



## GHB Dependence: Lessons from a Small Case Series

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### Abstract

This case series identifies all patients presenting for GHB related problems to Western Hospital's Drug Health Service (between 2009-2012) and specifically focuses upon the small subgroup which have GHB Dependence and required hospitalisation. Of eight such cases, only one had a complicated inpatient course, reported the highest GHB daily dose consumption (~30 gm/day) and was concurrently Alcohol Dependent. All the other patients responded to supportive nursing care and simple pharmacotherapy with diazepam. The majority of patients with GHB Dependence in this review also took other drugs and also had an uncomplicated GHB withdrawal process. Hence, the outcome of this review questions the need for hospital admission in most cases of GHB Dependence except for cases involving high dose Dependence (e.g. >30 gm/day); this finding is consistent with recent literature reports.

**Keywords:** GHB dependence; Krebs cycle; Endogenous substance

### Introduction

During the past decade, increasing numbers of patients with GHB dependence have presented to our hospital for treatment. Some of the past literature relating to GHB dependence has suggested that the withdrawal syndrome and related complications may be severe [1-7] however more recent reports including one case series [7-10] suggests otherwise. GHB and more recently, the precursors gamma-butyrolactone (GBL) and 1,4-butanediol (1,4-BD), in contrast to many other illicit drugs of abuse, were comparatively cheap, easy to obtain and considered as "legal highs" i.e. psychoactive substances of abuse that were not classified as illegal. In 2001, GHB was placed under Schedule 1V of substances under control by member countries; later, several countries enacted legislation to control the use of GHB and a number of precursor substances, including GBL [1]. Certain social groups have been reported as having higher prevalent use of GHB and these include night-clubbers, bodybuilders (unsubstantiated claims of GHB inducing growth hormone release related muscle development) and polydrug users [6]. In some countries, GHB is used medically for the treatment of certain sleep disorders such as cataplexy and narcolepsy (some evidence that GHB improves aspects of REM-sleep efficiency) and used in the treatment of alcohol dependence [7,11].

GHB is a naturally occurring or endogenous substance found within the central nervous system which appears to have its own unique receptor locus within the GABA receptor complex [10]. GHB was synthesised as an analogue of GABA (gamma aminobutyric acid), the major neurotransmitter for inhibition. GHB is principally metabolised by the liver by conversion to succinate which enters the Krebs Cycle; some GHB is also converted to GABA. GHB receptor binding facilitates GABA related central inhibition and also leads to Dopamine release into the Nucleus Accumbens, which functions as a reward stimulus; to a lesser extent, GHB also acts at the GABA(B) receptor as an agonist. It is suggested that the combined actions of GHB at its own receptor, plus its effects at the GABA(B) receptor and with indirect effects at the GABA(A) receptor account for the sedation observed in patients especially those with intoxication. GHB can be detected in some post-mortem blood, urine, CSF specimens making it difficult sometimes to determine whether GHB ingestion occurred antemortem (and might have played some role in course of death) or whether any GHB detected represents only endogenous levels [12]. As with most other substances of abuse, it appears that many users of GHB do not proceed to develop a dependence syndrome however those who do, require frequent

dosing with the drug (e.g. 2 to 4 hourly) in order to avoid withdrawal symptoms.

In the absence of Best Practise practice guidelines for the management of GHB dependence and particularly the withdrawal syndrome, we decided to review the cases of GHB dependence presenting to our hospital's Drug Health Service over the past two years in order to review how many patients were able to managed in an outpatient/home setting without the need for hospitalisation.

### Aim

Over a four year period (2009-2012) at Western Hospital, to review all cases of GHB Dependence and specifically identify which patients required hospital admission, describe what clinical characteristics were common and might be useful as potential indicators of a need for hospitalisation for GHB withdrawal.

### Methods

Aretrospective medical record search was conducted, for the four year period including January 2009 until December 2012, to identify all cases presenting to the Drug Health Service at Western Hospital requesting GHB detoxification. Patients who reported using GHB but used such intermittently and without specific mention of withdrawal symptoms were therefore excluded. Only patients who self-reported GHB daily use and specifically requested detoxification assistance were identified. All such patients were assessed by a specialist clinician employed within the Drug Health Service of Western Hospital, Melbourne, Australia. This service has access to acute hospital beds, a community-based (low level care) drug and alcohol detoxification unit and outpatient withdrawal support program. The Western Hospital is located in the major industrial region of Melbourne which has a higher prevalence of social disadvantage in comparison with other regions. Data collected included basic demographics, drug use history,

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presenting problem and withdrawal assessment. Only basic descriptive statistics were employed to characterise ages and drug doses. No validated withdrawal scale or methodology for GHB withdrawal in humans has yet been developed therefore physician assessment of severity based upon observed signs, duration of admission and amount of medication received was relied upon. This review process was undertaken as a quality assurance Project (clinical audit) for our institution and thereby approved by the Western Hospital Low Risk Research Ethics Committee.

