COMA AFTER INTAKE OF GAMMA-HYDROXYBUTYRIC ACID (GHB): TWO CASE REPORTS

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ABSTRACT: We are presenting the first cases of gamma hydroxybutyric acid (GHB) overdosing in Switzerland, describing an analytical method and summarizing general GHB effects. Two patients became unconscious – one even deeply comatose – after the intake of GHB. After a couple of hours in hospital, they awoke, recovered rapidly without any after effects, and left the hospital.

KEY WORDS: Gamma-hydroxybutyric acid (GHB); Case reports; GC/MS.

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TWO CASE REPORTS

The new drug gamma-hydroxybutyrate (GHB, "liquid ecstasy") has been abused in the USA since the beginning of the nineties. In Europe the first reported cases were in 1995 [21]. The main abusers are young people at raves, discos and on the drug scene, where GHB is popular for its euphorigenic and sedative properties. Furthermore, it is taken as an alleged anabolic agent among bodybuilders. Criminals use it to narcotize potential victims [4]. We describe the first Swiss cases from 1998 and 1999, as summarized in Table I. Both patients ingested GHB in addition to other drugs. Remarkably, both persons were distinctly hypothermic, a condition which might be due to GHB and which could also be useful for diagnostic purposes [13, 14]. Typical for a GHB overdose was the rapid onset of unconsciousness, the quick awakening from this state and the lack of after effects.

GHB analysis

GHB analyses were conducted by a modified method of Louagie et al. [12]. 20 µl of blood, urine or diluted GHB liquid and 5 µl of the internal standard GHB-d6 were added into a 0.5 ml Eppendorf tube. Then 45 µl of methanol were added, the mixture was vortexed and centrifuged (12000 rpm,

TABLE I. CASE REPORTS OF THE TWO PATIENTS SUFFERING FROM GHB OVERDOSING

Sex, age	Case no.1 Male, 26	Case no.2 Male, 23
Condition during hospitalization	Comatose (GCS 3)	Agitated, responds poorly, uncontrolled defensive movements
Body temperature	34.7°C	33.8°C, 1 h later 35.0°C
Blood pressurepulse	120/80 mm Hg 100/min	125/85 mm Hg 72/min
Pupils	Small, delayed reaction to light	Middle,normal reaction to light
Laboratory results	Hematology and chemistry including electrolytes normal	Hematology and chemistry including electrolytes normal
Drug screening positive for	Amphetamines, cannabis	Amphetamines, cannabis
Treatment	0.8 mg naloxon and 0.5 mg flumazenil, both without effect	5 mg diazepam (for sedation)
Clinical course	After 3 h of deep coma rapid awakening, full orientation, no residue, left hospital quickly	After 5 h of unconsciousness rapid awakening, full orientation, no residue, left hospital 2 h later
GHB concentration	No blood or urine 0.5 g/ml in the GHB liquid. Maximum intake: 17.5 g GHB	Blood: 9.9 µg/ml (normal: 0–0.4 µg/ml) Urine: 990 µg/ml (normal: 0–5.7 µg/ml) Sample time of body fluids: approx. 4.5 h after admission
Other drugs		Blood: 1160 ng/ml amphetamine, 185 ng/ml MDMA, 30 ng/ml diazepam Urine: 205 ng/ml THC-COOH
Anamnesis	Consumption of alcohol, speed, ecstasy, cannabis and GHB (purchased via Internet) in discos	Consumption of amphetamine, ecstasy and a clear liquid (GHB) during a techno-party

5 min). 50 µl of the supernatant was evaporated to dryness under a stream of nitrogen at room temperature. For silylation 20 µl MSTFA were added, vortexed and incubated at 85°C for 15 min. Gas chromatography mass spectrometry (GC/MS) analyses were performed with a Fisons MD 800, full scan mode, electron ionization (70 eV). A DB5-MS column (J & W Scientific, 30 m, 0.25 mm i.d., 0.25 µm film thickness) was used. The injection port temperature was 230°C, the interface temperature was 250°C and the temperature in the ion source was 200°C. 1 µl of sample was injected into the GC/MS. The initial column temperature was at 80°C, held 1 min, ramped at 5°C/min to 140°C, and then ramped at 40°C/min to 250°C with a final hold of 5 min. Helium with a pressure of 80 kPa was used as the carrier gas. The mass m/z 233 for GHB and m/z 239 for GHB-d6, respectively, were used for quantitation, see Figure 1 and 2.

Pharmacology and toxicology of GHB

GHB is a metabolite of the neurotransmitter gamma-aminobutyric acid (GABA) and on the other hand GHB is also probably metabolised to GABA [1]. GHB seems to affect gabaergic, opioid, dopaminergic and cholinergic neurotransmitter-systems in the brain [1, 19].

