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GHB and Driving Impairment

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ABSTRACT: Gamma hydroxybutyrate (GHB) was identified in the blood of 13 subjects arrested for impaired driving. GHB concentrations ranged from 26 to 155 mg/L (mean 87 mg/L, median 95 mg/L). In eight cases, GHB was the only drug detected, and signs of impairment were consistent with those of a CNS depressant, including erratic driving (weaving, swerving, ignoring road signs), confusion, incoherent speech, unresponsiveness, lack of balance, unsteady coordination, poor performances on field sobriety tests, and varying states of wakefulness. Given the ability of GHB to induce sleep and unconsciousness, it is evident from these cases that recreational use of the drug has the potential to impair a person's driving ability.

KEYWORDS: forensic science, GHB, driving, impairment

Gamma hydroxybutyrate (GHB) was first used clinically in Europe as an anesthetic in the 1960s; however, its use was discontinued as it lacked analgesic properties, and side effects of petit mal and grand mal seizures, and coma were reported (1). GHB is currently still available in Europe as an anesthetic adjunct and a hypnotic agent, and is also used to treat symptoms of alcohol dependence and opiate withdrawal syndrome (2–5). GHB is abused by bodybuilders as an alternative to anabolic steroids to enhance muscle growth, and recreationally by others for its intoxicating effects such as euphoria, reduced inhibitions, and sedation (4,6–9).

Substances such as gamma butyrolactone (GBL; also known as 2(3H) furanone di-hydro) and 1,4-butanediol (1,4-BD) convert into GHB in vivo following oral administration (10–12). In March 2000, GHB was federally reclassified as a Schedule 1 substance [H.R.2130.ENR]; however, the precursor GBL is a listed substance only. GHB is available illicitly as a powder and as a solution, while GBL and 1,4-butanediol are liquids. Typical recreational doses administered by users are usually in excess of 1 teaspoon of GHB powder, or 1 "capful" of liquid GHB, GBL, or 1,4-BD, which is approximately equivalent to at least 2.5 g, or 35 mg/kg of GHB for a 70 kg person (1,4,13). Administration of up to 4 tablespoons of GHB has been previously reported (1).

The primary effects of GHB are those of a CNS depressant. Clinical and adverse effects range from relaxation and euphoria, confusion, dizziness, drowsiness, nausea, agitation, loss of peripheral vision, short-term amnesia and somnolence, to uncontrollable shaking or seizures, combativeness, respiratory depression, hallucinations, and unarousable unconsciousness (1,3,4,9,14–15). These classical clinical symptoms are clearly contraindicated for the safe operation of a motor vehicle. Several deaths have also been reported following overdoses from GHB or GBL alone, and in combination with other drugs (16–19).

Previous authors have reported subjects taking GHB and being arrested for impaired driving (16,20,21), and we have encountered a number of similar cases in our own jurisdiction. This prompted us to document the clinical symptoms, circumstances, driving behavior, and indicia of impairment in these cases.

Methods

Cases of suspected drug-impaired driving are referred to the Washington State Toxicology Laboratory by law enforcement agencies for alcohol and/or drug testing. Cases where the alcohol or drug concentration could not reasonably account for the degree of impairment observed in the subject were additionally tested for GHB. Specimens were also analyzed for GHB if this substance or one of its precursor drugs were found in the driver's possession, or if the driver admitted to using GHB, or one of its pseudonyms or precursors. On receipt of blood specimens at the laboratory, samples were stored at 4°C in tubes containing sodium fluoride and potassium oxalate, until tested.

All specimens underwent blood alcohol analysis for ethanol, methanol, acetone, and isopropanol by headspace gas chromatography. The limit of detection for ethanol was 0.005 g/100 mL. Methanolic extracts of blood specimens underwent a screen for drugs of abuse and several prescription drug classes using an Enzyme Multiplied Immunoassay Technique (EMIT). The EMIT procedure screened for cocaine metabolites (cutoff limit 100 ng/mL), opiates (10 ng/mL), amphetamines (100 ng/mL), carboxy-tetrahydrocannabinol (10 ng/mL), methadone (100 ng/mL), phencyclidine (10 ng/mL), propoxyphene (100 ng/mL), barbiturates (100 ng/mL), benzodiazepines (50 ng/mL), and tricyclic antidepressants (100 ng/mL). Additionally, *n*-butylchloride and ethyl acetate extracts of blood specimens underwent separate screens for weak acid, neutral, and basic compounds using GC-MS.

