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Review Article

Gamma Hydroxy Butyrate: A New Fangled Date Rape Drug

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Abstract

Most of the drugs that have the properties of altering the state and perception of mind have always been abused more than being used for the purpose for which they were intended. Gamma Hydroxy Butyrate is one such drug which has the potential of wide range of therapeutic and criminal applications. GHB is often included in the group of 'club drugs' and has been implicated in cases of 'date rape', usually in combination with alcohol. GHB is a Central Nervous System depressant and is related to neuro-modulator gamma-aminobutyric acid.

Keywords: Gamma Hydroxy Butyrate; Dopamine; Gamma-aminobutyric acid; Date rape drug; Narcotics Drugs and Psychotropic Substances Act, 1985.

Introduction

Every development in science has its own advantages and disadvantages, strengths and short comings. Most of the drugs that have been designed or have the properties of altering the state and perception of mind have always been misused more than being used for the purpose for which they were intended. Misuses extending from their use in recreation to commission of crimes like drug facilitated sexual assault and robbery or even to steady one's nerves before commission of any crime. Gamma Hydroxy Butyrate (GHB), also known as 4-hydroxybutanoic acid and sodium oxybate[1] is one such drug which has the potential of wide range of therapeutic and criminal applications. It has many street names like *Georgie Home Boy, Liquid Ecstasy, Liquid X, Liquid G and Fantasy* etc.[1] Literature on initialism and prevalence of GHB abuse is incomplete; however, various qualitative measures indicate that a mini-epidemic of abuse began in the late 1980s.[2] GHB is often included in the group of 'club drugs' and has been implicated in cases of 'date rape', usually in combination with alcohol.[2]

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Synthesis[1]

GHB is a substance naturally present in the central nervous system of human, wine, small citrus fruits and almost all animals in small amounts. GHB is also produced as a result of fermentation and is found in small quantities in some beers and wines; but, the amount found is insignificant and not sufficient to produce any effects. Synthesis of GHB was first reported in 1874 by Alexander Zaytsey. In the typical scenario, GHB has been synthesised from gamma-buyrolactone (GBL) by adding sodium hydroxide in ethanol or water.

Pro-drugs and Analogues of GHB

Important pro-drugs of GHB are 1,4-Butanediol and Gamma Butyrolactone (GBL).[3] GBL tends to be more potent and faster acting than GHB but has a shorter

duration; whereas, the related compound 1,4-Butanediol tends to be slightly less potent, slower to take effect but longer acting than GHB. GBL and 1,4-Butanediol are used to bypass GHB restriction laws. In the human body the analogue is rapidly converted into GHB.[4] Analogues of GHB such as 4-hydroxy-4-methylpentanoic acid, 3-methyl-GHB, 4-methyl-GHB and 4-phenyl-GHB have been shown to produce similar effects to GHB in animal studies, but these compounds are even less well researched than GHB itself. Of these analogues, only 4-methyl-GHB and its prodrug form gamma valerolactone have been reported as drugs of abuse in humans and on the available evidence seem to be potent but more toxic than GHB.[1]

Pharmacological actions[1]

GHB is a Central Nervous System (CNS) depressant and is related to neuro-modulator GABA. GHB has at least two distinct binding sites in the CNS. It is an agonist at the GHB receptor, which is excitatory and it is a weak agonist at the GABA-b receptor, which is inhibitory. GHB is a naturally occurring substance that acts in a similar fashion to some neurotransmitters in the mammalian brain. GHB is probably synthesized from GABA in GABAergic neurons and released when the neurons fire. At pharmacological doses, GHB reaches much higher concentration in the brain and activates GABA-b receptors, which are primarily responsible for its sedative effects. GHB's sedative effects are blocked by GABA-b antagonists.

GHB induces the accumulation of tryptophan in the extracellular space. The blood content of tryptophan is increased by peripheral GHB administration. GHB induced stimulation of tissue serotonin turnover may be due to an increase in tryptophan transport to the brain and in its uptake by serotonergic cells. As the serotonergic system may be involved in the regulation of sleep, mood and anxiety, the stimulation of this system by high doses of GHB may be involved in certain neuropharmacological events induced by GHB administration.

GHB's effect on dopamine release is biphasic. Lower concentrations stimulate dopamine release via the GHB receptor; whereas, higher concentrations inhibit dopamine release via GABA-b receptors. After the initial phase of inhibition, dopamine release is increased via the GHB receptor. This explains the paradoxical mix of sedative and stimulatory properties of GHB as well as the so-called "rebound" effect, experienced by individuals using GHB as a sleeping agent, wherein they awake suddenly after several hours of GHB induced deep sleep. This is because, over time, the concentration of GHB in the system decreases below the threshold for significant GABA-b receptor activation and activates predominantly the GHB receptor. The growth hormone elevating effects of GHB are mediated through muscarinic acetylcholine receptor blocking agent.

