Sudden leg paralysis in a 26-year-old nurse

Silvia Ulrich[a], *Veronique Müller*[a], *Marius Keel*[b], *Jörg D. Seebach*[a]

[a] Department of Internal Medicine, University Hospital of Zurich, Switzerland
[b] Division of Traumatology, University Hospital of Zurich, Switzerland

An analysis of overdose cases with γ-hydroxybutyrate (GHB) and its precursor γ-butyrolactone (GBL) reported to the Swiss Toxicological Information Centre was recently published by Liechti and Kupferschmid in this journal [1]. We want to add to the evolving clinical picture of GHB and GBL intoxications by reporting a recent case from our institution presenting with a hitherto unknown severe sequelae of GBL intake.

Case report: A 26-year-old nurse woke up in the morning before Christmas and realized that she was unable to move and feel here legs. She crawled to the phone, called for help and was admitted to the emergency room. Upon arrival she was afebrile, fully orientated and conscious. Her past medical history was unremarkable and she repeatedly denied any substance abuse besides moderate cigarette smoking. Physical examination showed sensomotoric, painful paraparesis of both legs at the level L2–3 without clinical signs of meningitis. Both feet were cold with week arterial pulses. Toxic neuropathy, traumatic and neoplastic nerve compression, and Guillain-Barré syndrome were considered. However, computed tomography of the lumbar spine and liquor samples were normal whereas laboratory tests revealed elevated muscle enzymes (creatine kinase 135'905 U/l, myoglobulin >30'000 U/l, lactate dehydrogenase 4'114 U/l, aspartate aminotransferase 1'877 U/l), creatinine (166 µmol/l), blood urea nitrogen (10.2 mmol/l), phosphate (2.2 mmol/l) and potassium (5 mmol/l), moderate anaemia (Hb10 g/dl) and neutrophilia (9.14×10^3/µl). Drug screening in the urine revealed the presence of cocain, benzodiazepine and cannabis, but no amphetamines or opiates. The medical history was reiterated and the patient disclosed having sniffed cocaine at a party four days earlier for the first time in her life. Despite vigorous volume replacement acute renal failure developed necessitating continuous hemodiafiltration and both legs exhibited progressive bluish discoloration. A clinical diagnosis of acute compartment syndrome was made. Elevated intracompartmental pressures (25–47 mm Hg, normal <10 mm Hg) were measured in both lower legs by the method of Stryker [2] and immediate surgical fasciotomia and decompression was performed. Thereafter, the patient's condition improved within a week, the muscle compartments were closed and hemodiafiltration was stopped. Upon repeated compassionate history taking the patient reported occasional intake of GHB and a massive intake of GBL with a suicidal intention on the evening before admission.

Mimicking sensomotoric palsy, this patient suffered from severe rhabdomyolysis leading to acute renal failure and compartment syndrome after GBL use. Since GBL induces rapid coma that only lasts a few hours [3] it is likely that the combination of sedative substances was responsible for a prolonged unconsciousness and immobility leading to muscle compression and damage. Alternatively, GBL might have direct myotoxic effects possibly in combination with cocaine. In this regard it is noteworthy that GHB is used as muscle building agent and that Liechti and Kupferschmid described elevated creatine kinase levels [1]. The short half-life restricts detection of GHB/GBL by gas or liquid chromatography-mass spectrometry in serum or urine samples to 6–12 hours after intake [4, 5], which was not feasible in the present case. In summary, rhabdomyolysis is a rare but well recognized complication of methylenedioxymethamphetamine (MDMA; "Ecstasy") and cocaine abuse [6, 7] but it has not yet been recognised as a potential lethal sequelae of GHB/GBL intoxication.

