Episode 41: Can One Dose Cure Addiction? The Promise and Peril of Ibogaine

Transcript

Hi everyone, welcome back to the Tox Lab. I'm Rebecca. I'm Rob. Rebecca, what if I told you there was a pill that could take away your lifelong addiction, but it comes with a downside, it just might kill you. There's always a downside to good things.

This sounds a little bit too good to be true, doesn't it? The idea of a single pill that could cure you of addiction. But remarkably, that's what we're gonna be talking about this week. We are, of course, talking about Ibogaine, and it sits between ancient tradition and modern experimental treatment.

So I want you to imagine you're someone who has many years of addiction behind them, stimulant addiction, opiate addiction, in theory, any addiction. They're in a darkened room, they take a brown capsule, swallow it, half an hour or so later, the room is as if it's vibrating. Strobe light effects, you start twitching, shaking, you feel like you're being electrocuted, you close your eyes, orbs float past, dancing gods and goddesses, your whole life replays before your eyes. And this carries on for what feels like hours.

And then suddenly the visions stop, as does the shaking, but you can't move, and it feels like you've been there for days. And actually only 12 hours have passed, but it feels like an entire lifetime. But yet remarkably, the cravings, the drug addictions you had, they're no longer there. The question we're gonna be looking at this week is, how can a plant-derived psychedelic cause healing but also potentially very significant harm all at the same time?

Before we jump into today's episode, if you wanna stay up to date with our content, you can find us on Instagram at @the_tox_lab. You can also find us on LinkedIn, we're quite active over there. And if you don't use social media, but still wanna get in touch with episode suggestions or comments about our episodes, you can email us at thetoxlab@gmail.com. So as we've already alluded to this week, we're gonna be taking a look at Ibogaine, which is a compound derived from a plant that grows in Africa.

Ibogaine has become a thing in a few TV shows of recent years. I certainly recall seeing it in Homeland and I think Law and Order might've had an episode on Ibogaine. And it's easy to see why. It's captured the imagination of storytellers because this molecule can cause significant psychedelic and hallucination effects whilst at the same time bringing about healing to addiction, which as we know is notoriously hard to treat.

You can see why it's featured in some of these dramatized stories, but there's actually a lot of truth to the dramatization and we're gonna be looking at that this week. So what's the history of Ibogaine? Well, it comes from a shrub native to parts of Africa. So Gabon, Cameroon, parts of the Congo, and it's used by indigenous peoples in ritualistic settings.

So similar to Ayahuasca in South America. In low doses, it's actually a stimulant drug. So similar to a lot of drugs, actually caffeine, cat we've talked about before, coca leaf. At low doses, it's used really as a stimulant, but at higher doses, you get this significant psychedelic experience and initiation into the tribes is done by taking a large dose of Ibogaine.

And this causes intense visions and an introspective life review. And this has a history going back a long time, but in the 19th century, French explorers brought samples of Ibogaine to Europe. In the 1960s, an American scientist pioneered the use of Ibogaine as a treatment for substance addiction. And so the story goes that Howard Losthoff was a 19 year old heroin addict.

And him and six friends all consumed this bitter powder derived from the root of Tabernanthe iboga, and underwent this psychedelic experience, revisiting his early memories. And 30 hours later, his cravings for heroin had gone. And actually he then became a pharmacologist and in 1985 actually patented the ibogaine molecule, but he couldn't get his treatment approved. At that point, psychedelic drugs had moved from being freely researchable to quite tightly controlled.

We talked about this a few times, haven't we? Looking at LSD in both the Tusco episode and also the Albert Hoffman episode. And so at that point, Ibogaine was considered schedule one, and therefore he wasn't able to carry out his research. Chemically, it's a fairly interesting molecule.

It's an indole alkaloid, as so many plant compounds are. It has a really, really mixed receptor pattern in terms of its action. So it acts like an NMDA receptor antagonist, similar to ketamine, which is linked to neuroplasticity. It's postulated.

This can reset some of the addiction pathways. It's also an opioid, but at the kappa receptors. And these receptors are less well studied than the mu opioid receptor, but these seem to modulate mood and have a role in perception changes. And there's also effects on serotonin and dopamine reuptake, affecting mood and reward.

