

Episode 55: Space Oil - Etomidate in the Drug Supply and Its Toxicological Risks

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Transcript

Hi everyone, welcome back to the Tox Lab. I'm Rebecca. I'm Rob. This week we're going to be looking at the strangest drug you've probably never heard of. It's called Etomidate.

It's actually got an awful lot of street names. I'm going to throw a few Etomidate street names at you and you tell me if they're true or false. Ooh, I did have a good quiz. So the first one, space oil, true or false?

True. True, correct. One puff faint. Oh, that's got to be false, right?

No, this is true. So I do have to point out these are literal translations of some Chinese words. So there may be some nuance lost. In Korea, it's known as dream juice.

True or false? False. False. I couldn't find any evidence of Korean street names.

Spaceman's milkshake. I so want this to be true because it'd be amazing if it was. This one's also false. Oh, sad times.

And one more, magic smoke cartridge. False. That one is also true. Oh, I'm doing really poorly on my quiz today.

And it's an interesting drug because it seems to have emerged pretty much exclusively in China, Hong Kong, Taiwan, and it's starting to spread outside of that. But actually, it's a drug that's been present on the streets in those countries for some time. And we thought we'd do a bit of a deep dive this week. Before we jump into today's episode, if you want to stay up to date with our content, you can find us on Instagram at @the_tox_lab.

We also have a page on LinkedIn, and we're fairly active on there. And for those of you who don't use social media, but still want to get in touch with episode suggestions or comments about episodes, you can email us at thetoxlab@gmail.com. So Rebecca, it's home today. Space oil, zombie juice, all of those things we've just discussed.

What is it? It's actually a short acting anesthetic drug. And it's used in anesthesia for surgical procedures and things like that relatively commonly. And it was another drug that was developed by Janssen Pharmaceuticals, same company that developed fentanyl.

And it's had relatively wide medical use for quite some time, introduced as early as 1972 in Europe and in the 80s in the US. It's a very, very short acting anesthetic. And when it's used medically, it's normally used intravenously. It can induce a loss of consciousness within 30 to 60 seconds and a sort of hypnotic state lasting three to five minutes.

So it's very, very short acting, very, very fast onset. It binds to the GABA A receptor and it enhances GABA uptake, which is what leads to this loss of consciousness. It's to say its general medical role is in the operating theater. It's used to induce anesthesia, similar to drugs like propofol.

So why are we talking about it? And why does it seem to have all of these slightly strange names in China? So the use of space oil and e-cigarette vaping has surged in Hong Kong and mainland China since about 2023. And the Hong Kong Poison Center recorded 45 cases of space oil misuse presented to hospital between May and December 2024.

And the mean age of people presenting was 17. This case series looks at three cases that presented between April and May 2024 to the pediatric emergency department after vaping, a time date via e-cigarettes. So case one involves a 17 year old male with ADHD who was admitted to the hospital with ketamine cystitis. He had a mild hypokalemia and was hypertensive with a blood pressure of 137 over 84.

A urine tox screen detected cocaine, ketamine, and a time date. He reported daily vaping of space oil e-cigarettes for approximately four months. They then went on to do some follow-up blood tests, which showed a raised ACTH and an inadequate response to a short synactin test. And he was diagnosed with adrenal insufficiency.

Case two involved a 16 year old male who presented with confusion, insomnia, and unsteady gait after vaping space oil weekly for approximately a month. Blood pressure and electrolytes on admission were normal. A urine toxicology revealed a time date and its analog propoxate. His ACTH was within the reference range, but the short synactin test showed an inadequate response and both renin and aldosterone were below the reference range.

Based on this, he was also diagnosed with adrenal insufficiency. Case three involved a 15 year old male with substance abuse induced psychosis who presented with emotional instability. He also reported vaping space oil via e-cigarettes weekly for several months. He had normal blood pressure and electrolytes on admission, but was diagnosed with partial adrenal insufficiency based on a borderline short synactin test result.

