Complex Management of Gamma Hydroxyl Butyrate Withdrawal

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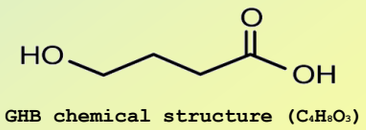
Introduction:

GHB is a naturally occurring short chain fatty acid related to GABA and increasingly popular drug to abuse; is unfamiliar to many clinicians. GHB could rapidly produce effects and dependence that have been likened to a combination of ecstasy (heightened sexuality, emotional warmth) and alcohol (reduced anxiety, drowsiness, loss of motor control) Recent cases of severe GHB withdrawal delirium have occurred in psychiatric and emergency settings making it necessary for the professionals to be informed about the management of these patients.

Case Report:

- A 29 year old single man was assessed with history of poly substance misuse (including alcohol) and use of GHB for last 1 year. He was using GHB (dependence use) every 2-3 hourly and used up to 300ml per day with half the dose at night time to aid sleep.



GHB chemical structure ($C_4H_8O_3$)

- GHB detoxification was commenced in hospital setting using withdrawal rating scales (CIWA-AR, used for alcohol withdrawal) every half hourly with regular review of his vital signs. GABA agonists such as baclofen 40mg qds, acamprosate 999mg tds were prescribed and need for benzodiazepines was minimal.
- Baclofen was very gradually reduced over the two week period and he was discharged on 30 mg qds, acamprosate 999mg tds and also he was commenced on sodium valproate and naltrexone. Baclofen was gradually reduced eventually during which he relapsed twice.
- Currently he is maintaining abstinence and actively involved in relapse prevention work. He was recently diagnosed with features of depression and started on mirtazapine and shown good improvement.

COMPARISON BETWEEN VARIOUS WITHDRAWAL SYNDROMES

Substance	Onset/ Duration	Autonomic Instability	Neuropsychiatric Symptoms	Mortality	Possible Mechanism inducing W/D State
GHB	1-3 hrs/ 6-12 days	Mild	Severe	?	Loss GHB, GABA A, and GABA B mediated inhibition
Benzodiazepine	1-3 days/ 5-9 days	Moderate	Moderate	1%	Loss of GABA A mediated inhibition
Ethanol	Usually >6 hrs/ 10-14 days	Severe	Moderate to Severe	5-15%	Loss of GABA A mediated inhibition, disinhibition of NMDA receptors

Discussion:

- Symptoms of GHB withdrawal syndrome can occur rapidly after 1to 6 hours of last dose due to short duration of action and rapid elimination.
- The average dose and frequency associated with GHB withdrawal is 18gms and 2-3 hourly dose. GHB withdrawal was even after as little as 2 to 3 months use.
- Peak manifestations of withdrawal symptoms may occur within 24 hours.
- A review of 30 cases published has shown that tremor, tachycardia, anxiety symptoms, perceptual disturbances occurred in more than 50%. Some people could with present with just with tremor and changes in blood pressure and were prescribed anti hypertensive and eventually presented with withdrawal delirium after discharge.

CYCLE OF ABUSE, PHYSIOLOGIC TOLERANCE AND GHB WITHDRAWAL PATHOPHYSIOLOGY

Pathophysiology:

- The most important activity GHB possesses with regards to withdrawal syndrome is close metabolite relationship with GABA.
- GHB modulates both GABA A and GABA B receptors (predominant) and that explains the similarity of withdrawal syndrome with benzodiazepines and alcohol
- GABA b is important mediator of GHB psychotropic effects (Hechler et al., 1997)
- Cross tolerance has been demonstrated between GHB and alcohol in rats, and GHB has been used to suppress the alcohol withdrawal syndrome.

Treatment with current research evidence:

- Most of the published evidence is about benzodiazepines in the treatment of GHB withdrawal.
- Milder forms of withdrawal may be successfully treated with benzodiazepines on an out patient basis. (Addolorato et al 1999c; Galloway et al.1997)
- Severe withdrawal states require medical support, high doses of benzodiazepines and capacity for physical restraint to prevent the patient from harming self or others during bouts of psychotic agitation (Dyer et al.2001; Miotto and Roth 2001)
- Craig and Colleagues reported a case of a patient who needed 507 mg of lorazepam plus 120 mg of diazepam over 90 hours to control agitation.
- Other drugs used in the management are Barbiturates (Benzodiazepine Resistant cases), antipsychotic, chloral hydrate, anticonvulsants.
- In the above described patient we used drugs which share same pharmacological action such as Baclofen (acts on GABA B receptors) and drugs like acamprosate (acts on GABA A receptors); sodiumvalproate (acts on GABA transaminase and slow down degradation of GABA).
- Symptomatic and supportive care in addition to sedation is required in medical setting to prevent injury, hyperthermia and rhabdomyolysis

Drawbacks:

- Close monitoring of vital signs during usage of high doses of benzodiazepines.
- Baclofen could cause severe dependence in short time and also present with severe with drawl.
- Anti-psychotics are not efficient and could cause effects such as dystonic reactions and neuroleptic malignant syndrome.
- Anti-hypertensives could be used only in milder cases but could cause paradoxical vasospasm in severe withdrawal.

Recommendations:

- GHB withdrawal should be considered as medical emergency and ideally should be treated in hospital setting for at least 2 weeks due to high rates of mortality.
- GHB should be suspected in cases of coma, seizures or withdrawal when no other etiology can be found and urine drug test is negative (young adults, body builders).
- If suspected or known patient should be monitored in critical care setting until symptoms resolve.
- GHB usage should be enquired as routine measure while obtaining psychiatric history.
- Patients are at increased risk of relapse because they cannot remember the aversive experience of withdrawal and also suffer with severe depression with suicidal ideation, anxiety symptoms up to 3 to 6 months after detoxification.

Conclusion:

GHB is emerging drug of abuse which has sedating and anesthetic properties Even though emerging medical information provides new insights into GHB dependence and withdrawal, research on treatment is an important area to be developed. Psychiatric, emergency and critical care professional need to be aware of GHB withdrawal signs and should coordinate their care to provide safe management of these patients.

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Case Finding

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