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Risk Factors of γ -Hydroxybutyrate Overdosing

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Key Words

Recreational drug · Overdosing · γ -Hydroxybutyrate · Side effects

Abstract

The aim of this study was to identify in recreational drug users the factors which increase the risk of overdosing (OD) with γ -hydroxybutyrate (GHB). A purposive sample of 45 experienced GHB users was interviewed, equally divided into three groups (never OD, occasional OD, and repeat OD). The repeat OD group scored highest on many risk factors regarding GHB use, the occasional OD group scored intermediate, and the never OD group scored lowest. Participants, whether or not they had overdosed on GHB, most often perceived GHB use (e.g. using more GHB than usual, using GHB doses too closely together) as the main reason for GHB OD, and many participants who had overdosed on GHB reported that they had taken more GHB than usual at their most recent occasion of GHB OD. No significant differences in co-use of GHB with other substances were found between the three groups. Our findings indicate that using GHB in the company of groups of friends probably reduces, but does not eliminate, the risk of OD.

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Introduction

γ -Hydroxybutyrate (GHB) acid is a potent depressant of the central nervous system which rapidly enters the bloodstream and produces its effects shortly after ingestion [1]. Though GHB was marketed as an anesthetic in 1960 [2], it is no longer applied as an anesthetic because of its negative side effects, poor control of dosage and duration of effect [3]. The current study refers to recreational GHB use, not the clinical use of GHB. GHB is clinically applied to treat cataplexy in narcoleptic patients [4], to suppress symptoms of alcohol withdrawal [5], and to achieve and to maintain alcohol abstinence in alcoholic patients [6]. In contrast to recreational use, however, it is important to note that dependency on GHB is seldom seen in its clinical use, which is due to the about 3-fold lower doses of GHB applied in clinical settings (4–7 g daily p.o., spread over 3–6 doses) as compared to recreationally used doses [4, 5].

As GHB also increases feelings like euphoria, well-being, relaxation, tranquility, sociability, sexuality, and enjoyment of dancing [7, 8], it has become increasingly popular as a recreational drug, mainly as a ‘club drug’, since the early 1990s [9–13]. For example, in the Netherlands, the use of GHB gained popularity as a recreational drug [14–18] as evidenced by data from a large national survey among clubbers and party goers in 2008–2009. Preva-

lence of GHB use among clubbers and party goers was 6.4 and 14.3% (lifetime use); 3.4 and 7.8% (last year), and 1.7 and 4.6% (last month), respectively [19]. These rates are significantly higher as compared to the general population (aged 15–64 years) with prevalence rates of 1.3% (lifetime), 0.4% (last year), and 0.2% (last month) [20].

Recreational users consider GHB as a safe drug because, in their view, it produces no side effects, i.e. no hangover or other serious adverse somatic effects. This may well be the case when used very moderately, but is a false assumption when GHB is used frequently or in higher doses. In the latter case, GHB has a high addictive potential. Moreover, after initial stimulation GHB may easily induce loss of consciousness, because the dose-response margin between stimulation and the loss of consciousness (intoxication) is very narrow [21]. Indeed, several emergency department case studies have reported GHB use as one of the major causes of drug-related intoxications [9, 22–27]. In Australia, large increases in ambulance attendances related to GHB intoxication were reported between 2001 and 2005 [22, 26]. Due to respiratory depression, GHB use may even be lethal [9, 11]. According to figures of the Dutch Drug Incidents Monitor 2011, 740 out of 3,652 registered drug-related incidents (ambulance called and/or arrived at emergency departments) were related to the use of GHB [28]. In addition to sudden intoxications, GHB retains a high addictive potential. Recently, the number of clients in outpatient care with GHB as their main drug problem sharply increased in the Netherlands from a few dozen in 2007 to 659 in 2011 [29, 30]. It should be noted that the variability in the quality of recreational GHB (strength and purity) poses an additional risk for such accidents [31]. Despite the high potential of lethality and intoxication, recreational users of GHB consider the drug as safe and non-toxic [9, 32]. Still, 52% of respondents reported that they had lost consciousness at least once after using GHB [33]. Others confirmed the frequent loss of consciousness after use of GHB: 66% reported ‘loss-of-consciousness’ episodes, 28% ‘overdose’ [32], 41% ‘passing out or coma’ [7], and 18% ‘complete loss of consciousness’ [34]. Users do even not perceive GHB overdosing (OD) leading to a coma as a serious problem [7, 33, 35], mainly because a GHB-induced coma usually resolves within 4–8 h and patients often awake swiftly from deep coma to full consciousness without any residual complaints [27]. This also explains why many GHB users experience GHB OD more than once [25, 32, 33]. Note that the repeated OD may be associated with residual adverse health effects on cognition [36].