GHB was analyzed by GC-MS as previously described (22). Calibration was determined to be linear over a range 1 to 100 mg/L in blood, and the correlation coefficient was typically better than 0.990. The limit of quantitation (LOQ) was defined as 1 mg/L, the lowest concentration at which the assay was determined to be linear. Specimens with GHB concentrations above 100 mg/L were reanalyzed after dilution to within the linear range of the assay.

In cases where GHB was identified, the circumstances of the incident, including alcohol or other drugs detected, driving behavior, subjects' appearance, statements, and performance in field sobriety tests were recorded from the police report.

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Results

In total, 13 cases of suspected impaired driving, in which GHB was identified, were encountered between November 1998 and June 2000. Concentrations ranged from 26 to 155 mg/L (mean 87 mg/L, median 95 mg/L). In eight cases, GHB was the only drug detected. One case was additionally positive for ethanol (0.06 g/100 mL) and carboxy-tetrahydrocannabinol (9 ng/mL), and another case was positive for carboxy-tetrahydrocannabinol (5 ng/mL) and dextromethorphan (~0.01 mg/L). Diazepam (0.08 mg/L) and thiopental (8.7 mg/L), diphenhydramine (~0.01 mg/L), and bupropion metabolites were also detected in combination with GHB in one case each.

In the eight subjects where GHB was the only drug present, symptoms reported were generally those of a CNS depressant. The subjects were typically stopped because of erratic driving, such as weaving, ignoring road signs, and near-collisions. Common signs of impairment included confusion and disorientation, incoherent speech, short-term memory loss, dilated pupils, lack of balance and unsteady gait, poor coordination, poor performance of field sobriety tests, copious vomiting, unresponsiveness, somnolence, and loss of consciousness.

The following histories are from the 13 cases submitted to the Washington State Toxicology Laboratory with requests for GHB analysis. These 13 subjects had all been arrested for driving under the influence (DUI) of a drug.

Case 1—A 24-year-old female was observed driving through several red lights, before stopping her car on the side of the road. When contacted by police, the subject was sitting in the driver's seat, marginally conscious. She appeared anxious, jittery, confused, incoherent, unresponsive to questions, and attempted to start the car without keys. The subject had dilated pupils, continually lost her balance, and repeatedly fell in and out of consciousness. There was no smell of alcohol, and the subject was taken to a hospital for evaluation.

The subject stated she had taken a "nutrition supplement" (called G3), which she had purchased from a gymnasium and was told that the supplement was "a legal form of GHB." Entries in a diary belonging to the subject revealed that she had taken GHB on several previous occasions.

Blood was drawn approximately 3.5 h after first police contact. The subject's blood was positive for GHB at a concentration of 26 mg/L. Blood alcohol analysis, an EMIT screen for drugs of abuse and several prescription drug classes, and a GC-MS screen for acid, neutral, and basic compounds did not reveal the presence of any other substances.

Case 2—A 33-year-old male was arrested for DUI after being stopped by police for driving with three flat tires. At the time of the incident, the subject was negative for breath alcohol; however, he was disorientated and easily distracted, slow to respond, had slurred speech, and his coordination was unsteady. A drug recognition expert (DRE) evaluation was conducted. The subject's eyes were bloodshot, his pulse ranged from 88 to 108 bpm, his blood pressure was 124/58 mmHg, and his body temperature was 98.88°F. His muscle tone was near normal. Horizontal gaze nystagmus was present (six clues) and the subject performed poorly during the standardized field sobriety tests (Romberg balance, walk and turn, and one-leg stand). No vertical gaze nystagmus was present. His pupils were dilated with slow reaction to light. The DRE officer's opinion was that the driver was under the influence of a CNS depressant. The subject had a bottle of liquid labeled "RenewTrient" (2(3H)-furanone di-hydro) in his possession.

Blood was drawn approximately 2.25 h after the arrest. The subject's blood and urine were positive for GHB at a concentration of 33 mg/L and 714 mg/L, respectively. A screen for alcohol, basic, neutral and acidic drugs did not reveal the presence of other substances.