And what is interesting about Ibogaine is it's converted to nor Ibogaine. It's breakdown product. And Ibogaine has been shown to have a half life. So the time it takes for half the substance to leave the bloodstream of about four to seven hours in most individuals.

But nor Ibogaine, the breakdown product, has been reported to have a half life of up to 50 hours. So it hangs around for a very, very long time. And this is also active, possibly in a slightly different receptor profile, which might explain why individuals who take Ibogaine describe experiences lasting well past 12, 24, 36 hours sometimes. So what is the clinical impact of this compound?

We mentioned that Howard Lostoff tried to patent this in 1985 and couldn't actually get approval to do any studies. But we have in the last 10, 15 years or so started to see studies come out looking at Ibogaine's potential as a therapeutic. So Rebecca, why don't you take us through our first paper this week? So the first paper we're gonna look at today is a prospective observation study involving 14 participants seeking Ibogaine treatment for opioid dependence.

So purified Ibogaine has been marketed at doses of between five and eight milligrams three to four times a day as an antidepressant and an enhancer of mental and physical ability. And at doses around 19 milligrams per kilogram have been associated with attenuation of opioid withdrawal as well as cessation of use. So this study enrolled participants who were dependent on opioids and orally administered staggered doses of 200 milligram capsules of Ibogaine, approximately 12 and 33 hours after the last dose of opioids.

They commenced treatment in early evening and gave multiple doses over a period of 24 to 96 hours with the aim of giving 25 to 55 milligrams per kilogram of Ibogaine with a concomitant benzo and sleep aids. Initial dose was based off of patient characteristics and the experience of the different providers and was adjusted based on patient response and assessment. They were all given a test dose of 200 milligrams. And then when patients were in withdrawal approximately one to four hours after they were given a large dose between 400 and 600 milligrams and then rapidly received smaller doses of about 200 milligrams.

These patients were interviewed pre-treatment, post-treatment and then once a month for 12 months. They also completed addiction severity index light assessments at baseline one, three, six, nine and 12 months post-treatment. They also received random urine tox screens and had to complete depression assessments. So 20 people on treatment expressed interest in the study.

15 people were enrolled. Unfortunately, one died during treatment and 14 completed. They were all aged between 28 and 47 years. All were Caucasian and 50% were female.

And on average, these patients had previously received 4.7 treatments for substance dependence with 58% of these being a detoxification program of some kind and 10 of them were receiving methadone maintenance treatment at the time. In their baseline interviews, they were asked about their opioid use 30 days prior. And on average, individuals had used opioids for 28.8 days. Methadone was the primary drug of dependence.

Three were dependent on codeine and one individuals dependent on poppy seeds. Of those reporting methadone use as their primary drug, six individuals also reported using other opioids including morphine, DHC and buprenorphine. Moving on to the results of this study, subjective opioid withdrawal scores showed a significant reduction in withdrawal symptoms from baseline, but only the drug component of the addiction severity index showed a statistically significant decrease of about 80% from baseline to their 12 month follow-up.

Depression assessments also showed a significant reduction over time, but the medical component of one of the assessments showed a significant increase suggesting an increase in reported health problems or motivation to seek medical care. Unfortunately, the drug data from the urine samples was quite patchy in this case. Only a small percentage of participants tested positive for opioids. One subject tested positive at three and six months.

Two tested positive at 12 months. Of the 11 participants who were followed up all the way to 12 months, 55% of them reported a reduction in drug use and 36% reported a reduction in alcohol use. And they concluded from the study that outcomes were consistent with currently accepted treatments. So relatively small study, but they did follow up for 12 months, which is relatively long.

And actually a lot of people were still abstinent at 12 months. Although the data was perhaps patchy. Depression scores seem to improve. This sounds like relatively positive outcome, right?

Apart from one patient died during treatment. And Ibogaine really seems to carry with it some really severe risks. The reward appears to be great, potentially one dose treatment from addiction. The risks are very real, aren't they?

