

Interesting Cases - Salsitz

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 00:00

This presentation is entitled Interesting Cases: Applying Concepts to Unexpected Real Life Scenarios. I'll now pass it over to Dr. Edwin Salsitz to begin our presentation.

 00:10

Good afternoon, everyone, and congratulations for making it to the end of the review course marathon. This is the last presentation and I'm sure that you have received a lot of very important and good information. One of the things about addiction medicine is that usually we don't have that much of a problem in making a diagnosis, we usually know which drug the person is using and if they're presenting with an overdose or withdrawal syndrome, but occasionally cases present themselves which are a little bit more difficult to figure out. And I'm going to present three such cases and I hope that you will find them to be interesting and educational. I have no financial disclosures.

 00:54

So the first case is called "Name the Event." It involves a 64 year old female. She was admitted to our rehab unit for treatment of alcohol use disorder following a detox protocol. She was treated- she has been treated with methadone maintenance, 60 milligrams for many years. And her opioid use disorder is in remission. She's married, she has a spouse that doesn't have a substance use disorder. There's a little bit of a family history of alcoholism in the family in her father but not in her other close relatives. High school graduate, she's employed in sales. She's in a sort of social occasional alcohol user until the age of 56. An event occurred at that time, which led to increased alcohol intake one year after the event. Eventually she'd met criteria for alcohol use disorder.

 01:47

Her physical exam was unremarkable. Her laboratory work- her comprehensive metabolic profile CBC and lipids were all within normal limits. And her urine drug toxicology tests was positive for methadone as we would expect.

 02:03

So what was the event? Since we're not really live, we're virtual. I'll give you a moment to think about it. You'd have to kind of know about this. There's no real way to figure it out. But the event was bariatric surgery. And the rest of history is that at when she was 56 years old, she had bariatric surgery at that time, she had a BMI of 41.

 02:31

Now, if you know about this, you would you would also say Well, I wonder what type of bariatric surgery did she have. Did she have a Roux-en-Y bypass surgery? Did she have a sleeve gastrectomy. Or did she have laparoscopic gastric banding? And in this particular case, the patient had a sleeve gastrectomy. It has been successful in terms of weight loss, she went from a BMI of 41 to a BMI of 24. However, she now drinks two liters of vodka a day.

 03:04

So here are the different bariatric surgeries which are performed most commonly in the United States. This is the Roux-en-Y procedure where a small gastric pouch is created. And the jejunum is anastomosed to that gastric pouch. So the food contents go from the mouth the esophagus into the pouch and right into the jej- jejunum. The duodenum is left intact so that the gas- the biliary and the pancreatic secretions can go into the jejunum and the rest of the stomach is left inside. This is the Roux-en-Y named after the surgeon whose name was Cesar Roux.

 03:44

This is the most common type of bariatric surgery performed in the United States, the sleeve gastrectomy. So the small stomach was created and the larger part of the stomach is removed, and the rest of the anatomy is left intact, so that the gastric contents empty into the into the duodenum and then into the jejunum.

 04:09

This is the laparoscopic gastric banding, which puts a band between the esophagus and the stomach. And this can be adjusted in terms of the pressure through a port on the outside. And the idea is that as you make this tighter, it is harder to eat a lot of food. This isn't done very often any longer and did not have very good results in terms of weight loss. Again, the most common type of gastric bypass surgery performed these days is the sleeve gastrectomy.

 04:41

So here's an article demonstrating why after bariatric surgery, there can be problems with alcohol. So these are 19 patients. 84% of them were female and by the way, about 80% of bariatric surgery and the United States is performed on women. See these are 19 patients who have had the Roux-en-Y

gastric bypass, they were able to test them preoperatively, three months after the procedure and six months after the procedure by giving them five ounces of red wine on each one of these occasions.

 05:22

So this is the preop, they take five ounces of red wine, and they get a blood alcohol level of approximately point two up of 25 milligrams per deciliter where 80 would be the legal level of intoxication. Three months after the procedure, they've lost some weight. And now they're given the same five ounces of red wine. And now they go up to a level of 60 milligrams per deciliter. And then three months later, at six months, they go above the legal limit in New York with the same amount of red wine. So this is the problem after bariatric surgery, that the pharmacokinetics of the alcohol intake are changing because of the bypass of the stomach.