Now both case one and two required regular hydrocortisone replacement and follow-up testing in these cases was carried out. And in case one, testing five months after cessation of etomidate showed that he continued to have persistent adrenal insufficiency. So etomidate is a very popular drug in China. So national drug surveillance data from China in 2024 showed that etomidate was the most frequently misused substance on an aquatic and psychotropic drugs and 86.4% of individuals who were using were below the age of 35.

So let's have a bit of a dive onto our cases then and have a look at some of those big words that you said that many of our listeners might not be familiar with, but we probably fire around the lab without really thinking about. Etomidate is weird because it has that gabaergic effect that we talked about that leads to that loss of consciousness and the hypnotic state, which is what the users desire. But it also has another effect and chronic use can actually lead to quite serious hormonal disturbances. And in particular, it can cause what we call adrenal suppression.

So let's dive into the biochemistry a little bit. Rebecca, you're a biochemist. Why don't you take us through the biochemistry aspects? So etomidate can affect how the body produces steroids and the steroid production pathway in humans is really complicated.

So we're not going to dive into it, but essentially it inhibits 11 beta-hydroxylase, which is one of the enzymes that's involved in the production of cortisol, corticosterone and aldosterone. And cortisol, many people have probably heard of the stress response hormone that our body produces when it's under physiological stress, and it helps it deal with external things like starvation. Aldosterone, people might not have heard of, but that's another adrenal hormone that leads to sodium retention and maintains blood pressure. So it's a really, really important hormone for general homeostasis.

And what's interesting is this effect can last up to eight hours after a single dose of etomidate. So it's not surprising that these individuals who've been chronically using it were experiencing these effects for longer. And compare that to the time the drug actually has an effect on the individual. It could be worn off within 20 minutes, and yet they could have eight hours worth of adrenal suppression.

So to unpack a little bit more about what Rebecca mentioned in those cases, there was two other big, long words. ACTH measurement. ACTH is a pituitary hormone, and it drives the adrenal response. So if you've got a blockade in your steroid pathway, there's no feedback and ACTH increases.

So these patients had high levels of ACTH, adrenocorticotrophic hormone. And the other test that they carried out on these individuals was what we call a Shorts and Actin test. And this is where a dose of artificial ACTH is given to see whether the adrenals respond. And in this case, they didn't, did they?

Not only was their pituitary working hard to try and drive their adrenals, but their adrenals didn't actually respond when given a dose of ACTH. And what I found really interesting with this case was actually the first patient, they were hyper-intensive, weren't they? They had high blood pressure. And there is actually an even bigger knock-on effect.

Not only do you not produce cortisol, there's actually a buildup of a steroid intermediate called 11-deoxycortisol, and that can cross-react with the aldosterone receptors. And that's what was leading to this hyper-tensive effect, even though they've got this adrenal suppression. And we do see this in patients occasionally, don't we? There are certain inherited conditions whereby people have inherited blockades of these steroid pathways.

What we're seeing here is effectively an induced form. So, etomidate use is a big thing, particularly as we said in China, Hong Kong, particularly amongst younger individuals. And some of these people are using it quite regularly. And it is leading to some of these slightly surprising medical effects.

Why don't we look at now a more extreme case? So, this next case involves a 47-year-old male who experienced a sudden loss of consciousness while drinking coffee on a boat. Emergency services were called to his aid, but after one hour of resuscitation efforts, the man was pronounced dead. A bottle labelled guava, which contained a clear liquid, was found at the scene, and video footage showed him taking a sip from the bottle before losing consciousness 20 minutes later.

Further investigations by the police found that this man had been known for selling etomidate illegally. A post-mortem examination was carried out which revealed pulmonary congestion and edema with dark red frothy fluid in the trachea and bronchi, approximately 50 mL of coffee-coloured fluid found in his stomach. Histopathological examination revealed tissue, hyperemia and edema, and this also showed degeneration and necrosis of the adrenal gland cells, hepatocyte chord dissociation, degeneration and necrosis of hepatocytes, and a lack of secretion of glucocorticoids from the zona fasciculata gland cells.