Therapeutic uses

GHB had been used as a general anaesthetic[1] (but it did not become an established agent due to adverse effects including nausea, vomiting and seizure-like activity [5]), for the treatment of insomnia, clinical depression, narcolepsy, cataplexy alcoholism and to improve athletic performance.[1,6] It is an approved therapeutic agent for cataplexy with narcolepsy.[1,6] It was used in France, Italy and other European countries for several decades as a sleeping agent and as anaesthetic in child birth, but problems with its abuse potential and development of newer drugs have led to decrease in legitimate medical use of GHB in recent times.[1] In Netherlands, GHB could be bought as aphrodisiac and euphoriant in a smart shop for several years, until several incidents caused it to become regulated which no longer made it possible to buy it at smart shops. The only common medical applications for GHB today are in the treatment of narcolepsy and more rarely alcoholism.[1]

Addictive potential[1]

GHB and its analogues cause physical

dependency. The dependency syndrome can be characterized as "round the clock" use, where users may have to dose from as frequently as every forty minutes to an hour. There appears to be a temporal pattern of withdrawal symptoms which include extreme anxiety, sleeplessness, feeling shaky, confusion, nausea, vomiting. In addition, further withdrawal symptoms can be mistaken for psychosis. Activation of both the GHB and GABA-b receptor is responsible for the addictive profile of GHB.

Abusive potential

When used as a recreational drug, GHB is available as sodium or potassium salt (white crystalline powder) or GHB salt dissolved in water to form a clear solution. The sodium salt of GHB has a salty taste. Other salt forms such as calcium GHB and magnesium GHB have also been reported but sodium salt is by far the most common. Common recreational doses of GHB are in the range of 1.8 to 2.7 gms, a large amount compared with most other sedative drugs, which can be active in amounts measured in milligrams. Doses required to induce complete sedation are even higher in most individuals. GHB at low doses has a euphoric effect (sometimes referred as 'liquid ecstasy'), whereas at higher doses it acts like sedative. GHB users feel that it enhances the experience of being in a club or party (club drug). It has quickly found a wide range of users due to its minimal side effects and short duration of action.[1]

GHB has been described as "very easy to add to drinks" as it is colourless and odourless. GHB has been used in cases of drug-related sexual assault, but, it is difficult to establish how often GHB is used to facilitate rape as it is difficult to detect in the urine sample after a day and many victims may not recall the rape.[1] It has also been reported that there is high use of GHB, amongst homosexual men. Several large gay clubs offer prolonged clubbing promotions have been documented in United Kingdom.[5] Recently, GHB has also gained popularity among body builders, athletes due to reported beneficial effects on growth hormone concentrations.[7]

Features of acute intoxication[1]

Overdose of GHB and its precursors results in dose-dependent CNS effects. GHB tends to cause rapid unconsciousness at doses above 3500 mg with single doses over 7000 mg often causing life threatening respiratory depression and still higher doses inducing bradycardia and cardiac arrest. The greatest life threat due to GHB overdose is respiratory arrest. Other relatively common causes of death due to ingestion of GHB are aspiration of vomitus, positional asphyxia and trauma sustained while intoxicated.

Detection

Toxicological investigations on serum,[8] urine[8] or hair[9] allow to detect the substance used. GHB has a very short plasma half-life, the window of detection is small and in the majority of these specimens, levels of GHB are low.[8,10] Because, GHB is naturally occurring in humans, discrimination between endogenous and exogenous GHB is difficult particularly in those samples with low concentrations.[8] Gas chromatography-mass spectrometry is at present the most appropriate analytical method to detect these drugs in a biological specimen.[10,11]

Legal status

In India, GHB is included in the Narcotics Drugs and Psychotropic Substances Act, 1985. GHB can be imported under the Special Provisions for medical and scientific purposes as per Chapter VII-A of the NDPS Rules, 1985 after obtaining an import certificate from the Narcotics Commissioner under the proviso to Rule 53 of the NDPS Rules.[12] GHB and its analogues are labelled as regulated substances by the Laws of many countries.

Conclusion

Gama Hydroxy Butyrate is a potentially

lethal naive drug with a wide range of abusive and addictive potentials. In today's world, it has been the drug of choice for episodes of drug facilitated sexual crimes especially in the west. The magnitude of havoc such a drug can cause in the developing world is illusive. What makes the situation worse is, it has become one of the most preferred commodities for the drug mafia owing to its easy techniques of manufacture, widespread abuse and potential availability of its designer drugs by means of which law evasion has become easy. Strict regulation of the law, wide research towards treatment aspects of its acute intoxication / poisoning and rehabilitation of the addicts, along with strategies to increase the awareness level among the youth regarding health hazards of its abuse is the need of hour.

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