

Jeroen BOSCH ZIEKENHUIS



Toxicologie

GHB

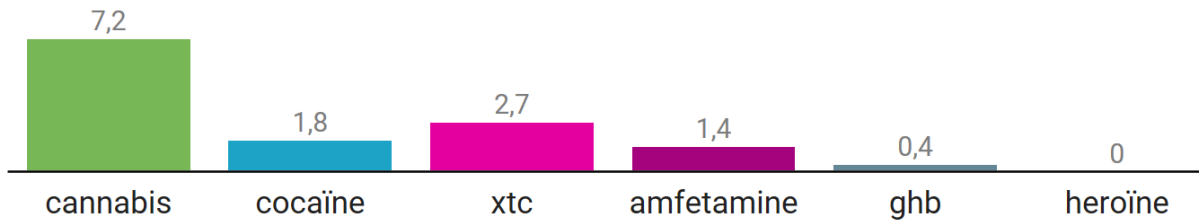
acute intoxicatie en detox bij chronisch gebruik

2017 | Drugsgebruik in de bevolking

Jaarprevalentie ▾

Totaal ▾

%



Bron: Gezondheidsenquête/Leefstijlmonitor CBS i.s.m. RIVM en Trimbos-instituut, 2017

- Wat is het?
- Er zat iets in m'n drankje
- EMV 3 en nu?
- Detox bij chronisch gebruik

GHB - Wat is het?

- Endogene stof –precursor en metaboliet van GABA
- Slaapmodulerend, exogeen verhoogt het tevens de glutamaat, dopamine, serotonine, groeihormoon en acetylcholine spiegels
- 1960 synthetische vorm: anestheticum
- 1970 gebruik door bodybuilders, over the counter sedativum, en als rape drug
- 1990 drugscene
- Geregistreerd als Xyrem voor narcolepsie, detox bij alcoholverslaving

