

Episode 88: Decongestants - When Nasal Sprays and Eye Drops Become Toxic

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Transcript

Hi everyone, welcome back to the Tox Lab. I'm Rebecca. I'm Rob. In September 2018, a 32-year-old woman in North Carolina suddenly collapsed at home.

Her husband was a paramedic. He knew CPR. He knew emergency medicine. He knew exactly what to do, but she could not be saved.

There was no full post-mortem examination and her body was cremated. To most people, that should have been the end of the story. Except one small tube of blood remained. Because she'd been an organ donor, a sample had been retained, and when investigators eventually tested it, they found something they were not expecting.

Not cyanide, not insulin, not some obscure hospital drug, they found tetrahydrozoline. Which sounds exotic, until you realise it's the active ingredient for some redness relief eye drops. Prosecutors allege that her husband, former flight paramedic Joshua Hansucker, had been putting eye drops into her drinks. A medicine designed to constrict tiny blood vessels on the surface of the eye had, when swallowed, allegedly caused profound sedation, cardiovascular collapse, and death.

And the story did not stop there. Years later, while Hansucker was awaiting trial, his own young daughter was taken to hospital with unexplained drowsiness, low blood pressure, and a dangerously slow heart rate. Once again, investigators said they found tetrahydrozoline. This week, we're talking about the poison hiding in some people's bathroom cabinets, and what it was in that tiny retained blood sample that may have transformed an apparently natural death into a murder investigation.

Before we dive 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 over there. And for those of you who don't use social media but still want to get in touch with episode suggestions or comments on episodes, why not reach out via our new website at thetoxlab.co.uk. So we are, of course, looking at the phenomenon of decongestant toxicity.

And this has a role both in accidental exposures, but also, as we've alluded to, has been implicated in not just one, but a number of homicides over the years. I want to give a shout out to Taylor Garcia, who messaged us on LinkedIn with this episode suggestion. So thank you so much. And if anyone's got any other episode suggestions that they want us to cover, please do send us a message on LinkedIn or Instagram or get in touch through our website.

Decongestant eyedrops, not just eyedrops. Actually, you can get nose sprays as well as a class of compounds. It's not just one thing, and they all work in broadly this similar way. Peripherally, you're supposed to expose them to parts of your body that you want to constrict blood vessels in.

And so that's eyedrops or whether that's nose sprays, and you have this peripheral alpha-1 adrenergic action. And so alpha-1 adrenergic receptors, if you stimulate them, they cause vasoconstriction. And that's the logic for eyedrops that can reduce the redness in your eyes or the nasal sprays that reduce the nasal congestion. You constrict those blood vessels.

But if you take these compounds and administer them centrally, maybe through putting them in a drink, for example, then they also have activity on central alpha-2 receptors. And alpha-2 receptors form part of your adrenergic system's natural feedback loop. And by stimulating these, you actually reduce the release of noradrenaline. This then leads to central nervous system depression, respiratory depression, low blood pressure, low heart rate.

Ultimately, it can lead to death. And we've talked on this podcast before about xylazine. That is an alpha-2 agonist. That works in this same way.

The difference here is these compounds are designed to be used on alpha-1 receptors, peripherally, by squirting them up the nose. And centrally, they can act on these alpha-2 receptors. So why don't we have a look at some of these compounds? So first, let's take a look at xylometazoline.

So xylometazoline is applied topically in the nose, either through sprays or drops. And this causes localized vasoconstriction, which can be used to treat nasal congestion, sinusitis, and allergic rhinitis. In this first case study, it involves a 40-year-old female who was found dead in her bathtub by a family member. She had been periodically treating allergy symptoms, but had no history of other chronic conditions.

There was no sign of third-party involvement or an explanation for the death, so a forensic autopsy was performed. On autopsy, an extensive hemorrhagic focus was found located in the right hemisphere of her brain, and this was penetrating into the subarachnoid space and into the ventricular system. There were also features of generalized cerebral edema, which alongside the hemorrhage led to brain compression and brain death. Pulmonary edema was also seen, and secondary agonal changes were seen in the heart.

And the cause of death was concluded to be hemorrhagic stroke. So what's the connection? So femoral blood was taken for toxicology, which only showed the presence of xylometazoline at a concentration of 18.6 nanograms per millilitre, and a urine concentration of 499 nanograms per millilitre, which the authors suggested that this showed that she'd likely taken more than the recommended daily dose. So how might xylometazoline have caused this?

So xylometazoline controls vascular tone and permeability on the central nervous system, which can alter blood pressure and lead to complications. You can get ischemic stroke, which can occur as a result of reversible cerebral vasoconstriction secondary to xylometazoline-mediated stimulation of the adrenergic receptor, and a possible mechanism of the hemorrhagic stroke seen in this case is due to hypertensive crisis and cerebral vasculitis, which can lead to intracranial and or subarachnoid hemorrhage.

An ischemic stroke tends to occur after long-term use of these nasal sympathomimetics, and a hemorrhagic stroke is generally associated with acute short-term use. So let's think about this for a moment. Firstly, these compounds are really easy to get hold of. Yeah.

