CASE REPORT

Gamma-hydroxybutyrate and cocaine intoxication in a Danish child

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Key Clinical Message
GHB intoxication must be considered in children with coma and a suspicion of drug intoxication. Furthermore, mixed intoxication with several substances and the possibility of unpredictable symptom profiles should be anticipated to ensure optimal symptomatic treatment of patients.

Keywords
gamma-hydroxybutyrate, gamma-hydroxybutyric acid, GHB, cocaine, pediatric, child, intoxication.

Introduction
Gamma-Hydroxybutyrate (GHB) is an endogenic gamma-aminobutyric acid analog originally used in the 1960s as an anesthetic drug. It was revoked due to side effects but later reintroduced as a drug for treatment of narcolepsy. In the 1980s GHB was promoted as a bodybuilding and weight loss aid due to its purported growth hormone stimulatory effects [1, 2]. After it was banned in the US in 1990, its use in body building [3] and as a recreational drug [4] expanded. GHB reached the UK in the mid 1990s [5] and shortly thereafter Denmark as a substance of abuse [6]. The prevalence of GHB use in Scandinavia is considered to be low, but the proportion of intoxications with GHB relative to other drugs-of-abuse is high and numerous fatalities have been described [7].

Gamma-butyrolactone (GBL) and 1,4-butanediol (BD) are prodrugs of GHB. Both substances are accessible as pure industrial solvents (>98%) and purchasing opportunities as well as recipes for converting these prodrugs into GHB are easily available [8]. The legal status of GBL and BD vary and only a few countries have classified the compounds as controlled substances.

GHB, GBL, and BD intoxication in children has been described. Accidental ingestion of GBL solvents [9–11], ingestion of BD coated toy beads [12–15], and cases of children and adolescents unintentionally drinking GHB laced soft drinks have been reported [16, 17]. We report a case of a 3-year-old boy ingesting GHB from a fluid container found in a fitness center. To our knowledge, GHB intoxication in children as a result of the substance’s supposed growth hormone stimulatory effects and misuse among bodybuilders has not been reported before.

Case
A 3-year-old Danish boy was admitted to hospital with sudden onset lethargy, vomiting, and unconsciousness. The child was with his father in a fitness center, where he was left unsupervised in a children’s play area. Shortly after, the child came up to his father and said that he had drunk something from a fluid container left on a nearby
The urine GHB concentration found in this case report (186 µg/mL) was 18 times higher than the maximum endogenous level. In comparison, a study of 8 healthy adult volunteers who were administered a single 25 mg/kg dose of GHB showed peak urine concentrations of 230 ± 86.3 µg/mL 60 min after ingestion [19]. Another study of 12 adult volunteers ingesting the same dose of GHB reported peak concentrations in the range 32.6–161.3 µg/mL (average 67.6 µg/mL) [20]. In a study of 16 adult volunteers, doses of 50 mg/kg resulted in peak urine concentrations averaging 150–200 µg/mL in samples collected 0–3 h after drug administration [21]. Due to insufficient urine sample volume, it was not possible to determine the creatinine level of our patient’s urine sample. We are, therefore, unable to comment on the degree of urinal dilution. We can, however, conclude that the urine GHB concentration in this case report corresponds to levels found in adults who are administered GHB doses of 25–50 mg/kg.

Our case demonstrates previously described symptoms of GHB toxicity. These are vomiting, lethargy, somnolence, respiratory distress, bradycardia, and CNS depression. The patient showed sudden onset of symptoms and spontaneous remission – two very characteristic traits of GHB intoxication [22]. One symptom that did not fit the profile of GHB intoxication, however, was the dilation of the patient’s pupils.

The patient’s symptom pattern exhibited a biphasic profile. Sedative symptoms with affected GCS appeared twice, initially 40 min after ingestion and then again 1.5–2 h after ingestion. GHB is known to show a mixed stimulant-sedative pattern where psychostimulant effects appear first and sedative effects appear later [23]. A double-peaked sedative effect, however, has not been described previously. It is known that elimination of GHB from the body is biphasic. The first phase follows linear, zero-order kinetics where the rate of elimination is independent of the drug concentration. Remaining elimination follows a inversely proportional, concentration-dependent first-order kinetic rate of elimination [19, 24, 25]. A biphasic symptom profile should, therefore, not be possible.

The biphasic clinical presentation of symptoms raises the suspicion of the possible involvement of other toxic agents. The observed dilated pupils support this suspicion but at the same time could have been the result of parasympathetic effects caused by vomiting and a fall in blood pressure, pulse, and respiration frequency. Subsequent comprehensive urine drug screening was, therefore, carried out to determine the possible presence of other drugs not detected in the immunoassay panel test. A low concentration of benzoylecgonine – a metabolite of cocaine – estimated to 20 ng/mL was found by LC-MS/MS. The combination of GHB and cocaine is well-known in the world of fitness and bodybuilding, where the stimulatory effects of cocaine are used to counteract the
sedative effects of GHB. The presence of cocaine in conjunction with GHB in our patient was, therefore, not surprising.

Initial urine analysis by immunoassay was false negative for cocaine. Screening tests for benzoylecgonine have cutoff concentrations between 150 and 300 ng/mL and concentrations less than this remain undetectable. Since the amount of cocaine in the urine sample was below the limit of quantification and because the patient received active charcoal within the appropriate time interval, we believe that this treatment may have terminated further absorption of cocaine.

Another factor that needs to be considered is the effect of food on the symptom profile of GHB and cocaine. The patient had eaten a meal shortly after ingesting the unknown fluid. Food could have played a role in the absorption rate of both GHB and cocaine and may have contributed to the biphasic symptom profile seen.

Another plausible cause of the biphasic profile seen in our patient may be ingestion of a mixture of GHB, GBL and/or BD. It is known that both prodrugs of GHB have the same toxic effects as GHB but GBL has more rapid absorption, greater lipid solubility, higher serum concentration, and more prolonged hypnotic effects than GHB [26–28]. The concentration of GBL and GHB in urine is, however, inconclusive with regard to GBL ingestion due to the dynamic equilibrium that exists between GHB and GBL in vitro [29].

Hence, it remains speculative whether a mixture of GBH, GBL and/or BD could produce the symptom profile observed in our patient or if it may have been caused by food ingestion or by the presence of other drugs that were not detected. On the basis of our patient’s clinical presentation and resolution of symptoms and a confirmatory high urine level of GHB, we conclude that GHB was the most likely cause of our patient’s symptoms.

**Conclusion**

GHB intoxication must be considered in children with coma and a suspicion of drug intoxication. Furthermore, mixed intoxication with several substances and the possibility of unpredictable symptom profiles should be anticipated to ensure optimal symptomatic treatment of patients. The use of GHB and cocaine in the world of bodybuilding and our account of a new child victim demonstrates a new area of concern.

**Consent**

Written informed consent was obtained from the parents of the patient for publication of this case report. A copy of the written consent is available for review by the Editor of this journal.

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**Conflict of Interests**

The authors declare that they have no competing interests. There are no relevant financial relationships that should be disclosed. There are no conflicts of interest.

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