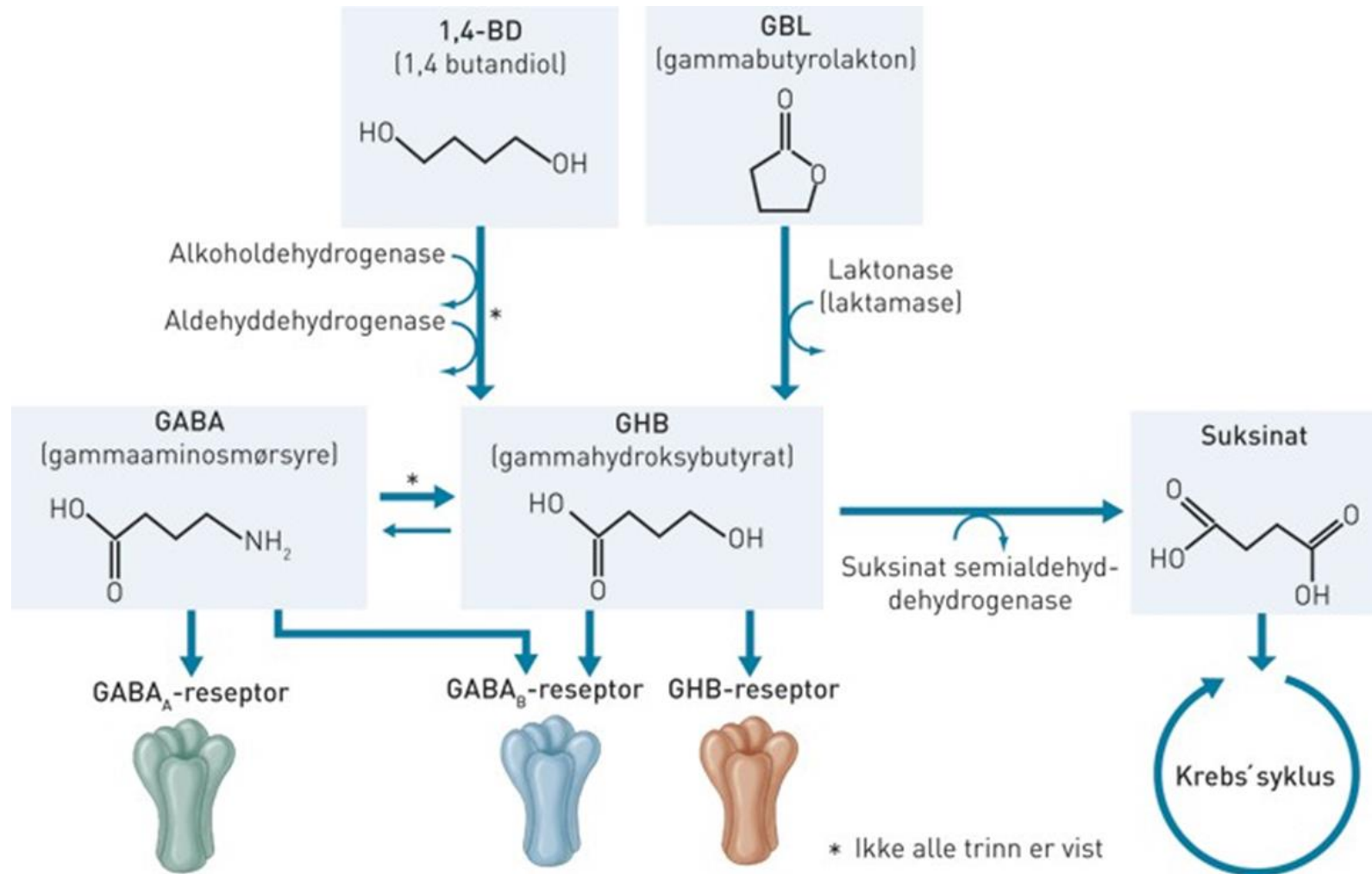
Henri Laborit



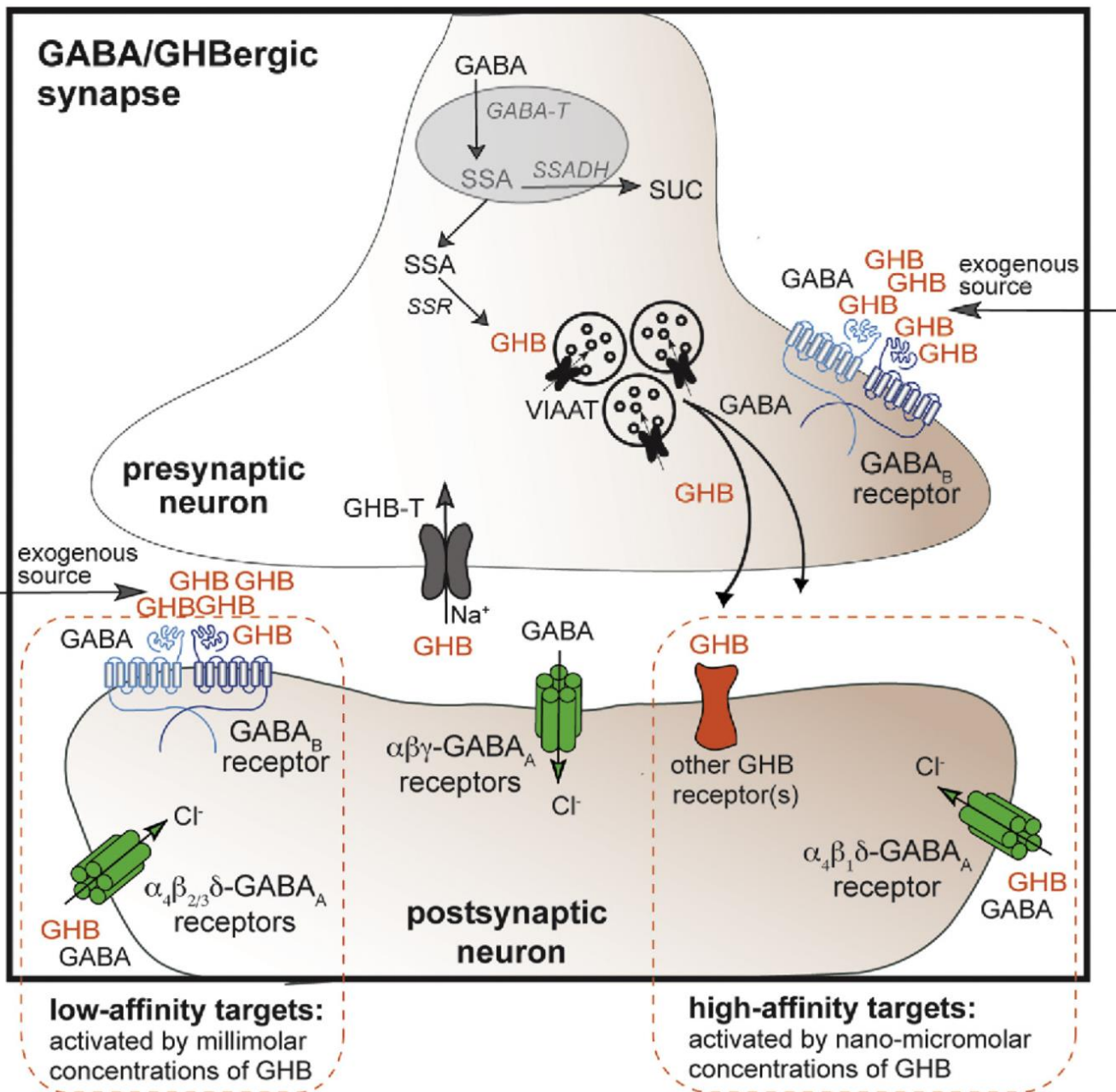
Laborit in 1991

Born	21 November 1914 Hanoi , French Indochina
Died	18 May 1995 (aged 80) Paris , France
Nationality	French
Known for	Discovery of the effects of chlorpromazine , GHB, gamma-OH, clomethiazole , minaprine
Awards	Chevalier of the Legion of Honor , Lasker-DeBakey Clinical Medical Research Award
Scientific career	
Fields	neurophysiology , pharmacology , psychiatry , psychosomatics
Institutions	Val-de-Grâce , Boucicault Hospital

GHB – Wat is het?



GABA/GHBergic synapse



Acute GHB intoxicatie

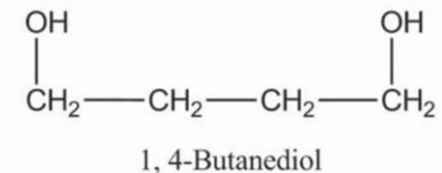
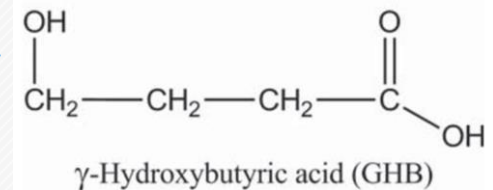
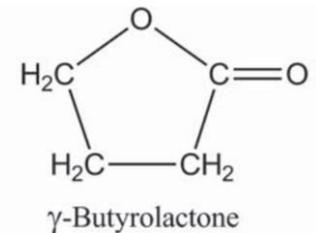
Symptomen bij gebruik van hydroxyboterzuur ¹²	
<i>dosering (in mg/kg)</i>	<i>belangrijkste verschijnselen</i>
10	kortdurende amnesie
20-30	hypotonie
	slaap
	somnolentie
	duizeligheid
50-70	euforie
	coma
	bradycardie
	hypotonie
	Cheyne-Stokes-ademhaling
	misselijkheid
> 70 niet dosisgerelateerd	braken
	cardiorespiratoire collaps
	agressie
	tonisch-klonische aanvallen
	hypothermie

'Uit eigen keuken'

Is het zo simpel om thuis een litertje GHB te brouwen? Ik neem de proef op de som. Uitgangstof voor de thuissynthese blijkt het ringvormige GBL (gamma-butyrolacton) dat **wordt verkocht als professioneel schoonmaakmiddel**. Door ringopening met loog ontstaat het natriumzout van GHB, de vorm waarin de drug meestal wordt ingenomen. **Recepten staan er genoeg op internet**.