Studies among users show a strong variation in self-reported prevalence of GHB-related overdoses, which is probably due to differences in the samples studied, i.e. the level and history of GHB use, and the applied definition of OD. For instance, when asked about the main risks of GHB, 83 [35] and 39% [33] of users mentioned overdose as the main risk, but these figures do not necessarily refer to self-experienced overdose. One of the most popular words in the argot among GHB users is ‘G-napping’, i.e. falling asleep or ‘taking a nap’ after using GHB. While this term might be more appropriate to describe a certain condition or effect, it could also serve as a euphemism for GHB-induced coma. For example, Barker et al. [7] observed that ‘falling out’ or ‘G-napping’ was accepted as part of the experience of using GHB and that ‘G-napping’ was not categorized by focus group participants as evidence of overdose. Similarly, Miotto et al. [32] found that participants considered unpredictable loss-of-consciousness episodes lasting minutes to hours as ‘falling asleep’, in contrast to an overdose.

Consequently, a clear definition is required to properly assess GHB OD in users. Barker et al. [7] explicitly excluded G-napping from ‘passing out or coma’, whereas Miotto et al. [32] distinguished ‘loss of consciousness’ from ‘overdose’, though they did not exactly define ‘overdose’ (or coma). In contrast, Degenhardt et al. [37] clearly defined overdose as ‘having lost consciousness and unable to be woken up’, and Duff [35] as the ‘full loss of consciousness’.

Many people who use GHB take the drug in combination with other drugs [7, 8, 10, 17, 33, 37]. The probability of coma increases when GHB is combined with other sedative drugs, such as alcohol and ketamine [38]. Accept for alcohol, most users were not aware that the combined use of GHB with other drugs is hazardous [7]. Remarkably, using severity of symptoms in first aid attendees, Krul and Girbes [24] found no differences between those who had used only GHB versus those who had used GHB in combination with other substances at large-scale parties.

Since the use of GHB may lead to loss of control, i.e. loss of consciousness, GHB is preferably not used at public events, but rather in company with a group of trusted friends and/or in a private setting, where the impact of this risk is limited [8, 39]. Moreover, GHB should be preferably used in company of peers to reduce the risk of overdose. Korf et al. [17] previously concluded that most GHB users regard OD in a private setting as less shameful than in a club or at a rave.

To conclude, the narrow dose-response margin of GHB between consciousness and overdose poses a poten-

tial risk which frequently leads to treatment in emergency stations. GHB OD, including repeated OD, appears to be rather common among recreational GHB users. Many GHB users are poly-drug users, but it is not clear to which extent the simultaneous use of GHB with other drugs increases the risk of OD.

To identify the factors which increase the risk of GHB OD, three groups of experienced GHB users, i.e. never OD, occasional OD, and repeat OD, were interviewed with respect to demographic characteristics, GHB use characteristics, poly-drug use, the co-use of GHB with other substances, and setting of GHB use. In line with Degenhardt et al. [37], we further investigated whether (1) a single experience with GHB OD was more prevalent among regular GHB users, and (2) whether those in the repeat OD group had used GHB more times during their lifetime than those in the occasional OD group. Furthermore, we assessed whether the use of GHB in a private setting and/or in company of peers diminished the risk of GHB OD, and explored other characteristics of GHB OD.