You go to the chemist and ask for a nasal decongestant, there's a reasonable chance you'll get xylometazoline. I don't think it even needs to be a pharmacist, actually. I think you can buy these in the supermarket. Yeah, I think you can also get them on Amazon and things like that too.

Yeah. So what's the rationale for the increase in blood pressure? Because this is different from my alpha-2 stimulation explanation. So I think it's just causing a more widespread vasoconstriction.

And that's then leading to an increase in blood pressure. Yep. Increasing the risk of stroke. And is there any indication as to how much more than the standard dose somebody needs to take to be at risk of this?

There isn't very clear therapeutic and toxic defined concentrations of drugs like xylometazoline. I think the authors had done a back calculation based on the blood concentration and what's in a dose to conclude that she would have taken more than the recommended daily dose, but I don't think they could convincingly say how much more. So I think at standard doses, the risk of stroke is fairly low. Yeah.

But it does rise as people go over and above that recommended dose. And it's more of an issue if you've already got existing risk factors. That is a point with this case. She had no known medical history, but there could have been something underlying that wasn't ever picked up on any doctors appointments.

That's fair. Yeah. So who knows what was actually going on behind the scenes. But it is a consideration that I think a lot of people won't have.

These sprays you go and buy on Amazon and you point up your nose and square and it makes your nose feel better. It doesn't feel like taking a tablet. Yeah. You know, it doesn't feel like I'm taking a medication here that if I use too much of, I might actually increase my risk of serious complication with.

Okay. So why don't we look at one of the other compounds now? So moving on to tetrahydrazoline, which is often found in over the counter eye drops, such as Visine, which is quite a popular brand in the US to treat conjunctivitis and is also found in nasal decongestants. So this review paper lit 18 case studies and two original research articles on tetrahydrazoline and the two original research articles both discussed the use of tetrahydrazoline eye drops, specifically Visine, to falsify positive urine immunoassay drug tests.

So both studies found that the addition of Visine led to a false negative THC result with the concentration below the cartel valley of the assay. That's interesting. I was going to guess that it was going to cause false positive amphetamines. No.

It interacts with the THC assay. I think in one of the papers, it also caused problems with the benzodiazepine immunoassay as well. Interesting. Of the 18 case reports they let out, two reported on drug facilitated sexual assault, two related to suicide, eight case reports reported accidental ingestion.

There were three cases of attempted murder, two intentional ingestions, and one was a combined drug facilitated sexual assault and attempted murder case. 39% of the individuals involved were male with five aged between 32 and 76, and the other 13 cases involved individuals aged between 18 months and 19 years. The most common symptom upon presentation to emergency departments was severe bradycardia, severe refractory hypotension, and loss of consciousness.

Severe clinical symptoms reported in the younger age groups in the form of ataxia, complete CNS depression requiring mechanical ventilation, Cheyne-Stokes respiration, and first degree AV block. At the time from ingestion to symptom presentation varied from as early as three hours after ingestion up to 38 hours. 17 of these cases involved the ingestion of tetrahydrozoline containing drops either directly from the bottle or via a drink, and one case involved forced intravenous injection.

In the majority of cases, the amount of tetrahydrozoline that was ingested was not known until the admission to hospital where they were able to determine the volume missing from the bottle or measure concentrations in biological samples. In 10 cases, the reported concentration of tetrahydrozoline using GCMS analysis ranged from 1.48 nanograms per millilitre to 114 nanograms per millilitre, with a mean concentration of 49.14 nanograms per millilitre, and this was detectable up to 24 hours post ingestion. So not low, low concentration. No.

In terms of treatment provided, 11 case reports mentioned treatments with five cases involving IV infusion of normal saline to maintain blood pressure. Naloxone was given in three cases. Two cases involved the administration of atropine. Three cases used activated charcoal.

Two cases required mechanical ventilation, and one was given supplemental oxygen. So a few of these cases, they were given naloxone. Presumably naloxone didn't do anything. I don't think there was any real response.

I've had a look at the literature and the reports are mixed as to whether there's improvement when naloxone is given in cases of tetrahydrozoline ingestion. But I think in those cases where it has had an effect, it was never ruled out that they were under the influence of opioids. I think that's it. They were given naloxone, really, because you had somebody who was unresponsive, had symptoms that could be considered an opioid overdose.

And so you give them naloxone, right? Yeah, because you do get those pinpoint pupils with a tetrahydrozoline overdose in this kind of class of drug. So it does present like an opioid overdose. So I can see why it was given.

So moving on to a tetrahydrozoline case study, this involved a 76-year-old male with a past medical history of Willis emphysema, a major depressive disorder, who presented to the emergency department 24 hours after ingesting 8 bottles of Visine eye drops, mixed in with wine with the intention of ending his life. He quickly fell asleep and woke up the following day, confused and complained of dizziness and was off balance. On arrival to the emergency department, he was orientated, but had irregular heartbeat and was bradycardic at 54 beats per minute.