 06:10

This is a follow up of a long term study of bariatric patients in Sweden. This is looking at for patients who have had the Roux-en-Y gastric bypass, and these are the folks that have had the sleeve gastrectomy. At the end of one year, not many patients have developed de novo alcohol use disorder. But the red bars represent the end of from year one to year two. So at the end of two years, these are the percentages of patients who have developed de novo alcohol use disorder. And you see it's approaching 10%, which is a pretty reasonable number.

 06:50

If you look at patients with bariatric surgery, and you look at other drugs, for example, this is looking at just drug use, in general, this is looking at tobacco, and they had some sort of a composite score for all substance use. There are there there are not there were not a lot of increases in these drug issues. But the big increase occurs with alcohol. So alcohol really is different from the other substance use disorders in terms of the impact of bariatric surgery.

 07:24

So how does this happen? Or why does it happen? And one popular way of looking at it, and many patients look at it this way, is that I substituted alcohol for food. And this has been called the addiction transfer/substitution theory. But if this is correct, then why would there be the two year delay? Why wouldn't it happen pretty quickly after the surgery? And why would it be procedure dependent? Why would it happen with certain procedures and not with others. It also is true that this occurs in patients who have gastrectomies for other reasons besides bariatric reasons, for example, people with peptic ulcers or people with stomach cancer.

 08:08

And in a rodent model, if you take a rat, and you perform the Roux-en-Y gastric bypass surgery on a rat, they will then drink more alcohol post the Roux-en-Y gastric bypass than they did prior to the bypass. And so the more accepted etiology for this problem or mechanism is that you have a different

pharmacokinetic profile of alcohol after the Roux, after bypassing the stomach than you do before.

 08:43

And that explains the difference in the different types of surgery. So the stomach lining has gastric ADH, alcohol dehydrogenase. And this is the first organ in the body that metabolizes alcohol. So when we talk about first pass metabolism, in this case, we're not speaking of the liver, but we're speaking of the stomach. So when you remove the gastric mucosa, you remove the first pass metabolic pathway of alcohol. When people lose weight, they tend to be able to socialize more, they're out in public more, they're at parties more, other events. And the increased socialization has a tendency to lead to more exposure to alcohol. So all the studies show that after a bypass, when people drink alcohol, they have increased absorption of the alcohol, they reach a higher maximal concentration of the alcohol and it takes less time to get to the maximal concentration. So in other words, the small stomach is not inhibiting the gastric emptying into the small intestine. And whatever you drink is going right into the small intestine and you're getting a much more more pronounced effect from the alcohol. So people report feeling more intoxicated after the surgery. And again, it seems to be restricted to alcohol use disorders and not other substance use disorders.

 10:13

The way I sometimes think about it, is the difference between intranasal and smoked cocaine. When people use intranasal cocaine, because it's a vasoconstricting drug, it limits its own absorption. And it takes a while for the cocaine to get into the brain at least minutes. But when people smoke cocaine, it gets into the brain within about eight seconds. And that really makes it feel different. And when we went from primarily intranasal cocaine use to crack cocaine and smoke cocaine in the 1980s, it really changed the landscape of what was happening with cocaine.

 10:53

So are there predictors of developing alcohol use disorder after weight loss surgery? Well, you have to have the type of surgery that removes the gas-, the gas-, bypasses the stomach either by leaving it in or taking it out. It happens more in men than women even though women have more weight loss surgery. Younger age is a little bit of a risk factor. So is family history of alcohol use disorder. And the more you drink before the procedure, the more likely you are to have a bigger problem after the procedure. Other drug use seems to increase the- the risk of this happening. ADHD as mentioned in some of the literature. People who are depressed have a lowest sense of belonging may be using the alcohol to try to deal with those with those dysphoric feelings. And as I mentioned before, the more weight loss, the more exposure to alcohol through socialization. So that in itself is a risk factor.