## Results

Overall, seventy four patients presented to our service reporting problems with GHB use with most reporting intermittent use (i.e. non-daily use), typically associated with use in night-club or “party” settings, and mostly report consumption levels in the range 1-5 gram per occasion. In our region, GHB use is usually reported by consumers as having been purchased from “Black Market” sources in either liquid or powder form, measured and sold in grams. The commonest initiation to GHB use was via social contacts particularly within nightclub environments. Within this population, twenty seven patients presented to our service specifically requesting help with GHB detoxification, each had been diagnosed by a specialist physician (Addiction Medicine) as having met DSM IV-tr criteria for a Dependence Syndrome. Eighteen of these were male, the mean age was 23 years (range: 19yrs – 41yrs) and all reported the regular use of at least one other drug, mostly the stimulant drugs (e.g. amphetamines) and alcohol, use being most commonly associated with “night-club” sub-culture; the female average age was 20 and their profile of use was essentially the same (although mostly being associated with a male partner’s use). None of the total cases had significant medical or psychiatric histories (i.e. likely impacting adversely upon their GHB withdrawal); details about employment, income and educational status was lacking, possibly reflecting the brief nature of the medical history recorded by the admitting hospital intern. Only 12 cases were re-presentations (i.e. had previously attended this service for the same problem), the majority being first time attendees. Apart from only eight cases, most patients were managed within the community, either by admission to the community-based drug and alcohol detoxification unit or by outpatient treatment. In both these latter settings, patients received some symptomatic medication typically diazepam (e.g. no more than 5 mg to 10 mg three or four times daily and reducing). Patients accepted for outpatient treatment were required to have their diazepam supervised by another person in their home or able to visit their home daily and to be a non-drug user. None of these patients, in either community location, deteriorated and required hospitalisation. Anxiety and insomnia with the commonest symptoms identified by patients undergoing detoxification in the community facility, the home and also the hospital setting.

Only eight cases, of the total twenty-seven identified with GHB Dependence, were considered to have particular risk for withdrawal complications and because of this, were admitted to the hospital ward (Table 1). The average estimated daily consumption of GHB in this group was ~ 17 gm/day; all used other drugs. Three of these cases were screened in the outpatient clinic as having particular risk for withdrawal complications because they also had significant poly-substance abuse including heavy alcohol use (i.e. >60 gm alcohol per drinking occasion). The other five cases admitted to hospital all had initially presented to the hospital’s Emergency Department with symptoms and/or signs of concern, prompting the decision to admit. One case had intentionally taken an overdose and with some persisting suicidal ideation, another had persistent tachycardia with symptomatic palpitations which did not

settle after initial diazepam treatment, another had recently collapsed and was transported to hospital by ambulance, another had psychotic symptoms (i.e. auditory hallucinosis) and the other had signs and symptoms e.g. tremors, anxiety, restlessness which did not settle after initial diazepam treatment.

This latter patient later developed a severe syndrome characterised by delirium with agitation which was protracted over a period of eight days, after which time, he appeared to make a spontaneous recovery. This patient was the older than the others admitted the heaviest and longest user of GHB (30 gm/day) and concurrently was Alcohol Dependent (80-100 gm /day, or more). His management included the provision of high doses of diazepam i.e. 20 mg four or five times per day together with Baclofen 20 mg three times daily (because his withdrawal was gauged to be severe despite high doses of diazepam). Further, occasional dosing with Olanzapine (from 10 to 20 mg at night) was also provided to assist with night-time sedation as anxiety/agitation at night was more problematic for nursing staff. In addition to specialised nursing care (utilising our “generic” protocol for delirium management), the patient required a nursing assistant present at all times. None of the patients, including the one severe case, suffered seizures, myoclonus or movement disorders apart from tremor; one case experienced auditory hallucinosis. All of the community-treated GHB dependent patients were polydrug (e.g. also using amphetamines, THC/Cannabis, alcohol most commonly), who typically reported consuming around 4-8 gm/day of GHB (e.g. 1-2 gm four times daily) and had essentially uncomplicated withdrawal reactions requiring fairly minimal doses of diazepam. All patients responded to diazepam, mostly receiving doses ranging between 10 mg and 20 mg three times a day which appeared to provide reasonable symptom management. Baclofen was only used in the one severe withdrawal case (described above), none of the others.

## Discussion

In this review of cases, only a small proportion of all cases required acute hospitalisation for GHB dependence and withdrawal management, the majority were able to be managed at home or within a community detoxification unit setting. The latter provides a supportive care environment within a home-like environment and cannot provide care for medical complications, hence if such occur, a hospital transfer is required. None of the community-treated patients required hospitalisation for medical attention, largely reflecting the experience of another case series [10]. Most who were hospitalised later required fairly minimal medical treatment, supportive nursing care and modest doses of diazepam. Only three cases, of the identified twenty seven GHB dependence cases in total, were considered to have particular risk for withdrawal complications and because of this, were admitted to the hospital ward. These cases all involved higher levels of poly-substance abuse and suspected alcohol dependent use. Another five cases (i.e. of the total twenty seven identified) were admitted to hospital after they had initially presented to the Emergency Department with symptoms and/or signs of concern, prompting the decision to admit. One of these latter cases had intentionally taken an overdose and had some persisting suicidal ideation, one had a tachycardia with symptomatic palpitations which did not settle after initial diazepam treatment, one had recently collapsed (uncertain cause; no neurological sequelae) and was transported to hospital by ambulance, one had anxiety and psychotic symptoms (i.e. auditory hallucinosis) and the other had severe symptoms including tremors, anxiety, and restlessness; all of these reasons prompted hospital admission rather than GHB Dependence alone.