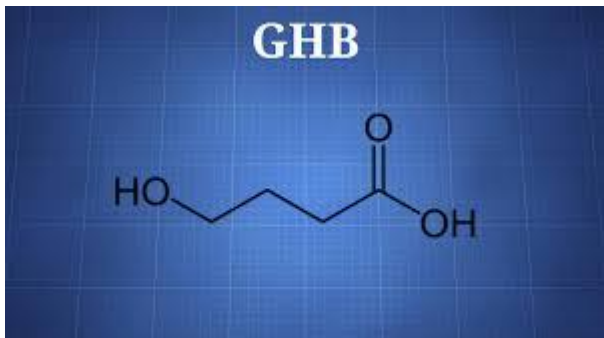
Na een bestelling op internet krijg ik GBL thuisgestuurd. De andere benodigdheden (een pH-test, gootsteenontstopper en gedestilleerd water) koop ik bij een bouwmarkt met tuinafdeling.

Drugs synthetiseren klinkt misschien spannend, maar de praktijk is nogal saai: een uur lang rustig loog toevoegen en goed roeren. Het product - een kleurloze vloeistof - gaat nog even door een koffiefilter. Dan gaat mijn 0,5 l keuken-GHB naar een echt laboratorium voor analyse.



Er zat iets in m'n drankje...





GammaHydroxyBoterzuur

Synoniem:	4-hydroxybutaanzuur
Straatnaam:	G, buisje, dopje, g-tje, liquid XTC
Toedieningsweg:	oraal (heel zout!)
Uiterlijk:	heldere/lichtstroperige vloeistof buisje met 3 tot 4,5 ml vloeistof en 2-3 gram GHB basisch (blaarvorming)
Productie:	GBL (= schoonmaakmiddel) en natronloog (gootsteenontstopper)

GHB meten

- Hoe?

- Serum → aantoonbaar zolang de patiënt out is
- Urine → tot ongeveer 8 uur na inname
- Vloeistof

- Wat?

- Serum → kwantitatieve waarde – relatie klinisch beeld.
- Urine → kwalitatief (aanwezig ja of nee)
- Vloeistof → kwalitatief

Plasma/serum

0-1 mg/L : endogene concentraties

25-75 mg/L : concentraties na gebruik bij "house party's; euforie, verhoogd libido

50-150 mg/L : slaap, spontane bewegingen, af en toe openen ogen

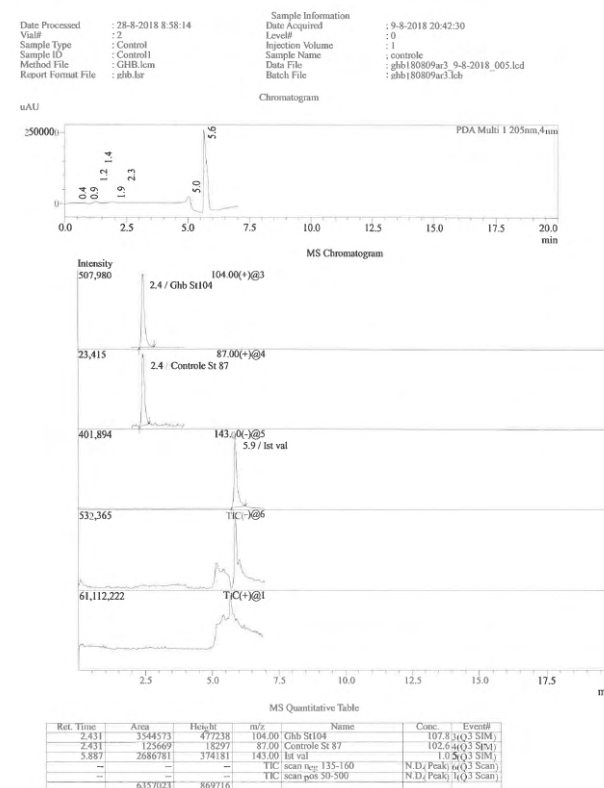
150-250 mg/L : coma, reageert op pijnprikkels

> 250 mg/L : diep coma niet reagerend op pijnprikkels, ernstige ademhalingsdepressie

GHB meten

- Hoe lang?
 - Tijdsduur bepaling: 1 uur
 - Dienst: minimaal 2 uur

- Wanneer?
 - Discussie!



