

CASE HISTORY

In July 2008 a 25 year old male was found unconscious in bed by his partner. A small amount of blood and vomit was present on his pillow. The previous evening the victim had ingested "GBL" but it was feared that too much had been taken as no measuring pipette had been used and he was "acting strangely". His heavy snoring that night had lead his partner to retreat to the lounge until the following morning when he discovered the victim.

Clinical Presentation: On arrival in the Emergency Department (ED), 40 minutes after being found collapsed, he was in asystole. Basic cardiopulmonary resuscitation (CPR) had been commenced by his partner and ambulance personnel. He was intubated (vomit noted in airways) and advanced life support used. Arterial blood gas showed PO₂ 0.9kPa, pCO₂ 10.9 kPa, pH <6.80, lactate >15.0. Resuscitation was discontinued in view of the prolonged out of hospital arrest.

Autopsy Report: The deceased was of average build. There was no evidence of external injury. The cardiovascular system was normal. The oral cavity, trachea and bronchi contained frothy bloody secretions although there was no evidence of aspirated gastric contents. Both lungs were heavy and the cut surface exuded oedematous fluid. The stomach contained bloody fluid. The liver showed mild congestion. There was blood within the distal tubules of the kidneys. All other internal examinations were unremarkable. Biological samples and the container of liquid consumed (Figure 4), were submitted for analysis.

EXPERIMENTAL

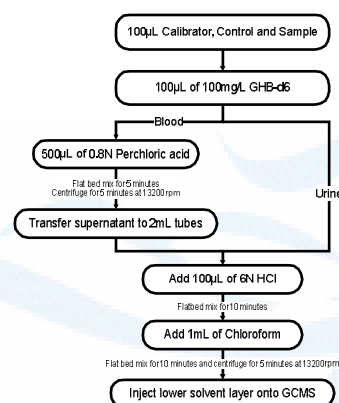


Figure 1. Sample Preparation.

Analysis of the biological samples for 'total' GBL was performed after conversion of any GHB present to GBL. A Shimadzu GC-MS-QP2010 with a AOC-20i autosampler and HP-5MS (30m x 0.25mm, 0.5µm) column was used. Helium was used as the carrier gas at a flow rate of 1mL/min. The injection volume was 1.0µL in splitless mode. The initial column temperature was set at 80°C and held for 4 mins. It was then ramped by 25°C/min up to 125°C. The total run time was 6 mins. Positive Electron Impact Ionisation (EI) mode was used and data were collected using single ion

monitoring (SIM). GBL and GBL-d6 were quantified monitoring *m/z*: 86 and 92 and their retention times were 4.64 and 4.68 minutes, respectively.

GHB and GBL can be easily differentiated by diamond ATR infra-red spectroscopy (IR). GHB has a strong band at ~3500cm⁻¹ which is not present in GBL. There are also marked differences in the fingerprint region allowing differentiation (Figure 2).

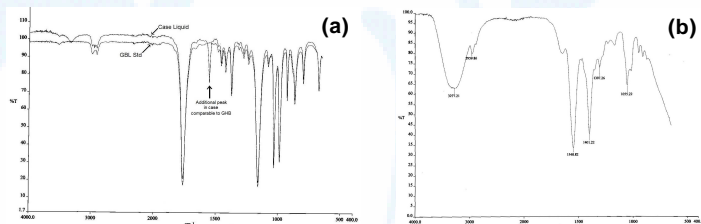


Figure 2. The IR of the case liquid overlaid with GBL (a) and GHB (b).

RESULTS

Total GBL was detected in the preserved femoral blood at a concentration of 282mg/L. Fatality has been associated with concentrations exceeding 280mg/L (1). Ephedrine was present at <0.05mg/L. No alcohol or other common drugs were detected.

The IR liquid screen was consistent with GBL (Figure 2). The pathologist attributed the cause of death to; 1a. Respiratory failure, 1b. GBL toxicity. The Coroner recorded a verdict of 'accident'.

DISCUSSION

Gamma-hydroxybutyrate (GHB) is produced endogenously as a by-product of gamma-aminobutyric acid (GABA) metabolism (2). It has become a popular recreational drug, which is associated with significant morbidity and mortality (3). It is therefore a class C drug under the Misuse of Drugs Act (1971). However, its prodrugs gamma-butyrolactone (GBL) and 1,4-butanediol (1,4-BD), which are widely used in the chemical industry, remain legally available despite having similar clinical effects. There have been suggestions in the medical and general press that there has been a shift amongst GHB users to GBL and other precursors such as 1,4-BD, due to the disparity in the current legislation (4-7). Whilst self reported use of GHB was more common in clubbers presenting to a ED in South London, significantly more GBL than GHB was seized from clubs within a London catchment area (8). There was no self-reported use of 1,4-BD, and none was found in samples collected from clubs (Figure 3).



GHB (17)



GBL (20)



Figure 4. GBL container associated with this case.

Figure 3. 41 liquids collected from club drug amnesty bins, of which 17 contained GHB and 20 GBL.

Despite the evolving trend towards GBL use, to date there are no publications attributing fatalities directly to GBL. However, due to the rapid *in-vivo* conversion of GBL and 1,4-BD to GHB in equimolar ratios, there are challenges associated with distinguishing between the use of these compounds through analysis of biological specimens alone. Methodologies involving conversion of GHB to GBL and measurement of 'total' GBL are common. Analysis of the liquid consumed, where available, offers conclusive identification. The pending change in legal status of GBL and 1,4-BD to Class C controlled drugs may result in a further change in the pattern of use or the use of new compounds.

CONCLUSION

GBL use may be more common than previously thought. There is a need for further work to determine whether GBL is associated with morbidity and mortality similar to GHB. Continued monitoring of the use of GBL, 1,4-BD and other GHB prodrugs and precursors will be invaluable to determine how the market adapts following the changes in legislation. New compounds with similar pharmacology may emerge.

Acknowledgements:

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References:

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