References

1 Liechti M, Kupferschmidt H. γ-hydroxybutyrate (GHB) and γ-butyrolactone (GBL): analysis of overdose cases reported to the Swiss Toxicological Information Centre. Swiss Med Wkly 2004;134: 534–37.
2 Uliasz A, Ishida JT, Fleming JK, Yamamoto LG. Comparing the methods of measuring compartment pressures in acute compartment syndrome. Am J Emerg Med 2003;21:143–45.
3 Sporer KA, Chin RL, Dyer JE, Lamb R. Gamma-hydroxybutyrate serum levels and clinical syndrome after severe overdose. Ann Emerg Med 2003;42:3–8.
4 Ferrara SD, Tedeschi L, Frison G, Castagna F, Gallimberti L, Giorgetti R, Gessa GL, Palatini P. Therapeutic gamma-hydroxybutyric acid monitoring in plasma and urine by gas chromatography-mass spectrometry. J Pharm Biomed Anal 1993; 11:483–87
5 Wood M, Laloup M, Samyn N, Morris MR, de Bruijn EA, Maes RA, Young MS, Maes V, De Boeck G. Simultaneous analysis of gamma-hydroxybutyric acid and its precursors in urine using liquid chromatography-tandem mass spectrometry. J Chromatogr A 2004;1056:83–90.
6 Horowitz BZ, Panacek EA, Jouriles NJ. Severe rhabdomyolysis with renal failure after intranasal cocaine use. J Emerg Med 1997;15:833–37.
7 Teter CJ, Guthrie SK. A comprehensive review of MDMA and GHB: two common club drugs. Pharmacotherapy 2001;21:1486–513.

Correspondence:
PD Dr. med. Jörg D. Seebach
Department of Internal Medicine
University Hospital
Rämistrasse 100, C HOER 31
CH-8091 Zürich
E-mail: Joerg.Seebach@usz.ch

Reply: Rhabdomyolysis and drugs of abuse

Matthias E. Liechti[a], *Hugo Kupferschmidt*[b]

[a] Department of Internal Medicine, University Hospital of Zurich, Switzerland
[b] Swiss Toxicological Information Centre, Zurich, Switzerland

The most common causes of rhabdomyolysis (creatine kinase (CK) level >1000 U/l) in emergency department (ED) patients are drugs of abuse, exercise, and immobilization [1]. Drugs of abuse associated with rhabdomyolysis include cocaine, heroin, ethanol, amphetamines, barbiturates, phencyclidine, and others [2]. The most frequent single cause of rhabdomyolysis in a series of ED patients was cocaine use [1]. Additional risk factors or causes for rhabdomyolysis and associated renal failure are agitation, hyperthermia, cardiac arrest, seizures, and trauma [3]. Pressure myonecrosis or compartment syndromes may occur as a rare complication primarily in patients with prolonged unconsciousness and immobility as a result of drug abuse [2, 4].

The patient described by Ulrich and colleagues took cocaine, benzodiazepines, and GBL (or GHB) and presented with rhabdomyolysis, acute compartment syndrome, and renal failure requiring surgical and intensive medical care. Cocaine use was confirmed by an urine drug screen. GBL use was not confirmed at admission to the hospital. Later, the patient admitted having used GBL, but it was then too late for a confirming analysis. Which of two drugs was responsible for the clinical picture? Cocaine has been widely reported to produce severe rhabdomyolysis [2, 3] while GBL has never been mentioned to be associated with this adverse effect. In contrast, GBL has been shown to have interesting tissue-protective effects in a wide range of organ systems on a variety of animal and human models [5]. GBL is therefore not expected to directly affect muscle tissue and to induce ischemic damage. As noted by Ulrich et al. we reported slightly increased levels of CK in patients with GBL intoxication (mean 626 U/l, range 176–1196) [6]. This slight increase in CK possibly indicates that GBL drug users suffer from minor muscle cell damages due to immobilization while being comatose. We assume that the patient in the present case vignette suffered from severe immobilization trauma secondary to GBL induced coma. Thus, GBL use indirectly led to the observed muscle damage, possibly in addition to a first ischemic damage induced by cocaine use two days before.