EMV 3 en nu?



Low GCS due to GHB intoxication is not an indication for intubation.

L.P.F.M. van Helmond¹, F.M.J. Gresnigt²

¹ Department of Emergency Medicine, OLVG, Amsterdam, the Netherlands. Present: Department of Emergency Medicine, Jeroen Bosch Ziekenhuis, 's Hertogenbosch, the Netherlands

² Department of Emergency Medicine, OLVG, Amsterdam, the Netherlands.

Background

In the literature, between similar hospitals there are different strategies regarding the management of gamma-hydroxybutyrate (GHB)-related presentations.¹ Based on different findings some suggest a "GCS-intubate" approach. Still up to 13% of the patients with a confirmed GHB-intoxication are intubated, in most cases only because of a low GCS.²⁻⁵ In our experience a conservative management in lateral tilt position with full observation of vital signs, is a safe way to treat these patients

Aim

The objectives of this study were to describe the clinical profile of our GHB intoxicated population with a decreased GCS and to determine if a conservative treatment strategy in the Emergency Department (ED) is safe without complications.

Methods

- Retrospective chart study
- Patients with a reduced level of consciousness related to GHB/GBL intoxication in the ED between April 2011 and December 2014
- Hypothesis: when there are no signs of major complications during primary survey, supportive care and close monitoring of vital signs in the ED is safe and in these patients there is no indication for intubation or admission to the Intensive Care Unit (ICU).

Results

All of our patients received supportive care, close monitoring of vital signs (including capnography) and neurological state, and non-invasive airway management.

Table 1 Main demographic and clinical findings during emergency department stay.

	Total = 209
	N (%)
Gender	176 (84,2)
Age 20-40 years	171 (81,8)
Dutch nationality	194 (92,8)
GCS <9	158 (75,6)
Life-threatening symptoms	
Airway impairment	48 (22)
Hypoxia	27 (12)
Bradypnea	12 (5,7)
Hypotension	14 (6,7)
Bradycardia	17 (8,1)
Hypothermia	31 (14,8)

There were 3 patients with major complications for which ICU admission was indicated. This was already evident after primary survey. Two of these patients consumed GHB in combination with other drugs (methamphetamine, amphetamine, cocaine, and THC). This combined intoxication is most likely the explanation for their worse clinical condition. The only admission to the ward was because of a trauma and not primary because of the GHB intoxication.

Table 2 Outcome.

	Total = 209
	N (%)
Admission to	
Ward	1 (0,5)
ICU	3 ((1,4)
Psychiatric institution	5 (2,4)
ED observation only	200 (95,7)
Intubation	3 (1,4)
Aspiration pneumonia	0
Death	0

We did not find any indication to admit GHB intoxicated patients after ED observation, they never deteriorated during observation. The mean length of ED stay was 179 minutes which is not a problem for the logistics in our department. Our conservative treatment strategy in the ED was sufficient to prevent major adverse events such as aspiration pneumonia, in all patients with a reduced level of consciousness.

Conclusion

Our study shows that in a GHB intoxicated patient, a low GCS alone is not an indication for intubation or admission in the hospital. It is save to closely monitor these patients in the ED if no ICU indication is found during primary survey.

GHB detox bij chronisch gebruik



Detox bij chronisch gebruik

Tabel 1 klinische onthoudingsverschijnselen op basis van prevalentie cijfers:

Tremor (67%)	Hallucinaties (63%)
Slapeloosheid (58%)	Tachycardie (63%)
Transpireren, misselijkheid en braken (35%)	Hevige angsten (46%)
Rusteloosheid	Hypertensie (44%)
Milde angst of onrust	Motorische onrust of agitatie (40%)
Spierkrampen	Delirium (12%)
Oogklachten	Rabdomyolyse (7%)
Diarree	Insulten (7%)

[J Forensic Leg Med.](#) 2018 Feb;54:74-75. doi: 10.1016/j.jflm.2017.12.008. Epub 2017 Dec 23.