Case 3—A 33-year-old male was arrested for DUI after being involved in a single vehicle accident. The subject was incoherent as to the direction of travel, or where he was going. The arresting officer had followed the subject for approximately six miles with activated lights and sirens before the subject responded and stopped. The driver's speeds ranged between 40 and 80 mph (in a 60 mph zone), and he had hit the highway barrier twice. There was no odor of alcohol on the subject; however, he indicated that he had taken GHB.

Blood was drawn approximately 2 h after driving. The subject's blood was positive for GHB at a concentration of 34 mg/L. A screen for alcohol, basic, neutral, and acidic drugs did not reveal the presence of other substances.

Case 4—A 42-year-old male was involved in a two-car collision. The arresting officer believed the subject to be under the influence of drugs and not alcohol, and the driver admitted using GHB. A DRE evaluation was conducted and the officer's opinion was that the driver was under the influence of a CNS stimulant, a narcotic analgesic, and GHB.

The subject's blood was positive for GHB at a concentration of 46 mg/L. A screen for alcohol, basic, neutral, and acidic drugs did not reveal the presence of other substances.

Case 5—A 23-year-old male was observed weaving and driving through a red light. Although the driver was cooperative, he was initially incoherent and unresponsive to questions. The driver was tense, agitated, combative and restless, and his coordination was unsteady. A DRE evaluation was conducted. The subject's eyes were bloodshot and watery, his pulse ranged from 64 to 76 bpm, his blood pressure was 170/120 mmHg, his body temperature was 98.5°F, and his muscle tone was normal-to-rigid. Horizontal gaze nystagmus (six clues) and vertical gaze nystagmus were present, and lack of convergence was also observed. His pupils were dilated with slow reaction to light. The subject performed extremely poorly and was unable to complete the standardized field sobriety tests. He was taken to a hospital for evaluation, where he fell asleep. The DRE officer's opinion was that the driver was under the influence of both a CNS depressant and a CNS stimulant. The subject stated he had taken two ephedrine tablets approximately 7 h earlier.

Blood was drawn approximately 2 h after the arrest. The subject's blood was positive for GHB at a concentration of 73 mg/L. A screen for alcohol, basic, neutral, and acidic drugs revealed the presence of no other drugs, including ephedrine.

Case 6—A 22-year-old male was observed driving slowly on a freeway, weaving in a serpentine motion between three lanes of traffic, and sideswiping another vehicle. The subject's pupils were dilated, unfocused, and bloodshot. His movements were slow and uncoordinated, and his speech was incoherent and repetitive. He had no memory of the events and claimed that he was not driving at all. He smelled of intoxicants and was copiously vomiting. He was unable to perform any field sobriety tests due to complete lack

of coordination and balance, and fell asleep during the police interview. The officer's opinion was that the driver was under the influence of a hallucinogen and marijuana.

Blood was drawn 1.75 h after first police contact. The subject's blood was positive for GHB at a concentration of 89 mg/L. Ethanol (0.06 g/100 mL) and delta-9-carboxy-tetrahydrocannabinol (9 ng/mL) were also detected in the subject's blood.

Case 7—A male (age unknown) was observed swerving and driving erratically. The subject stated he had taken a muscle-building supplement, which he knew to be GHB. The subject's blood was positive for GHB at a concentration of 95 mg/L. Diphenhydramine (~0.01 mg/L) was also detected in the subject's blood.

Case 8—A 20-year-old male was observed swerving over the centerline and shoulder. Despite being cooperative, the driver was dazed and confused, appeared nervous, and had trouble concentrating. His speech and movements were slow and deliberate, and his pupils were dilated, bloodshot, and unresponsive to light. He had difficulty maintaining his balance and performed poorly on the field sobriety tests; however, there was no smell of intoxicants. The driver claimed to have ingested a bodybuilding supplement "Re-Active" (2(3H) furanone dihydro) earlier in the day, and two bottles of the substance were found in the subject's vehicle. The subject also admitted blacking out while driving and had little memory of events.

Blood was drawn 2 h after first police contact. The subject's blood was positive for GHB at a concentration of 98 mg/L. A screen for alcohol, basic, neutral, and acidic drugs did not reveal the presence of other substances.