Cardiac blood and stomach contents were sent for toxicology, which showed the presence of etomidate in cardiac blood at a concentration of 3.63 micrograms per millilitre. Atomodate was also found in the stomach contents and was also detected in the bottle of clear liquid at the scene, but not in the remaining coffee that was found. ACTH and cortisol were also measured in cardiac blood, which were both low, and the official cause of death was determined to be etomidate poisoning. So this is a really interesting case, isn't it?

In general terms, etomidate is, as we've discussed with those first cases leading to medical outcomes, it's not commonly fatal, and this is one of the rare fatal cases that's been reported. Yeah, I believe from the literature all of the fatal cases that have been reported have been intentional injections. Now this one's a little bit strange, isn't it? He was on a boat.

We don't know much about circumstances. No, it just all sounded a bit strange. It's a very unusual case. What I found interesting was, well firstly, etomidate can be fatal, we think.

That's probably reasonable. Virtually anything in a high enough dose can be fatal. What I found interesting was the degree of necrosis of his adrenal glands. Do we think that was an acute effect, or whether that was, actually, he was a regular etomidate user?

I'm not sure. I don't know how quickly it would cause that effect, whether it is purely down to acute ingestion, or whether it is part of him chronically using and then taking this seemingly quite large dose. If any histopathologists are listening, do drop us an email. That would be amazing.

As we talked about in the previous cases, ACTA seemed to be high and corsets are seem to be low, where in this case both were low. And that I found quite surprising, but I don't know whether that's just a post-mortem artifact that ACTH is low in this case. Or that could indicate that he hasn't been using it regularly. Because if you were expecting regular use, then yeah, you would expect it to be high, wouldn't you?

Yeah. Or, as you say, actually it could be post-mortem. I've no idea what happens to ACTH post-mortem. I don't think I've ever tried to measure it.

No. A possible mechanism, if it was acute toxicity, is etomidate has been known to cause respiratory depression. So possibly the mechanical cause of death in this case was effectively respiratory failure. Yeah, and it did appear that he had lots of pulmonary congestion, so I feel like that fits.

Although I am constantly reminded by our histopathology colleagues that that is completely nonspecific. Okay, so let's move on and have a look at some of the other literature where etomidate has started emerging. So a report from the Philadelphia Department of Public Health dated 12 August 2024 showed that etomidate had been detected in combination with fentanyl and medetomidine in Philadelphia and had been involved in overdose deaths. It's thought that the use of etomidate may increase mortality in patients with sepsis and may increase the risk for respiratory depression when used with opioids.

And this is a real concern, isn't it? Because this is a complete change now from young people vaping it. Not to say that that's not a problem at all, but in Philadelphia we're seeing etomidate mixed in with fentanyl and medetomidine. We've talked a lot, haven't we, about drug adulteration and other drugs getting into the opioid supply.

And to see etomidate move in there as a very short-acting respiratory depressant on top of the fentanyl and the medetomidine is very concerning for people that use drugs, obviously. But it also shows that etomidate isn't limited to places like China, it really is present in the wider drug circulation. Etomidate has also been detected in drug-checking samples here in the UK as well, so it's definitely a bit more widespread than it has been. So analogues further complicate the picture, don't they?

According to the UN Office on Drugs and Crime 2025 Regional Report, etomidate analogues have been spotted and six new analogues were identified in 2024 in East and Southeast Asia. Some of these analogues such as MOC-etomidate are rapidly metabolised into inactive metabolites, so they have the desired therapeutic effect that people want from these drugs, but they don't come with that same risk of adrenal suppression. As we said earlier, this drug really started to emerge in China in 2023, but actually the earliest reports were in 2021, and China has now banned etomidate, which has led to this proliferation of ban-evading analogues.

And some of these analogues possibly are actually safer than etomidate and seem not to carry the same biochemical adrenal suppression risk. But nonetheless, it's going to complicate the picture, isn't it

it? It's one thing to know to be looking for one new drug, but to suddenly have to look for 12 new analogues. Enantiomers also further complicate the picture a little bit, so the R-enantiomer has significantly greater potency and is brought to clinical use, so that is something to be aware of.