Excited delirium syndrome after withdrawal from 10 days long recreationally used GHB.

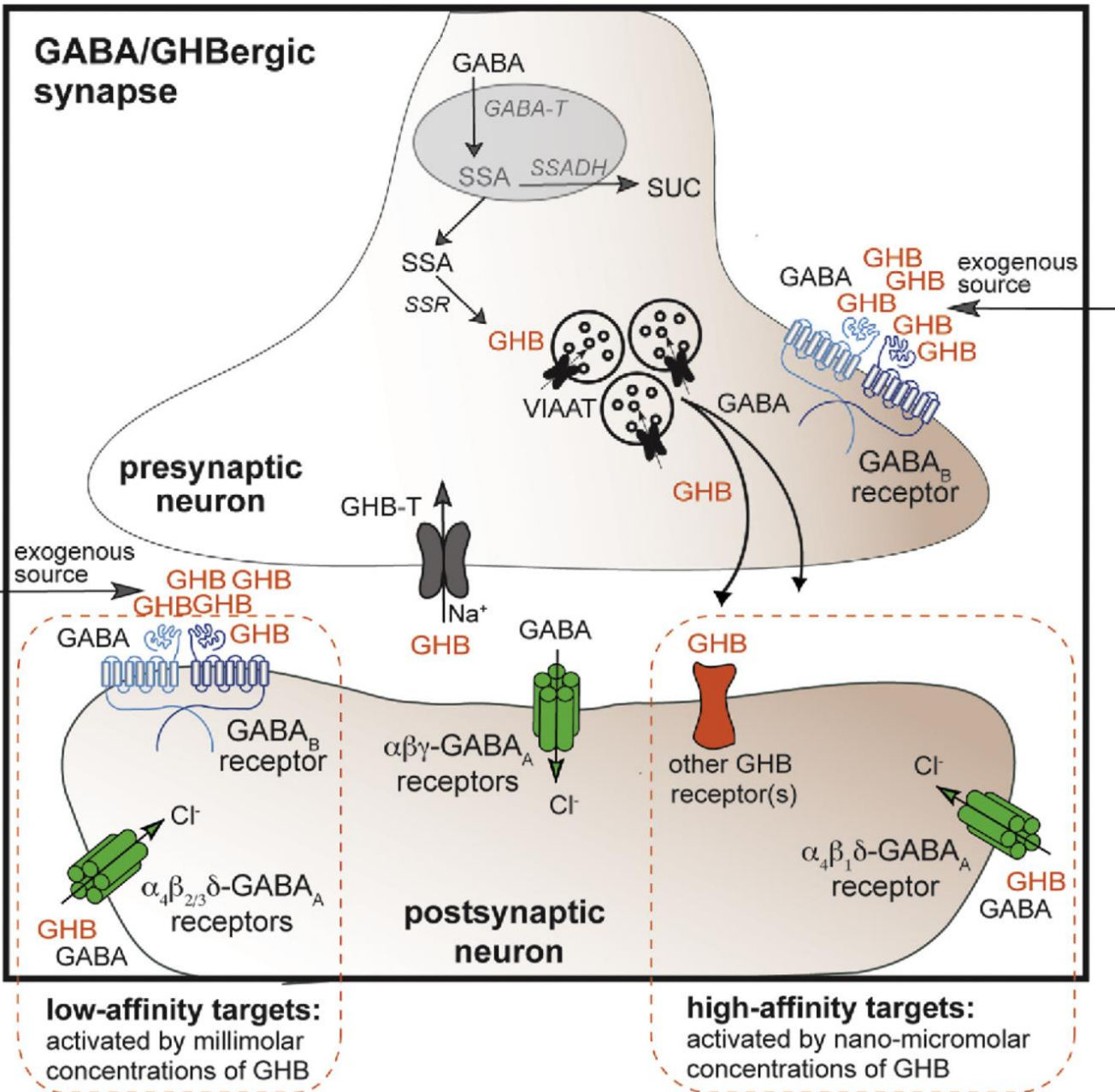
[Corstens D](#)¹.