Case 9—A 17-year-old male swerved into a lane of oncoming traffic, sideswiped two cars, then continued to drive recklessly before being forced off the side of the road by a citizen. The subject was intermittently unresponsive and unconscious. He began vomiting copiously and was transported to an emergency room. The subject smelled of alcohol and "another chemical."

Blood was drawn within 1 h of the hit-and-run accident. The subject's blood was positive for GHB at a concentration of 99 mg/L. Delta-9-carboxy-tetrahydrocannabinol (9 ng/mL) and a trace amount of dextromethorphan (~0.01 mg/L) were also detected in the subject's blood.

Case 10—A 21-year-old male was observed weaving all over the road, driving through a red light, and almost colliding with another vehicle. Observers stated that it appeared as though the driver and passenger were dancing in the car. The vehicle then stopped completely, and the driver was seen slumped over the steering wheel, although the driver did try to start the car and drive away. When police arrived, the passenger was vomiting and the driver was not responding to any questions. There was no smell of intoxicants, even though the driver appeared extremely intoxicated. Field sobriety tests were not performed, as the subject was intermittently unconscious and unresponsive. The driver was subsequently transported to a hospital where he became apneic and required intubation.

The subject admitted to nursing staff that he had ingested GHB. He had purchased the ingredients to make GHB over the Internet, and had been taking the mixture for 8 to 10 days to enhance muscle growth. On this occasion, he had taken a little more than two tablespoons of liquid GHB, which he stated was more than his usual dose. He also stated that he had thought his driving was fine and had only pulled over when another driver told him he was swerving. He then thinks he passed out.

Blood was drawn within 2 h of the alleged ingestion of GHB, and 1.25 h after the arrest. The subject's blood was positive for GHB at a concentration of 127 mg/L. A screen for alcohol, basic, neutral, and acidic drugs showed no other drugs present.

Case 11—A 38-year-old male drove his vehicle into a parked pickup truck. The arresting officer believed the subject to be severely impaired, and a DRE evaluation was conducted. The DRE officer's opinion was that the driver was under the influence of both a CNS depressant and a CNS stimulant. The subject stated he was a bodybuilder, and was found in possession of numerous bodybuilding supplements. The subject also admitted to taking GHB and Zoloft® (sertraline).

The subject's blood was positive for GHB at a concentration of 139 mg/L. Trace amounts of bupropion metabolites were also detected in the subject's blood; however, neither sertraline nor norsertraline were detected.

Case 12—A 38-year-old male rear-ended another vehicle. He was extremely disoriented and nervous, and appeared to be hallucinating. The subject performed poorly on standardized field sobriety tests and fell unconscious before completing the tests.

Blood was drawn within 1 h of the arrest. The subject's blood was positive for GHB at a concentration of 155 mg/L. A screen for alcohol, basic, neutral, and acidic drugs showed no other drugs present.

Case 13—Five weeks previously, the same subject as in Case 12 had been arrested for driving under the influence of drugs in similar circumstances. The driver had been observed driving erratically, and when stopped, he was continually shaking his head and slapping his own face. The subject continually fell in and out of consciousness, and standardized field sobriety tests could not be conducted. The driver was transported to hospital.

In this instance, the subject's blood was positive for GHB at a concentration of 117 mg/L. Diazepam (0.08 mg/L) and thiopental (8.7 mg/L) were also detected in the subject's blood.

Discussion

Instances of drivers seemingly impaired by GHB have been previously reported, and the symptoms, adverse reactions, and behavior of the subjects are consistent with observations made in the present study.

In one such report, a driver was found asleep behind the wheel of his vehicle (20). His symptoms included horizontal and vertical gaze nystagmus, muscle flaccidity, severe ataxia, and mental confusion. He was unable to stand unassisted. He admitted to ingesting a white powder given to him by an acquaintance at a gymnasium. A urine specimen collected approximately 2 h after drug administration contained 1975 mg/L of GHB and 26 ng/mL of 11-nor-9-carboxy-tetrahydrocannabinol. The urine GHB concentration measured was consistent with a dose of at least 100 mg/kg. The authors tentatively concluded that sufficient doses of GHB may cause impairment of the psychomotor skills required for safe operation of a motor vehicle.