Subjects and Methods

Definition of Overdose and Coma

Overdose was defined in line with Duff [35] ('full loss of consciousness') and Degenhardt et al. [37] ('having lost consciousness and unable to be woken up'), but it was specified more precisely in terms of coma, by applying the maximum score on the Glasgow Coma Scale, i.e. does not open eyes, makes no sounds, and makes no movements in response to painful stimuli during at least 30 min [40, 41].

Subjects

A purposive sample of 45 GHB users was interviewed between February 2012 and June 2012. Inclusion criteria were: 18 years of age or older, lifetime prevalence of GHB use at 25 or more occasions, and at 1 or more occasions in the past 12 months. Exclusion criteria were: neurological disorders (e.g. epilepsy, multiple sclerosis) and full medical narcosis in hospital (i.e. surgery) in the past 12 months. Participants were recruited through ethnographic fieldwork in public (clubs, festivals) and private settings (e.g. after-parties), and through snowball referrals.

Procedure

Our definition of overdose in terms of coma was not communicated to the respondents at the start of the interview, but during the interview, participants were asked first to tell what they understand as an overdose and whether they had ever experienced a 'G-nap' or alike. Later in the interview, the definition was presented and respondents were asked whether this applied to them, and if so, how often and under which circumstances this had happened. If the initial interview data could not unambiguously confirm that the respondent had never had an overdose (i.e. never lost consciousness, and never 'G-napped' and the like) after using GHB, the subject was excluded from the study.

Following this initial interview, the final sample of 45 participants was equally divided into three groups based on the frequency of overdose after GHB use. More precisely, the never OD group had never lost consciousness after using GHB; never taken GHB before going to bed, and never experienced waking up after having taken GHB without any memory of how and why they had arrived at that place. The occasional OD group had once or twice overdosed after using GHB (mean 1.2; SD 0.4; median 1.0), and the repeat OD group 3–20 times (mean 8.3; SD 5.4; median 7.0).

Participants were interviewed face-to-face, using a semistructured questionnaire that included questions about demographic characteristics, prevalence and frequency of GHB use, prevalence of other drug use, setting in which participants use GHB, experiences with and opinions about GHB overdose. All respondents provided written informed consent before the interview, acknowledging that their participation was voluntary. After completion, they received a financial compensation of 10 EUR.

Frequency of GHB use (lifetime, last year, and last month) was measured as number of times GHB was used, referring to the number of days or occasions, i.e. not the number of doses. Last-year GHB dependence was assessed with a 5-item Severity of Dependence Scale (SDS) with each item scoring never/almost never (0), sometimes (1), often (2), or very often (3), resulting in a value of 0–3 per item and of 0–15 in total [42]. Previous studies have applied various cutoffs for different substances. For example 2–4 for cannabis [43], 3 for heroin, 4 for cocaine [44], 5 for opiates [45], 3 for cocaine [46], 4 for amphetamines [47], 4 for ecstasy [48], 6 for khat [49], and 6 for benzodiazepines [50]. An arbitrary cutoff value of ≥ 4 (SDS score) was applied to define GHB dependence positivity. To determine their usual GHB unit dose, respondents were asked to fill their typical 'GHB tool' with water, and the volume was measured. Total amount of GHB per occasion was calculated by multiplying the volume with the number of doses. The same procedure was applied to measure the largest single dose ever taken as one single dose. Use of GHB in combination with other substances was measured using a 7-point Likert scale (0 = never, 6 = very often), for within 3 h *before or simultaneously* with GHB, as well as for within 3 h *after* GHB.

Statistical Analysis

Data were analyzed using SPSS v.20. For nominal variables, Fisher's exact statistics were calculated in comparisons between groups. Because distributions were skewed and/or standard deviations were very large for most continuous variables, medians are reported, and the Jonckheere-Terpstra (JT) test (an alternative test to the Kruskal-Wallis test applicable if samples have a natural ordering) was conducted to assign the statistical significance of differences. Significance was accepted at a conservative $p < 0.05$, but when p values ranged between 0.10 and 0.05, differences are mentioned in the text as 'tendencies'.

