Liquid ecstasy: a new kid on the dance floor

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The use of recreational drugs in the UK is on the increase, as is the range of available substances. One relative newcomer to the drugs of misuse that is achieving popularity in the UK among ‘ravers’ and bodybuilders is gamma-hydroxybutyrate (GHB), also known as ‘liquid ecstasy’.

WHAT IS GHB?

Gamma-hydroxybutyrate is an endogenous fatty acid found in every cell in the human body. In the brain it is widely distributed, reaching highest concentrations in the hypothalamus and basal ganglia (Gallimberti et al., 1989). It is available as a liquid or in powdered form and when taken by mouth it readily enters the brain and produces behavioural consequences that include anxiolytic, sedative and euphoric effects. It appears to have complex effects on both GABA$\alpha_1$ and GABA$\alpha_4$ receptors and has some actions similar to benzodiazepines, baclofen and alcohol (Barbaccia et al., 2002). The effects may result from potentiation of cerebral dopaminergic systems and there is evidence that the serotonin system also may be involved via stimulation of tissue serotonin turnover due to an increase in tryptophan transport (Gobaille et al., 2002). Gamma-hydroxybutyrate has been utilised in medical settings for a number of years to induce anaesthesia (Laborit, 1964), to aid with alcohol dependence and opioid withdrawal (Kam & Yoong, 1998; Tarricone, 2000; Nicholson & Balster, 2001) and as a treatment for sleep disorders (Mamelak, 1989; Chin et al., 1992).

LEGAL STATUS

During the 1980s GHB was popular in the USA as an over-the-counter food supplement. It enjoyed popularity among bodybuilders because it was believed to aid in fat reduction and muscle building (Miotto et al., 2001). Gamma-hydroxybutyrate stimulates growth hormone release and activates the ‘pentose pathway’, which plays an important role in the synthesis of protein within the body. It also results in a protein-sparing effect, which reduces the rate at which the body breaks down its own proteins and it is these properties that are believed to underlie its ability to aid in bodybuilding and fat loss (Miotto et al., 2001). In 1990 the Food and Drug Administration banned over-the-counter sales because of the growing body of evidence of the potential for misuse. This was followed in March 2000 by the placing of the substance in Schedule 1, making it illegal to possess or sell GHB without a licence in the USA. At the moment in the UK possession of GHB is not illegal, but manufacture and supply is illegal because the drug is a controlled substance under the Medicines Act 1968. Gamma-hydroxybutyrate became scheduled under the Misuse of Drugs Act in June 2003.

ON THE DANCE FLOOR

Reports from the USA, Australia and Europe indicate that GHB now is being consumed increasingly as a recreational drug (Colfax et al., 2001; Karch et al., 2001; Mattison et al., 2001; Miotto et al., 2001; Nicholson & Balster, 2001; Whitten, 2001; Deveaux et al., 2002; Iten & Oestreicher, 2002; Miro et al., 2002). Adverse acute effects are wide ranging and include dizziness, blurred vision, hot/cold flushes, excess sweating, confusion, vomiting, loss of consciousness, tremors, blackouts and memory lapses, agitation and death (Galloway et al., 1997; Nicholson & Balster, 2001; Degenhardt et al., 2002). In addition, evidence from both clinical and recreational settings indicates that GHB may induce seizures/ﬁts (Dyer, 1991; Degenhardt et al., 2002) and coma (Espinoza et al., 2001). Adverse reactions have been reported at a wide variety of doses (between 2 and 30g; Chin et al., 1992), indicating variable individual responses to the drug. In addition the