Frommhold and Busby (1998) described two cases where the subjects were most likely driving under the influence of GHB (21). In the first case, a police officer observed the front end of a pickup truck in the guardrail while the rear end of the vehicle was block-

ing the freeway lane. Two males were passed out in the front cab. No biological specimens were collected; however, a clear liquid found in a Gatorade© bottle was later identified analytically as being GBL. In the second case, a driver was stopped after narrowly avoiding a collision with another vehicle. No breath alcohol was detected; however, horizontal gaze nystagmus was present (six clues) and the subject failed the standardized field sobriety tests (Walk and Turn, and One-Leg Stand). Urine was positive for GHB (1041 mg/L), codeine, and phenothiazine metabolites. Pan et al. (1999) also detected GHB in the blood of six DUI cases; however, no corresponding symptoms or driving behavior were reported (16).

Two published reports investigating the effects of GHB on psychomotor performance failed to demonstrate gross impairment. Ferrara et al. (1999) concluded that oral doses of 12.5 and 25 mg/kg of GHB (i.e., 875 mg or 0.35 teaspoons, and 1750 mg or 0.7 teaspoons in a 70 kg individual) had no effect on attention, vigilance, alertness, short-term memory, or psychomotor coordination (23). Unfortunately, no corresponding GHB concentrations were obtained. These authors did report, however, that 66% and 50% of the subjects experienced either dizziness or dullness following dosages of 25 and 12.5 mg/kg, respectively. Mattila et al. (1978) concluded that oral doses of 1 and 2 g (i.e., 0.4 and 0.8 teaspoons) of GHB neither deteriorate driving skills (reactive and coordination skills, and attention) nor increase the effects of low doses of alcohol (24). There was only a slight increase in the number of reaction mistakes following the 2 g dose. Typical doses administered by GHB users, however, often exceed 1 teaspoon, which is equivalent to at least 2.5 g, or 35 mg/kg for a 70 kg person (1,4,13). Further studies on psychomotor performance using higher and more relevant doses of GHB would be valuable.

Table 1 summarizes the relationship between reported doses of GHB and observed clinical effects. The recommended therapeutic dose of GHB for sleep induction is approximately 1.5 to 2.25 g (20 to 30 mg/kg for a 70 kg person) orally at bedtime (25). GHB is rapidly eliminated and has a half-life of 20 to 53 min, which appears to increase with higher doses (3,26,27). Peak plasma concentrations are observed within 20 to 40 min, and peak urine concentrations are observed within 4 h of drug administration. Following single oral doses of 25 mg/kg GHB, peak serum concentrations in 10 alcohol-dependent patients ranged from 24 to 88 mg/L (26). Oral doses of 12.5, 25, and 50 mg/kg in eight healthy individuals produced mean plasma concentrations of 23, 46, and 80 mg/L at 25, 30, and 45 min, respectively (3). In another study, two separate doses of 26 to 52 mg/kg GHB were administered to six narcoleptic patients 4 h apart. The mean peak plasma GHB concentrations observed were 62.8 mg/L (range 30 to 102 mg/L) and 91.2 mg/L (range 48 to 125 mg/L), following the first and second dose, respectively (27).

Following a single dose of 30 mg/kg, subjects felt sluggish, sedated, fatigued, drunk, dazed, spaced, and carefree, compared to those subjects receiving a placebo (25). Doses above approximately 50 mg/kg resulted in transient unconciousness, hypotonia, slowed pulse, and slowed respiration. Other authors have reported that single doses of 10 mg/kg cause amnesia and hypotonia: 20 to 30 mg/kg causes drowsiness, euphoria, vertigo, and somnolence: 50 mg/kg causes loss of consciousness (although patients are still arousable): and doses of 60 mg/kg or greater result in coma or unarousable unconsciousness (8,9,15).

Since GHB has an extremely short half-life, any delay between the time of driving and the blood draw could result in a significant decrease in blood GHB concentrations. In Case 1, there was approximately a 3.5 h difference between when the driver was first contacted by police officers and when the blood was drawn. Consequently, a blood GHB concentration considerably higher than 26 mg/L can be assumed at the actual time of driving. At GHB concentrations above 50 mg/L, symptoms such as sedation, drowsiness, and dizziness are frequently observed (3).

