

GHB: PARTY DRUG, WEIGHT LOSS PILL, ANAESTHETIC, OR FLOOR CLEANER?

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My presentation today is related to the Australian, and predominantly the Melbourne experience with regards to GHB. For those of us who are from Australia or have seen the Australian newspapers recently, you will understand that, as far as Melbourne is concerned, this is a relatively new 'problem'.

GHB is an endogenous metabolite of GABA, a major neuro-inhibitory transmitter that will come into play later on when I get down to management problems. It is rapidly absorbed via the GIT; peak plasma levels are achieved in about the twenty to sixty minute mark, although there are durations of effect that have been prolonged beyond eight hours and one uncomplicated 'G' overdose, which was on 1,4-B, without sedation, was intubated for forty-eight hours. It defuses across the blood brain barrier readily, which causes a problem when it comes to making an antidote. Its half-life is in the ten to twenty minute range but we see probably the true duration of the effect beyond that. It is easily manufactured with basic skills, all you need is a little bit of salt and a bit of bleach or butyrolactone in the kitchen sink and you can mix it up; it is easy to find the directions, they are available on the Internet - all you type in is G and enter it into Google and you will get enough menus to keep you busy for a week. It is sold as a liquid, and the quality of the manufacture dictates its colour, odour and taste; from the Melbourne experience, the taste is not quite as horrendous as what they must have in New Zealand, but the colour and odour do prevail. And from our experience it depends on the clarity of the liquid as to what you are actually getting and to the quality of it.

As far as history goes, it was first made by the French, who are the only ones who still use it, and they use it in paediatrics. It was used as an anaesthetic agent, but it did not take off very well because the two predominant side effects are seizures or myoclonic activity and vomiting, not two things that people like when they are having an anaesthetic. It was used in the seventies as a narcolepsy treatment, which makes sense as it does help you sleep, and through the late seventies the Japanese released their papers, which saw it explode into the bodybuilding scene, suggesting that it enhanced growth hormone release and muscle building. It does not do anything to increase the rate of absorption or the effects of your steroids - it just makes you sleep more, which makes you feel better.

In the eighties it was used for alcohol and opium dependents and is still used in some settings for those two functions. It has also been used as a weight loss agent, though I do not believe it does anything but keep you sleeping which stops you eating, but that would be effective. It was not used in Australia, but in the nineties were the first social reports, which are consistent. In 1993 the reported death of River Phoenix was involving GHB and every other substance of abuse or misuse known to the human mind. In 1996 the first Australian reports came from Brisbane with nine unconscious patients pulled out of a nightclub and that is when it first appeared on the Australian scene. The heroin drought from 2000 saw a little bit of an increase in usage, but 2001 is consistent with the timelines we have just seen from across the Tasman and was

when Melbourne started to see its dramatic rise; 2002 was the first of our drug facilitated rape or sexual assault cases based around GHB and we do have that problem in Melbourne - there is no disputing that that occurs at this point in time.

The fish [refers to picture], there are three different colours - the clear one is the pure GHB, the red one was made in the sink at work, and that is why it has the slight pinkie tinge, and the blue one is 1,4-B because I could not get all the cartridge ink out of it. And that gets us on to the precursors; 1,4-B is an aliphatic alcohol and it is endogenous in trace amounts. You need alcohol dehydrogenase to convert it, so if you take a bucket load of this and you have been drinking alcohol along with it, you have a competitive inhibition - you only have a certain amount of alcohol dehydrogenase to break it down, therefore you either have an enhanced effect or you have an increased duration of your effect, which can see you remain unconscious or adversely affected for longer periods. GBL, or Gamma-butyrolactone, a lactone ring analogue rapidly converted, does not require the alcohol dehydrogenase.

We get into the demographics of the use, and we see that there are particular genetical dispositions which show smaller amounts of alcohol dehydrogenase, these being the Asian population, African Americans, the Inuits and the Aboriginal population. They are not as readily able to convert 1,4-B into GHB. Both require ingestion for the metabolism to occur.

In Melbourne, mostly we see males, although for the last six months the difference between males and females has been approaching zero; mean age is twenty-seven years and falling; most have completed high school and are either employed or in tertiary education. That comes into the fact that the reason the police haven't been particularly interested in GHB and the other party drugs is that they are self-funded; there is not a lot of crime associated with funding of the party drugs with the exception of the methamphetamines. Most users were homosexual or bi-sexual men up to 2002, but through 2003 the difference between the homosexual and heterosexual community has essentially evened out.

There is concomitant use with MDMA, or Ecstasy - given that the majority of the Ecstasy we see in Melbourne is not actually MDMA. There was a slight rise in the use of cocaine in the 2003-2004 period. Ketamine has been consistent at about 30% and alcohol is in about 75-80%. There has been no intravenous use of GHB in Melbourne and I have not heard of any in Australia - it would be fairly easy to identify them, they would be unconscious still with a needle in their arm. The risk is grossly underestimated by the using population in general. From personal experience, you will lie unconscious while they ring every number in your mobile phone and then when they are tired and they want to go home they will ring an ambulance, not because they think they need one, but because they do not want to leave you in the street by yourself. So I follow with Karl's suggestions that the misinformation that exists in the Victorian scene is horrendous.

Apparently there is a reduced effect on the use of marijuana if you have been using GHB; our presentations tend to be after the third dose and usually not before six hours into an event. So that for us correlates that most of our presentations occur some time after 4am, usually around the 6am mark and it is usually the 'third dose phenomenon.' A number of ideas have come from that, mostly that it might be used to come down

off some of the stimulant effects. Others are using it to end their evening as it is about the time the clubs are clearing out. We do not have too many twenty-four hour events in Melbourne. Most of our events start late at night and finish at about seven or eight in the morning, sometimes we see our clubs hosing people into the streets at about five-thirty, which is when the public transport starts and we see this is the time for most of our presentations.