What do we know about the combined use of GBL and cocaine? According to recent data from our hospital, cocaine was used in combination with GBL in 10 of 48 patients (21%) presenting with acute GBL poisoning

to our ED between 2001 and 2003. CK levels were (mean ± SD) 435 ± 701 U/l in 9 GBL mono-intoxicated patients and 420 ± 307 U/l in 8 patients with combined GBL and cocaine use. Thus, none suffered from a meaningful degree of rhabdomyolysis and the CK levels were not affected by cocaine use in this sample. However, we found that CK levels were positively correlated with the duration of coma in all patients (N = 30; Spearman R = 0,40; p <0.03) supporting the view that immobilization leads to increased levels of CK in these patients. Finally, we observed that the co-abuse of stimulant drugs such as cocaine or Ecstasy with GBL resulted in significantly deeper and more prolonged coma compared with patients who used GHB or GBL alone. In summary, the combined use of GBL with stimulant drugs may increase the risk for rhabdomyolysis due to prolonged coma and immobilization in addition to the known risk of the stimulant drugs.

The case of Ulrich and colleagues illustrates the risk of an increasing trend of combined party drug use in our country. In addition, it underscores the need to take sufficient blood and urine samples at first presentation to be at hand for additional analytical workups.

References

1 Fernandez WG, Hung O, Bruno GR, Galea S, Chiang WK. Factors predictive of acute renal failure and need for hemodialysis among ED patients with rhabdomyolysis. Am J Emerg Med 2005;23: 1–7.
2 Richards J. Rhabdomyolysis and Drugs of Abuse. J Emerg Med 2000;19:51–6.
3 Horowitz BZ, Panacek EA and Jouriles NJ. Severe rhabdomyolysis with renal failure after intranasal cocaine use. J Emerg Med 1997;15:833–7.
4 Kumar R, West DM, Jingree M and Laurence AS. Unusual consequences of heroin overdose: rhabdomyolysis, acute renal failure, paraplegia and hypercalcaemia. Br J Anaesth 1999;83:496–8.
5 Li J, Stokes SA and Woeckener A. A tale of novel intoxication: a review of the effects of gamma-hydroxybutyric acid with recommendations for management. Ann Emerg Med 1998;31:729–36.
6 Liechti ME, Kupferschmidt H. Gamma-hydroxybutyrate (GHB) and gamma-butyrolactone (GBL): analysis of overdose cases reported to the Swiss Toxicological Information Centre. Swiss Med Wkly 2004;134:534–7.

Correspondence:
Matthias E. Liechti
Department of Internal Medicine
University Hospital of Zurich
Rämistrasse 100
CH-8091 Zurich
Switzerland
E-Mail: meliechti@dplanet.ch

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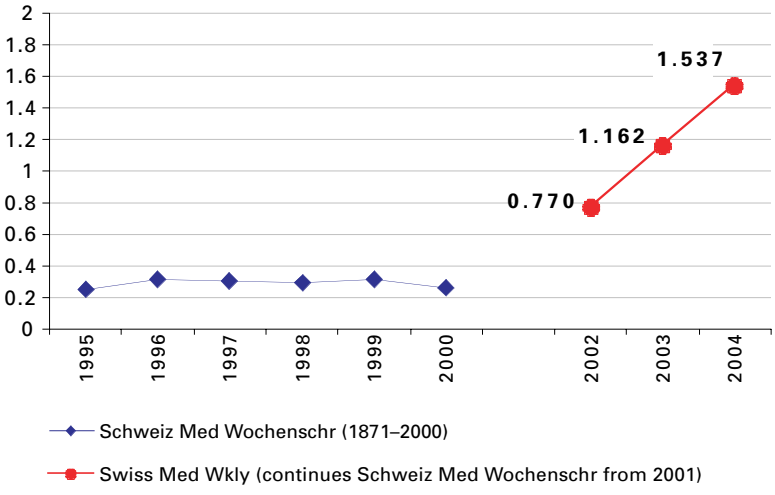

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