During x-ray, his heart rate dropped to 30 beats per minute, which required immediate intervention with atropine, and his heart rate then increased to 70 BPM. He was normotensive with a blood pressure of 115 over 72, and his pupils were of normal size and reactive to light. Blood test showed a low sodium and a raised anion gap metabolic acidosis. His troponin was also elevated, and he was also hypoglycemic.

An ECG was performed which showed third degree slash complete AV block, which is where the electrical signals aren't reaching the ventricles, and he had a heart rate of 37 beats per minute and a prolonged QT interval, and he was admitted to the ICU. There was no concern of acute coronary syndrome or myocarditis, and his elevated troponin was attributed to demand ischemia. He continued having ECGs, which demonstrated sinus rhythm with first degree AV block. So the electrical signal in the heart is now reaching the ventricles, but that signal is delayed, and he still had a prolonged QT interval.

A urine drug screen was performed which did confirm the presence of tetrahydrozoline, which fit with what he was presenting for, and the patient was eventually discharged after receiving inpatient therapy. So this is interesting. He had consumed quite a bit. Yeah.

And although he was clearly quite unwell, and I suspect would not have survived had he not gone to hospital. Yeah. Did survive long enough to get to hospital. So thinking with our toxicology hats on as we're going through our work, looking for drugs in people, are we thinking about these compounds as much as we should be?

I don't think so. They're not routinely tested for in the majority of cases, and when you're looking at what concentrations really mean, there isn't really any data on what constitutes a toxic concentration of these drugs. There was a little bit of work done to look at baseline levels in healthy volunteers, which is a good starting point to kind of establish a therapeutic concentration range. But I don't think there's any sort of established toxic or fatal ranges.

So I mean, two points. Firstly, you've pointed out here that they're clearly quite significant and have real toxicological potential. And secondly, on your point on therapeutic ranges, most of the time, people are either putting these in their eyes or up their nose. Yeah.

And so your peripheral concentration is probably going to be relatively low. Yeah. I'm really worried we're missing cases. Now you've described these things.

I mean, we might be. So because they're often not really screened for, we might be missing cases where they've been implicated in like a drug facilitated sexual assault or in murder cases. Because they're colorless, odorless, tasteless, they're very readily available. People aren't going to bat an eye if they see you whip out a bottle of Visine eye drops.

And because of their role of central nervous system depressant, they do kind of play a role in this more sinister world. Yeah, definitely. Do we have any indication as to how much of a bottle of eye drop it takes? What, to get a central nervous system depressant effect?

Yeah. I'm not sure. In the review article, they mentioned that people didn't know how much they'd taken until they'd like lit the bottle and seen that someone was missing and they could work out how much was missing. But I don't think they really stated what the minimum missing volume was.

And then it's hard to know whether they've been used as eye drops as they should be. And then someone's drunk a bit to know. Of course. What the minimum volume would be to cause these effects.

Yeah, that's fair. One of the groups of people here actually who are at risk is probably children and accidental ingestion. Yeah. Because as you say, these things are widely available.

We often have them. Maybe you don't even have them in our medicine cabinet, right? You might keep a nose spray in your handbag or some eye drops in your handbag. Yeah.

And we know children can get into everything. And so I think there is potentially a real risk here of accidental ingestion from children. And I think you did mention quite a few actually of your cases in that review article were children. Yeah, I think the youngest that they found was a case report of an 18 month old.

And so that's another angle actually thinking about it. Not only do we need to think about this from the context of drug-facilitated crime and death investigations, but actually, potentially clinical toxicity could be a real thing too. Child presents to hospital with unexplained bradycardia and sedation. Yeah.

Do we need to be thinking about eye drop toxicity? Because it's not like these aren't easy to find. It's not like this is a rare compound. One of the things with the nose sprays I found, I've had awful sinus problems in the past, and I've used xylometazoline spray.

And I found that they work for a first day or two, and then you get absolutely awful rebound congestion. Yeah. And I think the temptation there for some people might be, well, now I need two sprays. Yeah.

And that's where I think people might stray into this risk of stroke and potential more central toxicity. Not because this is a sort of deliberate abuse situation, but rather an innocuous spray that you don't think of as being a medicine suddenly stops working. So you squirt a bit more. Yeah, exactly.

So before we wrap up, then let's go back to our early opener of the paramedic who is accused of poisoning his wife and child with eye drops. Where is he now? Well, currently he's not yet been convicted. He's still reminded in custody, alleged to have murdered his wife and potentially poisoned

his daughter.

Interestingly, his lawyers have actually asked if he can be tried in a different court. One of the arguments for moving the trial location is that his lawyers claim that because he's become already, despite not being convicted, infamously known as the eyedrop killer, that juries simply aren't impartial, which I do understand. There is actually an interesting other point to this story and that there is actually another allegation pending. Allegedly, while working as a flight paramedic, he actually deliberately started a fire aboard a medical helicopter.

Oh, really? That's a separate case and currently is also unresolved. Well, I hope you've enjoyed listening to us this week as we explore the slightly surprising world, actually, of eye and nose drops. I hadn't quite realised just how poisonous they were, systemically.

As always, if you've liked what you've listened to, do give us a like, give us a follow, share us with your friends. Hope you all have an amazing week and we'll see you next time. Bye.