Yep. So we've got a couple more papers looking at some of the toxicity data associated with Ibogaine. So the next paper we're gonna talk about involves a 61 year old male who presented to a homeopathy clinic for alternative treatment to overcome a long standing opioid dependence related to his chronic pain. He had a past medical history of significant multiple spinal operations resulting in chronic cervical lumbar pain syndrome.

He also suffered with depression, mild hypertension and dyslipidemia. It's important to note that he had no cardiovascular disease history, no sustained palpitations or unexplained syncope, and there was no family history for unexplained arrhythmias or sudden cardiac death. So at this clinic, he was given Ibogaine capsules to blunt his opioid addiction. He ingested a single dose of 5.6 grams, which equated to approximately between 65 and 17 milligrams per kilogram of body weight.

Six to 12 hours post ingestion, he developed severe GI symptoms including heavy vomiting and diarrhea, and then developed altered levels of consciousness and was transferred to the emergency

room. On his admission to hospital, he was pale, barely arouseable and diaphoretic. He had no palpable radial pulse and no measurable blood pressure. A 12 lead ECG showed monomorphic wide QRS complex tachycardia at 270 beats per minute.

He was defibrillated, which corrected his rhythm back to a sinus rhythm, but he did still have a massive QC prolongation associated with ventricular biogenomy, which is a normal beat, and then an abnormally quick beat and then a pause. He was also suffering with a low potassium and was transferred to the ICU where this was corrected. He underwent lots of investigations and there was no evidence of heart disease found, but his prolonged QT interval took about seven days to correct. Luckily, this story ends on a positive note.

He had no further ventricular arrhythmias and passed an exercise treadmill test when all results were normal. They concluded that he was suffering with an Ibogaine-induced QT prolongation co-triggered by secondary hypokalemia. So very, very severe cardiac issues, had he not been transferred to hospital, likely would have died. Yeah.

This is one of many case reports in the literature, isn't it, about how people have taken Ibogaine and either died or come very close to dying due to cardiac issues. And it seems to be particularly cardiotoxic. We think it blocks potassium channels in the heart as one of the off-target effects. This leads to this prolonged QT interval.

It's basically the heart's recharge time between beats where the heart muscles are repolarizing. And this is a relatively common effect seen by lots and lots of drugs, but Ibogaine seems to do it particularly severely. And therefore it really does carry with it this risk of very severe cardiac rhythm abnormalities and potentially therefore death. So we're also going to look at a paper looking at data from the National Poison Information Service here in the UK from calls mentioning Ibogaine from the 1st of January, 2012 to the 31st of December, 2022.

And there were 11 inquiries related to seven different patients, five which were male, all aged between 19 and 41 years. All patients were symptomatic on presentation. All were classed as recreational abuse. And for some of these cases, we do have information as to why they've taken Ibogaine.

So two cases they were trying to manage their insomnia and two were trying to alleviate heroin use. And in all seven cases, neuropsychological symptoms developed, six developed cardiovascular features and two suffered hypoxic brain injuries from Ibogaine-induced cardiac arrest. So one of these cases occurred in February, 2016 involving a 41 year old male with a history of heroin use who had an out of hospital cardiac arrest lasting 29 minutes. He had taken Ibogaine to alleviate his heroin use and had taken an unknown amount between five and six hours prior to his arrest.

He then arrested twice more in hospital 11 and 18 hours after his initial collapse. Once they had returned spontaneous circulation, he was sedated and they managed to narrow his widened QC interval. And unfortunately after three days of supportive care, his neurological function did not recover. His GCS remained at three after his sedation had weaned off.

It was likely a hypoxic brain injury secondary to his first after hospital cardiac arrest as a result of his Ibogaine use. So interestingly, this is UK data showing that Ibogaine is in fact occasionally implicated in toxic cases here in the UK. It really is a two-sided substance, isn't it? On the one hand, there seems to be this emerging data and certainly strong anecdotal data that it can cure something that historically has been incredibly difficult to cure.

We know that addiction treatment is really, really challenging. Modern conventional medicine is either complete detox in a medical facility, which can be awful, substitution treatment, which sometimes

doses are tapered down and people come off the substitution, but actually sometimes they don't. Ibogaine seems to offer an alternative, a third way out, a effectively magic bullet, but at the same time seems to carry with it such extreme cardiac risk that we'd be really unlikely to get this licensed as a medicine. I can see why people choose to try and use it.