As physiologically normal for humans, GHB concentrations of approx. 0.1 µg/ml in

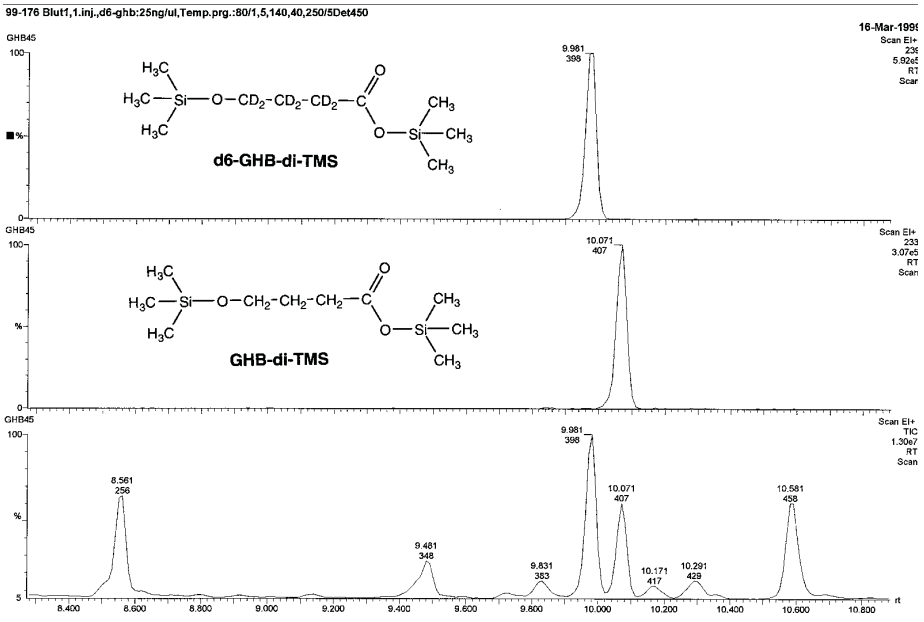

Fig. 1. GC/MS analysis (full scan) of a blood sample of case #2. Chromatogram of the characteristic mass of TMS-derivatized d6-GHB (top) and GHB (middle) and of the total ion current (TIC, bottom), respectively.

plasma (standard deviation: 0.3 µg/ml) and of approx. 2.5 µg/ml in urine (standard deviation: 3.2 µg/ml) respectively, were described [8]. Ingested GHB is quickly resorbed, metabolised and eliminated. The terminal half-life is approx. 30 min and with high doses (> 50 mg/kg bw) both resorption and elimination are slowed down [6, 16]. A dose of approx. 1 g leads to a maximum plasma concentration of approx. 25 µg/ml [16]. In the awakening phase Helrich et al. [9] were able to establish a good correlation between plasma concentration and effects: deep coma at GHB concentrations > 60 µg/ml, spontaneous blinking and responses occurred to deep pressure at 160–260 µg/ml, spontaneous movements with occasional opening of eyes at 50–160 µg/ml and awakening with concentrations below 50 µg/ml.

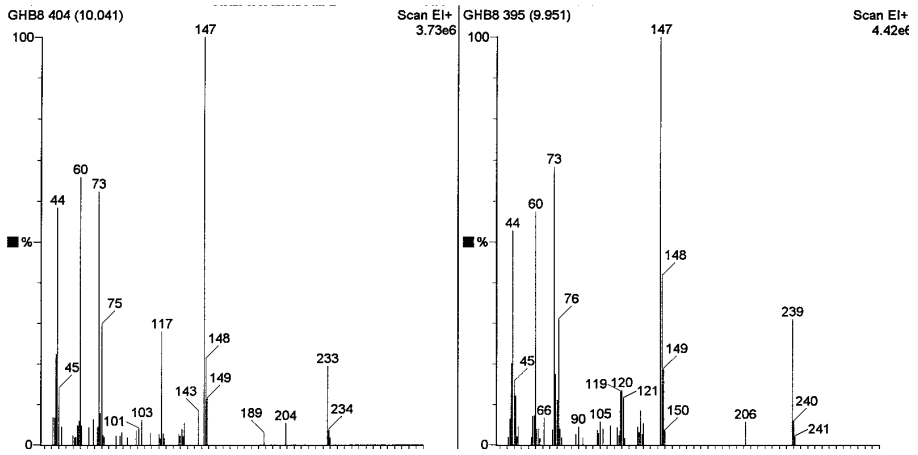

Fig. 2. EI mass spectra of GHB-di-TMS (left) and d6-GHB-di-TMS (right).

Single doses of 1–2 g have an euphorising effect; the consumer feels at ease, relaxed and slightly inebriated, the senses are intensified, the wish to contact other people is increased and a stronger physical sensitivity is noticed [7, 10, 17]. It is also suggested that it acts as an aphrodisiac [7, 17]. Doses of approx. 2.5 g lead to sleepiness, dizziness, nausea, vomiting, convulsions, cramps, bradycardia and hallucinations [2, 3]. Intake of 3–4 g (50 mg/kg bw) normally leads to unconsciousness within minutes, and doses of more than 4–5 g (doses up to 30 g have been described) to deep coma [2, 3, 21]. In almost all cases the coma is reversible and the patient free from after effects [3, 12, 18, 21]. There is a rapid onset of unconsciousness in addition to a rapid awakening [12, 14, 20, 21]. The observed amnesia is evidently anterograde. Particularly for the inexperienced consumer the steep dose-response curve can be fatal as the doubling of a normal dose can lead to coma instead of the desired euphoria. One should take into account that the dosing of GHB – particularly in its liquid form – is difficult because the consumer normally doesn't know the concentration.

In rats the LD_{50} is 1.7 g/kg bw [11]. The cause of death is respiratory depression [11]. In humans the lethal dose is unknown so far. Until now there has been no credible description of lethal cases that were caused solely by GHB. So far only two letal cases are described where GHB was consumed together with other central depressing substances [5, 15].

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