In the cases we have presented, the symptoms reported are consistent with those adverse effects noted in the literature, and are uniformly those of central nervous system depression. While there is no attempt here to correlate any blood concentration with a specific degree of effect, there is clearly evidence for a dose- or concentration-dependent increase in impairment when viewed across all cases. Given the complexity of the driving task, effects on driving could be expected in several areas. The first and most obvious was the tendency of many of these subjects to fall asleep or lose consciousness during the investigation. Interestingly, on the bottle

TABLE 1—*Literature review: Relationship between doses of GHB and reported clinical effects.*

Reference	GHB Dose: mg/kg (for 70 kg)	(g)†	(Teaspoons)†	Corresponding Clinical Effects
8,9,13,15	10	0.70	0.28	ammnesia, hypotonia
23	12.5	0.88	0.35	dizziness or dullness*; no effect on attention, vigilance, alertness, coordination
3	12.5	0.88	0.35	slight dizziness*
24	14	1.00	0.40	no effect on reactive and coordination skills, or attention
23	25	1.75	0.70	dizziness or dullness*; no effect on attention, vigilance, alertness, coordination
3	25	1.75	0.70	dizziness or drowsiness
32	25	1.75	0.70	drowsiness, dizziness, nausea*
26	25	1.75	0.70	slight transient drowsiness*
24	28	2.00	0.80	no effect on reactive and coordination skills, or attention
14	28	2.00	0.80	sleep
8,9,13,15	20–30	1.40–2.10	0.56–0.84	drowsiness, euphoria, vertigo, somnolence
25	30	2.10	0.84	sluggish, sedated, fatigued, drunk, dazed, spaced, carefree
4	40–50	2.80–3.50	1.14–1.40	somnolence leading to arousable sleep
26	50	3.50	1.40	slight transient drowsiness*
3	50	3.50	1.40	dizziness or drowsiness
8,9,13,15	50	3.50	1.40	loss of consciousness (arousable)
25	>50	>3.50	>1.40	transient unconsciousness
14	56	4.00	1.60	coma
8,9,13,15	>60	>4.20	>1.70	coma, unarousable unconsciousness
4	60–70	4.20–5.00	1.70–2.00	coma

* effects not observed in all subjects.

† equivalent dose of GHB for comparison, based on 1 teaspoon = 1 capful = 2.5 g or 35 mg/kg for a 70 kg person (1,29).

NOTE: recreational doses and purity of GHB vary widely, and often exceed 'recommended' doses.

HGN: horizontal gaze nystagmus; VGN: vertical gaze nystagmus.

of "ReActive" found in the possession of Case 8, the label stated ". . . a dose will induce stage 3 and 4 (deep) sleep in most people . . . within 30 minutes. Sleep normally lasts 3 to 6 hours . . . if ingested, do not operate machinery." Falling asleep at the wheel is recognized as a major cause of vehicle crashes (28,29), and has also been advanced as a causative mechanism in many crashes related to the withdrawal effects associated with stimulant abuse (30). The second series of effects impacting driving skills would be those affects on mental acuity and decision making, including inattention, distractibility, mental confusion, loss of critical thinking, and decreased ability to appropriately divide attention between the many components of the driving task (31). The third mechanism would be psychomotor impairment, deterioration in complex reaction time and tracking skills, muscular incoordination, loss of balance and orientation, and effects on vision. A fourth mechanism would be physical interruptions to driving such as caused by the uncontrolled vomiting observed in several of these subjects, and frequently associated with the recreational use of this drug.

Five of the cases we reviewed had additional drugs present. The patterns of effect documented are more attributable to GHB than to marijuana use, the only significant other drug present (Cases 6 and 9). The lack of evidence in our cases for polydrug use involving GHB is probably not significant, since the test for GHB was not uniformly applied in all our impaired driving cases, rather only when it was specifically indicated, or when there was obvious impairment which could not be accounted for by drugs revealed in routine tests for alcohol, weakly acidic, neutral, and basic drugs.

This popular recreational drug and bodybuilding aid is clearly capable of causing impairment in driving skills, and should be considered and tested for when drivers exhibit symptoms of CNS depression not accounted for by alcohol or other drugs.

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