Neurologic examination showed the absence of light, oculocephalic, and gag reflexes. Laboratory results are provided in Table 1. Other serum and urine toxicology screening results were unremarkable. There was no intracranial lesion on noncontrast-enhanced cranial computed tomography. We intubated the patient and initiated mechanical ventilation due to respiratory distress, and he was admitted to the intensive care unit. Six hours postingestion, his consciousness gradually improved (E2VTM4). We collected his urine and stored the specimen at 4°C until analysis. His urine GHB concentration was 289.5 mg/L, as measured with liquid chromatography-tandem mass spectrometry. He regained consciousness (E4VTM6) at 8 h postingestion after the administration of supportive treatments. He admitted that he had occasionally been using GBL for 4 years; he described buying it at art supply shops in the form of an ink cleanser. He was successfully extubated on day 1 and discharged, disease-free, after 7 days of hospitalization. During hospitalization, he did not display symptoms of withdrawal, such as anxiety, tremor, diaphoresis, or agitation. He did not present at the outpatient clinic after discharge.

Case 2

The second case involved a 24-year-old male with a body weight of 60 kg. According to his friend, he ingested an unknown amount of 99.5% 1,4-BD to enhance his sexual activity. Bradypnea and loss of consciousness developed 45 min after ingestion, and he was sent to our ED 2 h postingestion. On arrival, physical examination revealed a GCS score of 3, respiratory rate of 21/min, the oxygenation saturation level of 98%, heart rate of 85 bpm, blood pressure of 128/98 mmHg, and temperature of 35.6°C. Neurologic examination revealed pupils 1.0 mm in diameter, with the absence of a light reflex, oculocephalic reflex, and gag reflex. His laboratory results are shown in Table 2. We collected his urine and stored the specimen at 4°C until the time for the analysis. Urine toxicology screening indicated positivity for 4-methylmethcathinone (mephedrone), amphetamine, and methamphetamine. His urine GHB concentration was 1192.4 mg/L and 2583.8 mg/L at 2 h and 6 h postingestion, respectively [Table 2]. Supportive treatments were administered, and he regained consciousness at 6 h postingestion. He purchased 1,4-BD on the Internet as an industrial solvent, combined it with an "instant coffee packet" and used it as a sexual stimulant. The patient was not intubated and was discharged after 2 days of hospitalization. After discharge, he did not visit our outpatient clinic.

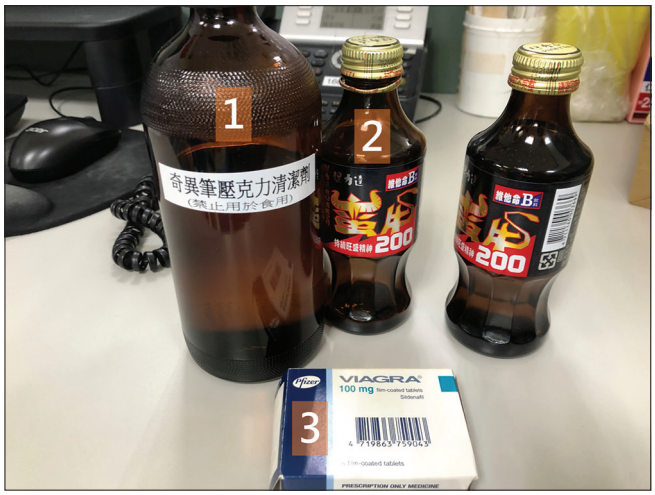

Figure 1: The patient took these substances to enhance his sexual activity. Number 1: Gamma-hydroxybutyrate (purity 99.95%); Number 2: Energy drink; Number 3: Sildenafil (Viagra)