 11:51

So the key takeaways on this topic is that 10% of patients with bypass surgery have a risk of developing de novo alcohol use disorder, more likely with the Roux-en-Y and the sleeve gastrectomy. Now, some patients after the surgery are very health conscious and will decrease their alcohol intake. But if the- if it's going to happen, it increases over time. It doesn't happen rapidly. It takes at least a year or two years for it to really set in. So I think we need to inform people and monitor them when

they have for weight loss surgery, particularly people that have had issues with drugs before that they have to be very careful. And maybe they should either not drink alcohol or be very careful and limit the amount that they drink. And I just want to give my special thanks to a colleague Alan Geliebter, who alerted me to this issue which unless you know about it, it's very mysterious. So that concludes the bariatric surgery case, and I will move on to the next case.

 12:56

The next case is titled "Rapid Sudden Death after IV Drug Use. So the history here, the case presentation is of a 26 year old male. He has an eight year history of opioid use disorder. Like so many patients he went from prescription opioids to intranasal heroin, to IV heroin/fentanyl over the last 12 months. He's three non fatal overdoses in the last eight months. He's been non compliant with his buprenorphine treatment and psychosocial treatment. He was at home he argued with his mother over dinner, he went up to his room, mother heard a loud thud. The mother went upstairs found him on the floor. He was unresponsive with a syringe and needle in his arm five minutes later. Naloxone nasal spray was administered four milligrams twice there was no response. patient could not be resuscitated by the EMS. In other words, this was a fatal overdose.

 13:59

So the question is what happened to this young man? And you might think, Well, what happened was what's happened to so many people who overdosed on opioids, that this was a typical opioid induced respiratory depression, where the opioid inhibits breathing in the medulla. The respiratory rate goes down, pO₂ goes down, pCO₂ goes up. And if it's not reversed, eventually it's fatal.

 14:25

The problem in this case is that it happens so rapidly. Within just five minutes after he left the dining room table. The mother found him to be dead, unresponsive, and usually an opioid overdose. A typical one, an opioid induced respiratory depression takes 45 minutes, an hour even longer. Otherwise there'd be no way for naloxone to be as effective as it has been in terms of having enough time to respond to the person who's overdosing and administer the naloxone. So on this person's post mortem toxicology, he was positive for fentanyl. And we know that most people who claim they're using heroin are either using a combination of heroin and fentanyl or now, only fentanyl, but he was negative for norfentanyl, which is the primary metabolite of fentanyl. He was positive for heroin, which is very unusual, since it's very short acting, but this this occurred so rapidly, and he was negative for 6-monoacetylmorphine, the first metabolite of heroin, which usually presents within minutes to hours after the heroin exposure, and he was positive for morphine, the second metabolite of heroin, because he had been using heroin and had been chronically exposed to the heroin.

 15:47

So what was this event that happened to him? This is called fentanyl induced chest wall rigidity. It's commonly called or expressed as "wooden chest." Another another term is fentanyl induced respiratory muscle rigidity, and laryngospasm.

 16:07

This phenomenon of fentanyl muscle chest wall rigidity has been known in the anesthesia literature for at least 50 years. The chest wall is most commonly involved in terms of the skeletal muscle rigidity. It's most- even though it's a opioid class effect to a certain extent, it's most common with fentanyl and its congeners. And the reason for that is because of the high lipid solubility of fentanyl. It's most common with rapid IV administration. So anesthesiologists are ready for this, they're ready to treat it and reverse it. And the mechanism has to do with activation of the coeruleospinal noradrenergic pathway following mu receptor activation in locus coeruleus by fentanyl. And I'll show you two or three slides on that a little bit later.

 17:05

Question Mark- dose related? Seems to be dose related, but it's it can happen at lower doses as well. And most of the time it's it's reversible with naloxone, but sometimes it's not. And a drug like succinylcholine needs to be used and that's routinely used in the OR. Ventilatory support is required. And one of the one of the telltale signs of this problem is low or absent norfentanyl in the postmortem toxicology.

 17:37

So this is in Ohio, Dayton, Ohio in 2017. They looked at 100 accidental overdose deaths in 2017 in the first quarter. 99% were positive for fentanyl only three cases positive for heroin. You know speaking to the way fentanyl has replaced heroin. However, if you look over here, the 99% positive of fentanyl, but only two-thirds of those had detectable norfentanyl and norfentanyl appears within two minutes of exposure to fentanyl through the 3A4 cytochrome system in the liver. So the way to think about this is that about 1/3 of these patients died so rapidly that they didn't even pro- they could not produce any norfentanyl- pointing towards the wooden chest syndrome rather than an opioid- typical opioid respiratory overdose. And there's a significant literature on this fentanyl induced chest wall rigidity.