Results

Demographic Characteristics

Approximately half of the sample was male (47%), equally divided over the three groups (7 males and 8 females in each group). Age ranged from 18 to 32 years

Table 1. GHB use according to history of GHB overdose

	Total (n = 45)	Never OD (n = 15)	Occasional OD (n = 15)	Repeat OD (n = 15)	Test statistic	p
Median age at first use, years	21	23	21	20	3.694 ^b	<0.001
Median frequency of use, n						
Lifetime	50	35	55	60	2.711 ^b	0.007
Past 12 months	30	30	30	35	2.112 ^b	0.035
Past 30 days	3	2	3	5	2.918 ^b	0.004
Median SDS score	2	0	2	4	3.124 ^b	0.002
Dependent (SDS score ≥4)	24%	7%	13%	53%	9.203 ^a	0.014
Median amount per occasion						
Dose per unit, ml	3.7	3	4	3.7	1.242 ^b	0.214
Doses, n	5	4	5	8	4.003 ^b	<0.001
Total amount, ml	20	12	20	30	3.867 ^b	<0.001
Median time between first and last dose per occasion, h	10	9	8	15	3.027 ^b	<0.001
Median largest single dose ever at once, ml	5	4	5	7	4.038 ^b	<0.001

^a Fisher's exact test; ^b JT test.

(mean 23.8; SD 2.9). After leaving elementary school (in the Netherlands commonly at the age of 12 years), respondents had completed 4–16 years of education (mean 9.5; SD 2.6). Among respondents, 62% were students, 93% were employed (47% >20 h/week), and 22% had a stable partner relationship. Demographic characteristics showed no differences between the three groups.

Substance Use

The total sample consisted of experienced substance users. Current use was defined as the use of a substance at least once in the past 30 days. All respondents were current drinkers, and 69% had used 5 or more glasses of alcohol on one occasion at least once in the past 30 days. The latter was less prevalent in the occasional OD group (40%) as compared to never OD (80%) and repeat OD (87%) (Fisher's exact test = 8.183, $p = 0.016$).

All respondents had used amphetamines, ecstasy (MDMA) and cocaine; current use of these three drugs was 87, 84 and 58%, respectively. All except 1 had used cannabis, and 71% were current users. Most respondents (89%) had taken ketamine and 62% were current users. Experience with magic mushrooms and LSD was not uncommon (lifetime prevalence 47 and 68%, respectively), but current use was rare (2–4%). Only 1 respondent had used crack and none had ever taken heroin. Between the three groups, differences were only found for lifetime (but not current) use of magic mushrooms (50% never OD, 93% occasional OD, and 60% repeat OD; Fisher's exact test = 7.311, $p = 0.027$) and current cannabis use (87,

80 and 43%, respectively; Fisher's exact test = 6.975, $p = 0.027$).

GHB Use

Age at first time of GHB use was 16–28 years (mean 21.5; SD 2.9). All respondents had consumed GHB only orally, either pure or mixed in water or juice. The most common dose was a vial or part of a vial (e.g. half, three quarters), but some respondents used to take a bottle cap filled with GHB or measured it with a kitchen pipette or syringe. Thirty participants had experienced at least 1 GHB overdose. In total, they reported 142 overdoses, but only 3 occasions of these overdoses required medical assistance in the hospital (1 participant once, another participant twice; both from the repeat OD group).

Table 1 shows the characteristics of GHB use according to history of GHB overdose. At first-time use of GHB, repeat OD participants were youngest and never OD participants were oldest. The median frequency of GHB use (lifetime, past 12 months, and past 30 days) and GHB dependence was highest in the repeat OD group, lower in the occasional OD group, and lowest in the never OD group. While median dose per unit was similar across the three groups, median number of doses per occasion, median total amount of GHB used per occasion, and median largest single GHB dose ever taken at once were lowest in the never OD group, higher in the occasional OD group, and highest in the repeat OD group. Finally, median duration of 'GHB sessions' (i.e. time between first and last dose per occasion) was al-