Table 1: Laboratory data of case 1

Test	3.5 h	6 h	9 h	32 h	Reference range
Urine GHB	289.5	ND	ND	ND	<10 mg/L
Glucose	145	ND	ND	ND	74-100 mg/dL
White blood cell	15,530	ND	ND	14710	4500-11,000/uL
Hb	15.8	ND	ND	12.3	13.5-18.0 g/dL
Platelet	182	ND	ND	136	150-400 10^3/uL
pH	7.278	7.341	7.354	7.399	7.350-7.450
HCO_3	21.9	19.8	22.7	22.7	22-28 mEq/L
$PaCO_2$	48.0	37.5	40.4	36.5	35.0-45.0 mmHg
Creatinine	1.3	ND	1.3	1.3	0.7-1.2 mg/dL
Na	139	ND	140	140	136-145 mmol/L
K	4.1	ND	3.7	3.8	3.5-5.1 mmol/L

GHB=Gamma-hydroxybutyrate; ND=No data; Hb=Hemoglobin

Table 2: Laboratory data of case 2

Test	2 h	6 h	11 h	15 h	Reference range
Urine GHB	1229.2	3539.4	106.4	21.9	<10 mg/L
Glucose	144	ND	ND	ND	74-100 mg/dL
White blood cell	10,440	ND	ND	ND	4500-11,000/uL
Hb	14.8	ND	ND	ND	13.5-18.0 g/dL
Platelet	302	ND	ND	ND	150-400 10^3/uL
pH	7.319	7.360	ND	ND	7.350-7.450
HCO_3	21.9	22.1	ND	ND	22-28 mEq/L
$PaCO_2$	43.6	40.0	ND	ND	35.0-45.0 mmHg
Creatinine	0.7	ND	ND	ND	0.7-1.2 mg/dL
Na	139	ND	ND	ND	136-145 mmol/L
K	4.1	ND	ND	ND	3.5-5.1 mmol/L

GHB=Gamma-hydroxybutyrate; ND=No data; Hb=Hemoglobin

DISCUSSION

GBL is a colorless and water-miscible liquid with a weak odor that is rapidly metabolized to GHB by peripheral lactonase.[2,6] Having a strong odor, 1,4-BD is a colorless liquid that is metabolized to GHB by alcohol dehydrogenase and aldehyde dehydrogenase.[2,6] Both substances are widely used in the chemical industry as organic solvents; thus, they are less controlled than GHB. As GBL and 1,4-BD are rapidly metabolized, their clinical effects are almost identical to that of GHB; however, the onset of acute toxicity of 1,4-BD may be delayed when consumed with alcohol.[7]

GHB is a CNS depressant commonly referred to as an athletic-performance enhancer, a recreational drug, and a date-rape drug. The onset of GHB-induced CNS suppression occurs within 10–30 min of ingestion.[7] Suppression of the respiratory system and CNS are the main signs of GHB poisoning. Dose-related CNS effects include short-term anterograde amnesia, drowsiness, somnolence, myoclonus, and coma.[7] Other common clinical manifestations are bradycardia, hypotension, and mild hypothermia.[7] The clinical effects typically last 2–5 h, with complete recovery in 4–8 h.[7] Although approximately 95%–98% of GHB is metabolized hepatically and quickly eliminated, the detection window of GHB is short with 4–5 h in the blood and up to 12 h in the urine.[8] The recommended storage temperature for urine and blood specimens awaiting GHB analysis is-20°C or 4°C.[8] Furthermore, because GHB is also an endogenous metabolite, an administrative cutoff concentration of 10 mg/L GHB in the urine is recommended to distinguish between endogenous and exogenous GHB.[8] In the presented cases, they provided definite sources of GBL and 1,4-BD drug attempts. Although we did not detect the level of GBL or 1,4-BD in the urine, the level of GHB was significantly more than the cutoff value that exogenous GHB is highly suspected. However, GHB and its analogs are not detected by routine hospital toxicology screening. The clinical diagnosis is based on the patient's history and exclusion of other potentially serious etiologies. Supportive treatment with an emphasis on the respiratory system is the mainstay of management. On the other hand, cointoxication with other substances, such as ethanol, cocaine, and amphetamine, is common and may lead to the development of more severe clinical features.[9] In Taiwan, the "instant coffee packet" is a special recreational usage for mixing instant coffee powders with new psychoactive substances (NPS), such as cathinone derivatives and ketamine.[10] The prevalence of cointoxication with GHB and NPS may be underestimated in Taiwan.