And I don't know whether with analogues you'd also get an R and S variant, and one of those may be more potent than the other. And do we know what has been in space oil? No. We don't know whether it was a mix or whether it was just the active enantiomer.

I imagine it's a mix. That would be my guess. Usually easier to synthesise. Yeah, exactly.

So even though China has banned etomidate, the prevalence does seem to still be increasing. So in Hong Kong, the police reported that the proportion of drug users reporting the use of space oil had increased from 1.4% in the first quarter of 2024 to 12% in the first quarter of 2025. So it has increased massively. That's a huge increase, isn't it?

So etomidate is definitely a thing, seems to be more of a thing in China and increasingly a thing in China, but may be spreading wider across the US and the UK, possibly Europe. It's a really strange drug, isn't it? From what I understand, it doesn't have a particularly euphoric effect. And so there's no traditional high.

There is this really unpleasant biochemical side effect profile. Why is it being used recreationally at all? I mean, other than it's cheap and it dissolves in e-liquid, I can't really see why it's emerging in the way that it is. I think lots of people who use it enjoy the very quick loss of consciousness and that very quick recovery that comes with using etomidate.

Interesting. We've seen a rise in vaping traditional vapes amongst young people, haven't we? And perhaps this is the next evolution of that, people vaping things that have a more profound effect than nicotine. I think the adrenal suppression angle with etomidate is really interesting and slightly unexpected.

It's rare that we sit on this podcast and talk about steroid pathways. The fact that it has this weird side effect profile is interesting. And I think it probably does mean that if a patient like this presents to a health care facility, the link might not be picked up. This isn't somebody presenting with typical drug intoxication because the drugs long worn off.

This is somebody presenting with what looks like an endocrine disorder. And actually the fact that it's drug induced may possibly go under the radar a bit. Let's go back to the street names. Some of those were somewhat outlandish, would you say?

Yeah. Space oil. One other one was K-Pod. And the K stands for ketamine, despite the fact there's no ketamine in it.

And it's a very different drug from ketamine. Are these street names more youth orientated branding? Quite possibly. We've talked about this before, haven't we?

With like 2C and how that seemed to be almost marketed. Yeah. And possibly we're seeing the same thing with names like Space Oil. I don't know where Space Oils come from, whether that's a direct translation or whether that's a made up English name.

Yeah, I'm not sure. So what's the control situation? Currently it's been banned in China. Internationally recognized as a medicine, I guess.

So covered under medicine laws, but not internationally controlled in the same way that something like heroin would be. I mean, the fact that it's legitimately used as a medicine does complicate control

quite a bit. Yeah, that's very true. I know the ACMD have proposed further controls, haven't they, to make it a Class C drug.

I think concern that it could spread, particularly amongst younger people. Realistically, all it would take is a shipping container filled with vapes to turn up in a port somewhere. Yeah, exactly. So really in summary then, Etomidate is a thing.

It's here, although we don't really know how widespread it is in the UK and again, probably with the US. There's certainly some emerging evidence that it is cropping up in drug supplies. We don't seem to be at the same level of prevalence they're seeing in places like Hong Kong quite yet. I think it probably is one to watch for, particularly if you are a clinician and somebody does present with unexplained endocrine causes, which is probably a really strange thing to be thinking about in the drug context.

But actually, a picture that looks like congenital adrenal hyperplasia is the pattern we were seeing in these patients. It is possible to measure 11-deoxycortisol, which would be the marker, I think, in that situation, wouldn't it? That would tell you the clue as to whether there was a blockade in that pathway. Definitely one to think about, for sure, and particularly be aware that there are so many potential analogues and that they could well emerge soon.

Well, I hope you've enjoyed listening this week. Do give us a like, do give us a follow. Thank you so much again for tuning in. Hope you all have an amazing week and we'll see you next time.

Bye.