ACUTE SIDE-EFFECTS

The increasing popularity of GHB is indicated by a sharp rise in the number of accident and emergency cases associated with it across Europe and in the USA (Espinoza et al., 2001; Marinetti et al., 2001; Whitten, 2001; Deveaux et al., 2002; Iten & Oestreicher, 2002; Miro et al., 2002). Adverse acute effects are wide ranging and include dizziness, blurred vision, hot/cold flushes, excess sweating, confusion, vomiting, loss of consciousness, tremors, blackouts and memory lapses, agitation and death (Galloway et al., 1997; Nicholson & Balster, 2001; Degenhardt et al., 2002). In addition, evidence from both clinical and recreational settings indicates that GHB may induce seizures/ﬁts (Dyer, 1991; Degenhardt et al., 2002) and coma (Espinoza et al., 2001). Adverse reactions have been reported at a wide variety of doses (between 2 and 30g; Chin et al., 1992), indicating variable individual responses to the drug. In addition the
black-market manufacture of GHB inevitably leads to variations in potency; this, coupled with rapid onset and a steep dose-response curve, places recreational users at particular and unpredictable risk of experiencing adverse effects and/or overdose. Gamma-hydroxybutyrate is rapidly metabolised into carbon dioxide and water with no residue of toxic metabolites detectable in urine 4–5 h after ingestion (Laborit, 1964). Consequently this makes it difficult to detect use of the substance during routine drug screens or following emergency admission.

**TOLERANCE AND WITHDRAWAL**

There is evidence that users develop tolerance to and physical dependence on GHB. Animal studies provide evidence for the development of tolerance and the presence of reinforcing/rewarding properties (Itzhak & Ali, 2002). In humans a GHB withdrawal syndrome is reported to include insomnia, anxiety, tremor, confusion, delirium, hallucinations, tachycardia, hypertension, nausea, vomiting and diaphoresis (Galloway et al, 1997; Mahre et al, 2001; Miotto & Roth, 2001; Miotto et al, 2001). Rosenberg et al (2003) report two cases of severe withdrawal delirium on a psychiatric unit in the USA. It is likely that, as the use of the drug increases, the psychiatric profession will increasingly be faced with hallucinations, tachycardia, tremor, nystagmus and diaphoresis. In a similar report Sivillotti et al (2001) give data from five patients who presented with severe GBL withdrawal syndrome that included paranoid delusions, hallucinations, psychosis and autonomic instability. Initial treatment with lorazepam proved to be ineffective, but subsequent treatment with pentobarbital resulted in good recovery within 5 days. In the UK reports of misuse and withdrawal from these precursors should be expected.

**MODE OF ACTION**

The physiological mechanisms for withdrawal from GHB are not clearly understood. Research indicates that chronic use of GHB results in a down-regulation of inhibitory GABA<sub>B</sub> and GABA<sub>A</sub> receptors, resulting in the development of tolerance (Snead & Nichols, 1987; Hechler et al, 1997). Cessation or a decrease in GHB use then results in a disinhibition of excitatory neurotransmitters (glutamate, norepinephrine and dopamine) and leads to withdrawal symptomatology. Similarities in terms of the psychoactive properties of use and of the pathophysiological effects of withdrawal have been reported between GHB and benzodiazepines (Miotto & Roth, 2001). This suggests a common mechanism of action and Miotto & Roth (2001) suggest that withdrawal from GHB involves loss of GABA<sub>B</sub> and GABA<sub>A</sub>-mediated inhibition. Further support for the role of GABA is presented by Carai et al (2001). Their results indicate that the sedative/hypnotic effects of GHB result from activation of GABA<sub>B</sub> receptors and that the behavioural depression of GHB was similar to that produced by baclofen, a GABA<sub>B</sub> agonist. In addition, the effect of both drugs was completely prevented by the administration of specific GABA<sub>B</sub> antagonists SCH 50911 and CGP 46381.

**SUMMARY**

Gamma-hydroxybutyrate misuse is a relatively recent phenomenon and one that is far from clearly understood in terms of the likely cost to the user and to the wider community. There have been no systematic studies of the prevalence of dependency on GHB in the UK, nor do we have sufficient information relating to the demographic characteristics or the patterns of drug use among GHB users in this country. In addition, the mechanisms underlying the development of tolerance to and the rewarding effects of GHB, as well as any possible interaction effects with other drugs, are poorly understood. Similarly, although research has clearly demonstrated the acute risks of use, we know very little about long-term emotional, neuropsychological and behavioural costs. It is likely, however, that as use of the drug and its precursors increases in the UK the psychiatric profession increasingly will be faced with individuals experiencing the adverse effects of use and withdrawal. What is clear from the research so far is that misuse of GHB places the individual and the wider community at significant risk. Further studies of the use and misuse of this potentially harmful substance are clearly needed.

**DECLARATION OF INTEREST**

None.

**REFERENCES**


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