Author information

Abstract

We describe a case of a 51-year old man who used GHB only in the afternoon and evening during 10 consecutive days in a recreational way: 20 ml a day in 4 ml per 2-3 hrs. He developed an excited delirium syndrome at the second day after stopping. Apparently even after relatively short recreational use severe disruptive behavior can develop. This is a unique case in literature. References are provided.

GABA/GHBergic synapse





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Contents lists available at [ScienceDirect](#)

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep



Full length article

Detoxification with titration and tapering in gamma-hydroxybutyrate (GHB) dependent patients: The Dutch GHB monitor project



Boukje A.G. Dijkstra^{a,b,*}, Rama Kamal^{a,b}, Martijn S. van Noorden^c, Hein de Haan^{a,d}, Anton J.M. Loonen^e, Cor A.J. De Jong^{a,f}

^a Nijmegen Institute for Scientist-Practitioners in Addiction (NISPA), Radboud University Nijmegen, 6525 ED Nijmegen, the Netherlands

^b Novadic-Kentron, Network for Addiction Treatment Services, PO Box 243, 5260 AE Vught, the Netherlands

^c Department of Psychiatry, Leiden University Medical Centre, PO Box 9600, 2300 RC Leiden, the Netherlands

^d Tactus Addiction Treatment, PO Box 154, 7400 AD Deventer, the Netherlands

^e Pharmacotherapy of Psychiatric Patients, Department of Pharmacy, University of Groningen, Antonius Deusinglaan 1, 9713 AV Groningen, the Netherlands

^f Department of Clinical Psychology, Radboud University Nijmegen, 6525 HR Nijmegen, the Netherlands

- N 274, 85% succesvolle detox, gemiddelde duur 12,5 dag, echter relapse 69%!

Detoxificatie middels farmaceutische GHB

- De 'dosering' van illegale GHB bedraagt gemiddeld 600-650 mg/ml.
- De aanwezige farmaceutische GHB in het JBZ bevat 150 mg/ml.
- Xyrem bevat 500 mg/ml.
- bij het instellen op farmaceutisch GHB wordt de eerste proefdosering gesteld op 60-70% van de door de patiënt gerapporteerde hoeveelheid gebruikte GHB per dosis.
- Na 2-3 uur wordt het effect op onthoudingsverschijnselen geëvalueerd en zo nodig wordt de dosis naar boven of beneden aangepast.

GHB detoxificatie



Neuroreport. 2001 Jul 20;12(10):2243-6.

Baclofen antagonises intravenous self-administration of gamma-hydroxybutyric acid in mice.

Fattore L¹, Cossu G, Martellotta MC, Deiana S, Fratta W.

Author information

Abstract

gamma-Hydroxybutyric acid (GHB) is a widely used recreational drug known to exert positive reinforcing effects in animals and humans. The GABA(B) receptor agonist baclofen has been proved to possess antimotivational effect and to inhibit alcohol, cocaine, heroin and nicotine intake. In the present study we evaluated the effect of baclofen on i.v. self-administration of GHB in drug-naïve mice under a fixed-ratio (FR-1) schedule of reinforcement and nose-poking-like response as operandum. Results show that baclofen was able to completely prevent GHB seeking behaviour, decreasing the rate of responding to basal values, without showing any reinforcing properties when made contingent on nose-poking response. Our findings demonstrate that baclofen antagonises GHB i.v. self-administration, supporting an important role for the GABA(B) receptor in reward-related mechanisms underlying addictive behaviour.

Published in final edited form as:

Neurocrit Care. 2008 ; 8(3): 430–433. doi:10.1007/s12028-008-9062-2.

Baclofen and Gamma-Hydroxybutyrate Withdrawal

Jennifer L. LeTourneau, Daniel S. Hagg, and Stephen M. Smith

Abstract

Introduction—Benzodiazepine treatment of life-threatening gamma-hydroxybutyrate (GHB) withdrawal is frequently unsatisfactory. Animal studies suggest strongly that treatment with GABA_B agonists, such as baclofen, will be a more effective strategy.