After GHB was banned, users gradually switched to GBL and 1,4-BD, which remain legal.[3,6] Furthermore, a new trend in the use of these drugs has occurred in recent years, whereby people use them as weight loss medication and during chemsex, which is defined as sexualized substance use.[2,4] Despite the lack of large-scale studies, recreational use of GBL and 1,4-BD is not uncommon in Taiwan. In a case series of 12 patients with GHB/GBL-related ED visited at National Taiwan University Hospital, even though all of the patients used GBL to evade conviction, only 3 of them admitted to consuming GHB or GBL.[5]

CONCLUSION

By reporting these cases, we highlight the recreational use of GHB precursors, such as GBL and 1,4-BD, which is relatively unfamiliar to clinicians. GHB intoxication is a clinical diagnosis based on the patient's history and exclusion of other potentially serious etiologies. Patients who present with suppression of the respiratory system and CNS should be considered to have GHB intoxication, especially when substance abuse is suspected. The clinical effects of GHB intoxication typically last 2–5 h, with complete recovery in 4–8 h. Supportive treatment with an emphasis on the respiratory system is the mainstay of management.

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Ethical approval

This study proposal was approved by the Institutional Review Board of Tri-Service General Hospital. Approval number: TSGHIRB No.1-107-05-134. Date of Approval: 2021/9/9.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Data availability statement

All data generated or analyzed during this study are included in this published article.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Wood DM. Gamma-hydroxybutyrate and its related analogues gamma-butyrolactone and 1,4-butanediol. In: Brent J, Burkhart K, Dargan P, Hatten B, Megarbane B, Palmer R, editors. Critical Care Toxicology. Cham: Springer International Publishing; 2016. p. 1-32.
2. Palmer RB. Gamma-butyrolactone and 1,4-butanediol: Abused analogues of gamma-hydroxybutyrate. Toxicol Rev 2004;23:21-31.
3. Wood DM, Warren-Gash C, Ashraf T, Greene SL, Shather Z, Trivedy C, *et al.* Medical and legal confusion surrounding gamma-hydroxybutyrate (GHB) and its precursors gamma-butyrolactone (GBL) and 1,4-butanediol (1,4BD). QJM 2008;101:23-9.
4. Nimbi FM, Rosati F, Esposito RM, Stuart D, Simonelli C, Tambelli R. Chemsex in Italy: Experiences of men who have sex with men consuming illicit drugs to enhance and prolong their sexual activity. J Sex Med 2020;17:1875-84.
5. Weng TI, Chen LY, Chen JY, Chen GY, Mou CW, Chao YL, *et al.* Characteristics of patients with analytically confirmed γ-hydroxybutyric acid/ γ-butyrolactone (GHB/GBL)-related emergency department visits in Taiwan. J Formos Med Assoc 2021;120:1914-20.
6. van Amsterdam J, Brunt T, Pennings E, van den Brink W. Risk assessment of GBL as a substitute for the illicit drug GHB in the Netherlands. A comparison of the risks of GBL versus GHB. Regul Toxicol Pharmacol 2014;70:507-13.
7. Schep LJ, Knudsen K, Slaughter RJ, Vale JA, Mégarbane B. The clinical toxicology of γ-hydroxybutyrate, γ-butyrolactone and 1,4-butanediol. Clin Toxicol (Phila) 2012;50:458-70.
8. Busardò FP, Jones AW. GHB pharmacology and toxicology: Acute intoxication, concentrations in blood and urine in forensic cases and treatment of the withdrawal syndrome. Curr Neuropharmacol 2015;13:47-70.
9. Miró Ò, Galicia M, Dargan P, Dines AM, Giraudon I, Heyerdahl F, *et al.* Intoxication by gamma hydroxybutyrate and related analogues: Clinical characteristics and comparison between pure intoxication and that combined with other substances of abuse. Toxicol Lett 2017;277:84-91.
10. Weng TI, Su PI, Chen JY, Chen PS, Hwa HL, Fang CC. Analytically confirmed 4-Methyl-N-ethylnorpentedrone (4-MEAP), a synthetic cathinone, in cases presenting to an emergency department. Clin Toxicol (Phila) 2020;58:65-6.