We haven't really talked about the other adverse effects of Ibogaine, have we? We've talked about the extreme cardiac risk. The psychedelic phase carries with it common to a lot of psychedelics, nausea and vomiting, but also the hallucinations can be really psychologically distressing. And although on average in that New Zealand data, there was actually a generally positive increase in people's depression scores, people have reported very significant negative psychological harm as a result of Ibogaine.

So whether or not another service here in the UK where you can send your pills to and they will test them reported one Ibogaine detection in March 2018 and the individual had self-reported panic attacks and irregular heartbeat with its use. So broadly consistent with what we've been saying. I think the international control of Ibogaine is quite interesting, isn't it? Because as we said, in 1985 in the US, it was schedule one, in other words, completely banned, hard to even do research.

That's still the case in a lot of countries, but there are some countries where that's not the case. And so Mexico, New Zealand was one that we were sharing a study from. South Africa, there are these unregulated Ibogaine retreats where people can go and take Ibogaine in a setting, sometimes with the spiritual element, the shamanistic things, sometimes not, sometimes purely in a pseudo-medical capacity. There are some issues though.

There's no pre-screening for heart disease or cardiac risk. But even then, as we saw with that one case report, they had no previous history of cardiac disease and afterwards had no history of, like no evidence of real cardiac issues other than this instance after Ibogaine. So that's not necessarily a... That's fair, although absence of evidence isn't evidence of absence.

We don't know for sure they didn't have something underlying. Very true. Fair point. There's no standardized dose.

There's no established protocols. On the other hand though, there are anecdotal evidence of people coming away from these retreats and saying it completely changed their life and it's completely recalibrated their mindset towards addiction and completely changed how their brain is wired. Going back to that New Zealand data, people were on their 4-4-5th attempt at detoxing, weren't they, some of them? What I find interesting with that is a lot of people wanted to come off their opioid substitution therapy methadone.

And we're using Ibogaine as a way of coming off of that as well. It reportedly works for non-opioid addiction too. So stimulant addiction, certainly a lot of anecdotal evidence of people with lifelong cocaine or amphetamine addictions. In theory, I'm not sure we've got any evidence for it.

It might work for non-drug addictions. So gambling and things like that potentially. So what's the future of Ibogaine treatment? I suspect we're going to see continual studies coming out of places where it's not illegal, places like New Zealand.

There have been some research into structurally similar compounds or Ibogaine analogs to see whether they can provide some therapeutic benefit. I think the goal of a lot of this is to try and maintain the anti-addiction benefit but have a better safety profile or potentially remove that long hallucinatory phase. But my question is, is if you remove the vision quests and the introspection, will it still work? That's a really good point.

Is that part of the process? So I want to go back to that original story I was telling at the start. These were actually from somebody's self-reported experience from Aerowid. We can put a link with the episode description.

That individual that least months later reported to no longer be using drugs. So perhaps some positive there and they did survive their experience. I think there is a bit of a take-home message, isn't there? Firstly, that Ibogaine is a thing and when you see it dramatized on the TV, actually there's a lot of truth in the dramatization but it carries with it real risks and really severe cardiac issues which could potentially be fatal and indeed have been fatal in the past.

There is possibly a little lesson if anybody's listening who does work in emergency departments and somebody does present with Ibogaine, be aware of that very long half-life of nor Ibogaine. Some of these people took days before their cardiac arrhythmias settled and so it is one to probably monitor over a longer period of time. So I hope you've enjoyed listening this week. Ibogaine, part medicine, part cutting-edge experiment into addiction therapy, part high-stakes gamble all rolled into one.

I wanna thank everyone for listening. Really do appreciate all of you tuning in and listening to our content, it really means a lot. We recently hit 2,500 plays. So yeah, thank you to each and every one of you who come back and listen each week.

It's really great to think we've built up this little community talking about toxicology and so I really appreciate that. Hope you all have an amazing week and we'll see you next time, bye.