Table 2. Combined use with GHB

	Total (n = 45)	Never OD (n = 15)	Occasional OD (n = 15)	Repeat OD (n = 15)	Test statistic	p
<i>Median Likert score (0–6) of combined use before/simultaneously</i>						
Alcohol	2	2	3	2	–1.877 ^a	0.060
Cannabis	1	1	2	0	–1.782 ^a	0.075
Ecstasy	5	5	5	3	–0.455 ^a	0.649
Cocaine	1	0	1	1	0.959 ^a	0.338
Amphetamines	4	4	5	5	0.160 ^a	0.873
Ketamine	1	1	1	1	1.121 ^a	0.262
<i>Median Likert score (0–6) of combined use after</i>						
Alcohol	0	1	0	0	–1.372 ^a	0.170
Cannabis	1	2	2	0	–1.876 ^a	0.061
Ecstasy	0	0	0	0	0.097 ^a	0.923
Cocaine	0	0	0	0	–0.194 ^a	0.846
Amphetamines	0	0	0	0	0.378 ^a	0.706
Ketamine	0	0	0	0	–0.688 ^a	0.492
^a JT test.						

most twice as long in the repeat OD group as in both other groups.

Setting of GHB Use

At the 10 most recent occasions of GHB use, 60% had never used GHB outdoors (e.g. open air festival, park), 51% never in a nightlife setting (e.g. club, party), and 49% never at home (in own or friend's apartment, but not a party). A private party or after-party was the most frequently mentioned setting for all three groups, but less so for repeat OD participants (median 4 out of 10, as compared to 6 out of 10 for the other two groups; JT = –2.191, $p = 0.028$). The repeat OD group used GHB more often at home (2 out of 10; JT = 2.015, $p = 0.044$) and tended to have used GHB more often outdoors (1 out of 10 vs. 0 out of 10 for the other two groups).

At the 10 most recent occasions, GHB was most commonly used by all three groups in the company of friends: 89% had never used it alone, and 80% had never used it together with strangers met while going out. Never OD participants used GHB almost exclusively in the company of a group of friends at the 10 most recent occasions (median 10 out of 10 times), while in the occasional OD and repeat OD groups, this happened less often (8 out of 10; JT = –2.505, $p = 0.12$). GHB was never used with a partner or friend in the never OD group (0 out of 10), but sometimes in the occasional (1 out of 10) and the repeat OD group (2 out of 10; JT = 3.320, $p = 0.001$).

Combining GHB with Other Substances

As shown in table 2, using ecstasy and amphetamines before or simultaneously with GHB was rather common (median 5 and 4 on a 0–6 scale, respectively), whereas the combined use of alcohol, cocaine, cannabis, or ketamine was not. The use of all these substances within 3 h after (the only or last dose of) GHB was uncommon. If participants used other substances after GHB use, it was almost exclusively cannabis with no significant differences between the three groups.

GHB Overdose

The most recent (or only) GHB overdose was 1–48 months ago (mean 7.4; SD 9.3; median 5.0). Table 3 shows characteristics of the most recent (or only) GHB overdose for both OD groups. At that occasion, the vast majority of participants in the occasional and the repeat OD group were using GHB in the company of a group of friends; and in a private setting, either at a party/after-party or their own or a friend's place. While 50% reported that they had taken more GHB than usual, 23% reported to have consumed the same amount as usual, and 27% less than usual. In general, participants reported that at that occasion, they had used one or more other substances in addition to GHB. Only 2 participants had not co-used another substance. Participants in the repeat OD group tended to have used GHB more often in a home setting and the occasional OD group tended to have used alcohol in com-