Patient Age & Sex	History of consumption	"Other" Drug use	Presenting Problem	Withdrawal Syndrome
Male 19yrs	~ 15gm/day; ~8 months	Amphetamines, Keta mine, Alcohol Abuse.	Poly substance Overdose (intentional) attended ED following relationship problems.	Mild; responded to symptomatic Diazepam.
Male 26yrs	28gm/day; ~2 years	Amphetamines, Alcohol Abuse.	Pre sented requesting a "Detox" due inability to undertake at home because of insomnia.	Mild; responded to Diazepam.
Female 27yrs	4-6 gm/day; ~3 years	Amphetamines, THC	Anxiety with "Panic" episodes, initially attended ED with "palpitations" etc	Mild; responded to Diazepam.
Male 24yrs	~ 16gm/day; ~12 months	Amphetamines, Cocaine, THC, Alcohol Dependent.	Pre sented requesting a "Detox" because unable to stop use unless uses heavy alcohol intake instead.	Moderate; responded to Diazepam and small doses of Baclofen.
Female 24yrs	~ 12gm/day; ~ 18 months	Amphetamines, (" <i>Ice</i> "), THC, Alcohol Abuse.	Pre sented requesting a "Detox" because of withdrawal anxiety and insomnia problems.	Mild; responded to Diazepam and small doses of Baclofen.
Female 22yrs	~ 12-14 gm/day; for ~ 2 years	Alcohol Abuse, THC	Initially presented to ED following a witnessed collapse with LOC at a "party"	Mild; responded to Diazepam.
Male 30yrs	~ 30 gm/day; > 3 years	Alcohol Dependence.	Bought to ED by friend: severe anxiety and shakes; not "coping" at home trying to stop !	Severe symptoms and prolonged delirium (6 days) required large doses Diazepam and Baclofen.
Male 25yrs	~ 120 gm/day; > 6 months	Amphetamines, Alcohol Abuse.	Pre sented to ED with fear of "Self harming" and acknowledging "hearing voices" etc	Moderate; responded to Diazepam and small doses of Baclofen.

(GHB daily dose estimated in grams expressed as gm/day; THC = Tetrahydrocannabinol/Cannabis use).

**Table 1:** Profile of patients admitted to hospital with GHB dependence.

The latter case eventually experienced a severe withdrawal syndrome and in retrospect, this patient was the heaviest user (i.e. only case taking 30 gm/day) and reported needing to dose himself with GHB when at home almost every two or three hours; he was also alcohol dependent. During his admission, a full medical work-up for other possible causes of delirium was conducted excluding a lumbar puncture as no fever or signs of meningismus were evident; a CT scan of his brain (found normal) was conducted in the Emergency Department prior to admission under heavy sedation and with the patient temporarily intubated. A recent review of GHB withdrawal found that high daily dose intakes (e.g. 30 gm/day or more and more frequent consumers (i.e. having short dosing intervals) were more likely at risk for withdrawal complications [7].

This case series was presented for peer review at the December 2012 clinical meeting of the Victorian Addiction-Medicine Inter-Hospital Liaison Association (VAILA) wherein the attending members also acknowledged similar GHB treatment experience and supported the suggestion that high daily GHB intake (e.g. > 30 gm/day) was a reasonable screening indicator of GHB withdrawal severity risk, based upon most clinician's experience. Hence, the experience of GHB withdrawal management at Western Hospital's Drug Health Service, together with some external peer support, and concurring with findings reported in a recent detailed review [7] suggests that patients taking daily doses estimated at 30 gm/day or more, appear at increased risk for complicated withdrawal and are more likely to require hospitalisation. The algorithm proposed by these authors [7] has subsequently been adopted by our service as a likely "best practise" guideline for the screening of all patients with GHB dependence.

## Conclusion

The majority of cases of GHB dependence presenting to this service for withdrawal support, subsequently had mild withdrawal symptoms, were able to be managed with diazepam alone and only a small number required hospitalisation, most of these admissions being related also to other medical concerns. The one severe case was the heaviest user (30 gm/day) over the longest period of time and had

co-morbid alcohol dependence. This experience supports the findings and recommendations of other reviews of GHB withdrawal suggesting that the frequent use of high GHB doses and possibly also co-morbid alcohol dependence, are likely significant risk factors that may predict the need for admission to hospital.

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