Methods—A case report from the medical intensive care unit (ICU) of the university tertiary care hospital.

Results—A 61-year-old woman was admitted to the medical ICU for severe withdrawal symptoms from chronic GHB use. This manifested as delirium, tremor, and seizures despite only small decreases in GHB dose and treatment with benzodiazepines. The addition of baclofen allowed the rapid sequential decreases in the GHB dose without seizure or delirium and resulted in long-term improvement of her tremor.

Conclusions—Baclofen, a GABA_B agonist, may be a useful agent in the treatment of severe GHB withdrawal.

Baclofen in GHB detoxificatie?

European Journal of Clinical Pharmacology (2018) 74:349–356
<https://doi.org/10.1007/s00228-017-2387-z>

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION



Baclofen in gamma-hydroxybutyrate withdrawal: patterns of use and online availability

Christopher N. Floyd^{1,2} · David M. Wood^{1,2} · Paul I. Dargan^{1,2}

Received: 11 September 2017 / Accepted: 26 November 2017 / Published online: 3 December 2017
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Abstract

Purpose Gamma-hydroxybutyrate (GHB) withdrawal is a life-threatening condition that does not always respond to standard treatment with benzodiazepines. Baclofen has potential utility as a pharmacological adjunct and anecdotal reports suggest that it is being used by drug users to self-manage GHB withdrawal symptoms. Here, we investigate current patterns of use and the online availability of baclofen.

Methods Data triangulation techniques were applied to published scientific literature and publicly accessible Internet resources (grey literature) to assess the use of baclofen in GHB withdrawal. An Internet snapshot survey was performed to identify the availability of baclofen for online purchase and the compliance of retailers with the UK regulations. Data were collected according to pre-defined criteria.

Results A total of 37 cases of baclofen use in GHB withdrawal were identified in the scientific literature, as well as 51 relevant discussion threads across eight Internet forums in the grey literature. Baclofen was available to purchase from 38 online pharmacies, of which only one conformed to the UK regulations.

Conclusions There is limited published evidence on the use of baclofen in GHB withdrawal, but both scientific and grey literature suggests clinical utility. Online pharmacies are readily offering prescription-only-medication without prescription and due to inadequate regulation, pose a danger to the public.

CNS Drugs (2018) 32:437–442
<https://doi.org/10.1007/s40263-018-0516-6>



CrossMark

SHORT COMMUNICATION

Baclofen to Prevent Relapse in Gamma-Hydroxybutyrate (GHB)-Dependent Patients: A Multicentre, Open-Label, Non-Randomized, Controlled Trial

Harmen Beurmanjer^{1,2}  · Rama M. Kamal³ · Cor A. J. de Jong² ·
Boukje A. G. Dijkstra^{1,2} · Arnt F. A. Schellekens^{2,4}

Table 2 Comparison of (re)lapse in GHB use in the 3 months after detoxification between patients prescribed baclofen (ITT) and patients who received treatment as usual

	TAU	Baclofen + TAU	Test statistic	<i>p</i> value
Patient completed follow-up	55	35		
Lapse (any use)	47% (<i>n</i> = 26)	46% (<i>n</i> = 16)	$\chi^2 = 0.20$	0.885
Relapse (weekly use)	38% (<i>n</i> = 21)	20% (<i>n</i> = 7)	$\chi^2 = 3.29$	0.069
Patients including drop-out	70	37		
Relapse ^a	50% (<i>n</i> = 35)	24% (<i>n</i> = 9)	$\chi^2 = 6.59$	0.010

GHB Gamma-hydroxybutyrate, ITT intention to treat, TAU treatment as usual

^aDrop-out is considered relapse in GHB-dependent patients, therefore only relapse is mentioned

Take home message

- GHB werking op multiële aangrijpingspunten in het brein
- Acute intoxicatie: typisch klinisch beeld> hoeft geen tube
- Spiegelbepalingen?
- Detox bij chronisch gebruik:
 - Xyrem
 - 'Sedatie cocktail'
 - Baclofen?