Table 3. Characteristics of the most recent (or only) GHB overdose

	Total OD (n = 30)	Occasional OD (n = 15)	Repeat OD (n = 15)	Test statistic	p
Setting, %					
With group of friends	87	100	73	3.853 ^a	0.100
Home setting	37	13	60		
Private party/after-party	37	53	20	3.853 ^a	0.063
Nightlife setting	17	20	13		
Outdoors	10	13	7		
Median number of doses	3	3	2	-0.674 ^b	0.500
Median total amount of GHB, ml	12	12	9	0.208 ^b	0.835
More, same, or less GHB than usual, %					
More	50	47	53	0.337 ^a	1.00
Same	23	26	20		
Less	27	27	27		
Co-use with other substances, %					
Ecstasy	67	73	60	0.600 ^a	0.700
Alcohol	53	73	33	4.821 ^a	0.066
Amphetamine	37	33	40	0.144 ^a	1.00
Cannabis	27	40	13	2.727 ^a	0.215
Ketamine	13	0	27	4.615 ^a	0.100
Cocaine	13	20	7	1.154 ^a	0.598

^a Fisher's exact test; ^b JT test.

Table 4. Perceived reasons for GHB overdose and future risk perception

	Never OD (n = 15)	Occasional OD (n = 15)	Repeat OD (n = 15)	3 groups		Yes/no OD	
				test statistic	p	test statistic	p
Main reason for GHB overdose, %							
More GHB than usual	67	40	40	1.733 ^a	0.565		
GHB stronger than usual	-	13	7				
GHB doses too close together	7	-	27				
Alcohol	13	20	7				
Other drugs	-	13	13				
Coincidence	-	-	7				
Exhaustion	-	13	-				
Inexperienced user	13	-	-				
GHB ^c	73	53	73			0.450 ^a	0.738
Other reasons	27	47	27				
Risk of overdosing on GHB in the future, %							
Would not happen	33	7	0				
Very small	20	20	20				
Small	33	33	20				
Moderate	13	33	27				
Big	0	7	27				
Very big	0	0	0				
Would definitely happen	0	0	7				
Risk moderate to definite, %	13	40	60	6.980 ^a	0.038	5.720 ^a	0.023
Median Likert score (0-6)	1	2	3	3.207 ^b	0.001	2.878 ^b	0.004

^a Fisher's exact test; ^b JT test; ^c more/stronger than usual, doses too close together.

bination with GHB more often, but there were no statistically significant differences between the two OD groups.

Perceived Reasons for GHB Overdose and Future Risk Perception

The primary reason for accidental OD with GHB or for a deliberate overdose of GHB was investigated. This was done for the most recent (or only) overdose (occasional and repeat OD groups) and for GHB users in general (never OD group). Table 4 depicts the various reasons given by the respondents. Among those who had taken an overdose themselves, the most common reason referred to GHB dosing, i.e. the GHB solution was stronger than usual or GHB doses were taken in a too short time interval (27% of the repeat OD group gave the latter argument as the main reason, whereas no one in the occasional OD group). Some users ascribed the OD to the co-use of alcohol or use of other drugs, whereas others reported it was due to mental-physical exhaustion (e.g. having worked many hours on the previous days, partying too long) or believed it was simply coincidental. Diminished tolerance as a cause of overdose, i.e. that they had not been using GHB for some time, was not mentioned. Most participants in the never OD group (67%) mentioned the use of unusually high quantities of GHB as the main reason of OD, whereas only 13% mentioned lack of experience with GHB as the main cause of OD. Overall, no significant differences were found between the three groups, nor between those who never overdosed and those who did overdose.

Table 4 further presents the perceived risk of OD on GHB in the future, which varies from 'would not happen' to 'would definitely happen'. While 33% of participants in the never OD group reported the chance of OD to be nil, this applied to only 7 and 0%, respectively, in the occasional and the repeat OD group. On a Likert scale from 0 (OD would not happen in future) to 6 (OD would definitely happen in future), the median score ranked from 0 for the never OD group to 2 (or small) in the occasional OD group and 3 (or moderate) in the repeat OD group.