Given the fact that the low dose effects are what were intended, we do not see people presenting with GHB intoxication at low doses. So anyone who has had only about 10 milligrams per kilogram, we do not tend to see. There appears to be a progression of symptoms and it is linear and it goes in reverse as well. It starts with some myoclonic activity, which is usually associated with the onset of the nausea and vomiting; at this point respiratory depression commences. It starts off fairly invisibly, unless you actually hook these people up to a machine, and it is predominantly related to volume rather than rate in the early stages. They then progress through a horrendously difficult to manage labile conscious state period, where we have the emergence syndrome that you saw the pictures of, but they will quickly without stimulation revert to unconsciousness. Following from this we end up seeing some seizures, which is usually a progression of the initial myoclonic jerking and then they progress into unconsciousness becoming apnoeic and bradycardic.

The management plan is essentially supportive. Airway adjuncts were spoken about previously - there is a huge aspiration risk due to the vomiting. If they have no gag reflex then intubation is a hundred percent indicated in every case. Oxygen therapy for all patients will aid in their oxygenation needs, ventilation as is required based around their respiratory depression. If they become bradycardic, atropine may be indicated as may be adrenaline, also based around the fact that they are often hypotensive. Transport to a facility that has a critical care service is absolutely essential. There are people who have low dose effects who are not requiring critical care intervention. Not everybody has to go to hospital. If they are awake enough, and they are still able to swallow, and they are still able to breathe, and they are trending back towards normal, they are recovering from their drug ingestion and so appropriate referral, for the non critically ill patient, needs to be considered.

There are many things that do not work that have been tried though. Naloxone or Narcan - they may look as though they have had a heroin overdose, they may have pin point pupils, respiratory depression, they are unconscious on the floor and they are hypoventilating, and if you given them the Naloxone all that happens is a transient rise in heart rate and that is about it. It does not do anything to revive them. Flumazenil, the antidote for benzodiazepine overdoses, despite the GABA effects that we see with GHB, does not work either. Gastrointestinal detoxification and extracorporeal elimination do not work. In the quest for an antidote, we have been looking at things like physostigmine. It readily crosses the blood brain barrier, but there are huge side effects with its administration in normal populations. There has been a small amount of research done on it, it is expensive and it also does not work straight away – it is not like giving sugar to someone who is in a diabetic coma, these people do not wake up fast. It may be a consideration and I will talk about that with regard to mass intoxication.

When it comes to the use of party drugs, we see the media loves it when we get ten ambulances turning up at *Two Tribes*, to cart unconscious bodies to hospitals around Melbourne. That is not just a media problem it is a hospital problem, or an emergency health care problem. If we were to have thirty unconscious, non-breathing patients, present within a three hour period - there are not that many critical care beds in Melbourne, in the Emergency Departments; they just do not exist. So there is a lot of discussion going on around how we can minimise that occurring. But if we did have a mass intoxication, I would strongly suggest that you would reserve intubation for those without any gag, use non-invasive ventilation techniques for those who still maintain some gag reflex but were hypoventilating, and administer physostigmine to almost all of them, knowing that one in five of the people you give physostigmine to, is going to then develop side effects that require intensive care treatment. It is not a good drug, it is not the sort of thing you are going to see carried in the ambulances, and it certainly not going to be given out on the streets like Narcan to some of the street workers. There are great problems with using physostigmine, but in the setting of mass intoxication, I propose that it is probably the only thing that we have got to get round it.

I mentioned bradycardia and ECG abnormalities earlier - it is a common finding in GHB presentations that we see throughout Melbourne. It is consistent with the degree of intoxication, with sinus tachycardia and AF being in the higher conscious state areas, and these people are usually not requiring ventilation in the short term and tend to have a normal blood pressure. Junctional rhythms in the first and second degree AV blocks, either the mid range conscious states where ventilation usually commences, progressing to the hypotensive and all-but-dead apneic patient when they are presenting with third degree heart block.

As far as ventilation targets are concerned, when you intubate somebody and you have to give them some sedating drugs to keep the tube in, when do you wake them up? How long do you ventilate these people for, before you start weaning the sedation and hoping to wake them up? Once the ECG trends back towards normal i.e. sinus rhythm, if you wean the sedation at that point, the patient's level of intoxication is usually so small that there is no adverse sequelae.

Predicted usage pattern - I predict that GHB use in Melbourne is going to increase. It is going to increase similar to what we see in Sydney, but I think it is going to level out. There is a large amount of disquiet through the using community in Melbourne to the point of violence, and we now have 'G' and 'non-G' populations at our dance parties. It has really become that bad. The price and availability makes it highly attractive and so that is one of the reasons it is going to go up. If it moves outside the party scene, into our lower socioeconomic areas, which is generally the western suburbs of Melbourne, the impact on the health system will be essentially unsustainable. [Refers to picture] They are the headlines from the 8th and 9th of March this year, just a month ago.

In conclusion, it is an anaesthetic drug and that cannot be under-estimated. It is in widespread use across the Melbourne dance party scene. It has a really narrow therapeutic window, which is the reason that we see so many people unconscious on it. The price is now down to around a dollar fifty to two dollars per mil - it is essential made by people that are using it. There is no money in GHB as far as the

dealers are concerned. And if it migrates beyond the party scene, the health infrastructure in this State is not sufficient to cater for that occurring, in that it will see a huge number of presentations outside of the arena that most of you work, but from where I sit and for the people from Emergency Medicine, we are terrified of that occurring.

Thanks for your time.