Conclusion

The aim of this study was to identify the factors which increase the risk of OD with GHB. We compared three groups of experienced GHB users (never OD, occasional OD, and repeat OD). Similar to a previous Australian study [37], which compared never OD to ever OD, participants were generally employed and well educated. No

differences in terms of sociodemographic characteristics became apparent between those who had or had not overdosed. Participants were experienced substance users, current (= at least once during the last 30 days) users of alcohol, often had used 5 or more glasses of alcohol on one occasion at least once in the past 30 days, and many were current users of stimulants (amphetamines and ecstasy in particular), cannabis and ketamine, but not of heroin, LSD or crack-cocaine. Like Degenhardt et al. [37], we found no differences between those who had or had not overdosed in the extent of other illicit drug use. However, participants who had overdosed were twice as often current drinkers. The occasional OD group and the repeat OD group did not differ in terms of the extent of other drug use, except for a higher lifetime (but not current) use of magic mushrooms in the occasional OD group and less current cannabis use in the repeat OD group.

As hypothesized, those who had overdosed on GHB had used GHB more often during their lifetime. While our findings generally support the conclusion of Degenhardt et al. [37] that 'the only apparent distinguishing factor between those who had and those who had not overdosed on GHB was the amount of experience with GHB use', the present data enable a closer specification of the differences between the two groups. For instance, the repeat OD group scored highest on many other risk factors regarding GHB use (age at first-time use of GHB, past 12 months and past 30 days frequency of GHB use, GHB dependence, number of doses of GHB per occasion, total amount of GHB used per occasion, duration of 'GHB sessions', and largest single GHB dose), whereas the risks were lowest in the never OD group and intermediate in the occasional OD group (except for duration of 'GHB sessions', which did not differ from the never OD group). Participants, whether or not they had overdosed on GHB, most often perceived GHB use (e.g. using more GHB than usual, using GHB doses too close together) as the main reason for GHB OD. Moreover, many participants who had overdosed on GHB reported that they had taken more GHB than usual at their most recent GHB occasion of overdose. Regarding the co-use of GHB with other substances, the use of ecstasy and amphetamines before or simultaneously with GHB, but not alcohol, cocaine, cannabis, and ketamine, was very common. The co-use of these substances within 3 h after (the only or last dose of) GHB was uncommon, and if used after GHB use, it was exclusively cannabis. Apparently, GHB is preferably used to reverse the stimulation caused by ecstasy and amphetamines, but not to enhance the sedative effects of previ-

ously used drugs. Interestingly though, no significant differences in co-use were found between the three groups. Consequently, the co-use of sedative drugs like alcohol and ketamine as a major contributing risk factor of GHB OD can probably be excluded. Based on pharmacological principles it should, however, be noted that the co-use of sedative drugs will increase the risk of GHB OD when taken in relatively high amounts.

Regarding the physical and social setting, GHB was most often used at a private party/after-party and in the company of a group of friends. The hypothesis that participants who had overdosed on GHB used GHB more often when being alone (solus) than the never OD group (and the repeat OD more often than the occasional OD group) was confirmed. Still, using GHB in the company of others was most common in all three groups. Consequently, using GHB in the company of groups of friends probably reduces, but does not eliminate, the risk of OD as illustrated by the finding that the most recent (or only) overdose mostly occurred in a social setting. Remarkably, the hypothesis that participants who had overdosed on GHB used GHB more often in private settings than the never OD group (and the repeat OD group more often than the occasional OD group) was not confirmed. Note that GHB was hardly used in public settings, which is probably because publicly OD is perceived as shameful [17, 39]. The predominance of GHB OD in private set-

tings in this sample might explain why participants who had overdosed rarely required medical assistance in hospital (3 in 142 reported overdoses).

This study has several limitations. Firstly, data were collected from more experienced drug users than the general population so that the sample and their level of drug use is not representative of the general population. Secondly, all data were self-reported, though this is a common and generally accepted approach. Thirdly, the small sample size of 45 participants may be the reason why certain differences could not be assessed at a statistically significant level. Nevertheless, this study provides clear evidence that – in recreational drug use, but not in clinical settings – the frequency of GHB use and amount of GHB are important risk factors of GHB OD. The present findings may aid GHB users and policy makers to limit the potential adverse health effects of repeated GHB OD, assuming that this is associated with residual adverse health effects on cognition [36].

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