 18:36

This is a little bit older- 2013. This I think is 2016. And this is a paper that's often referred to in the literature. They looked at about 48 cases of sudden death. And in in 42% of those cases, they could not find any norfentanyl on the postmortem toxicology. And the assumption is that these people died of the fentanyl induced chest wall rigidity.

 19:04

So thank my colleague, Dr. Ferland for making these slides. This is a phenomenon having to do with the locus coeruleus, which is the main noradrenergic center in the brain. And the locus really sends neurons down the spinal column, spinal motor neurons, and these motor neurons maintain stability of

the intercostal muscles and the intercostal muscles have to have some rigidity so that our chest wall can breathe in and breathe out. However, that chest wall pressure rigidity has to be the right amount so we can breathe.

 19:43

And what happens when people are exposed to fentanyl... Again, very lipophilic- gets into the brain very quickly. The fentanyl activates norepinephrine because it inhibits GABA interneurons in the locus coeruleus which are inhibiting the release of norepinephrine and this results in increased muscle tone. So, the first mechanism that's been proposed to explain what this- why this happens is that the mu activation on the GABAergic interneurons inhibits their activity leading to disinhibition of the locus coeruleus and leads to hyper contraction of the chest wall, which is pictured here. That's mechanism number one. And that's the generally accepted mechanism of the chest wall rigidity.

 20:34

Mechanism Number two is that fentanyl in addition to activating mu opioid receptors, also blocks norepinephrine uptake in the locus coeruleus. And so that gives you more norepinephrine activity more noradrenergic activity. And as you see on the slide, naloxone does not necessarily reverse this mechanism as opposed to the prior mechanism. And that's why naloxone is not always effective in reversing this fentanyl muscle rigidity syndrome.

 21:14

Going back to just more information about fentanyl itself, a lot of immunoassays now contain fentanyl, contain the the the strip for fentanyl. However, there are many instances of false positive immunoassay results for fentanyl. Trazodone is relatively common. Risperidone and some of its cousins are common. Some of the fentanyl analogs not norfentanyl, and people have reported these other drugs where they had a positive immunoassay and a negative on the GCMS confirmation. And they could find no other drug that they thought could cause it except these particular drugs, but trazodone very, very common. And of course, we all use trazodone a lot for insomnia.

 22:03

Okay, now we'll move on to the next case. And the next case involves a 38 year old female who was admitted to our inpatient rehab unit following an alcohol detox with chlordiazepoxide. This is a number of years ago. This woman never felt happy, anxious, low self esteem. Her father physically abused her, mother ignored that abuse. The woman was raped on the street by a stranger while she was intoxicated with alcohol. She's tried other drugs, but alcohol is is her preferred drug. And that's what she's been using lately, along with some benzodiazepines.

 22:45

Our rehab used to be a locked unit. And we- patients were allowed to have visitors one time a week. And the one time a week was Sunday. She came into the unit I think on a Thursday or Friday, and she had a visitor on Sunday. We had started her on naltrexone for MAT for AUD. And the day after the

had a visitor on Sunday. we had started her on gabapentin for MAT for AUD. And the day after the visitor came in on Sunday. On a Monday, she had a change in her mental status at 9am. And she was found to be somnolent. A rapid response was called. Her O2 Sat was 91%. Glucose was 64, blood pressure and pulse for a little bit low. Her pupils were normal size, she was hydrated, she improved rapidly, and she remained on the unit. We did a urine drug test at the time, and this is what we were testing for back then in 2016. And she was negative for the analytes we usually test for however, we did a blood alcohol level on her at that time, and it was 312 milligrams per deciliter where 80 would be the legal limit in New York state.

 23:54

And so then what happened? We usually think or we usually suspect that maybe the visitor brought in some contraband, maybe a benzodiazepine, maybe alcohol. So we usually think, "Could it be the visitor?" In this case, it was not the visitor. Where did the alcohol come from? The alcohol came from hand sanitizer. This is a case of hand sanitizer ingestion. These are what our hand sanitizer dispensers look like. Inside those- a bag of hand sanitizer. We found this under her bed. She was able to get a bag of this hand sanitizer from a maintenance cart. She bit a hole in the bottom of it and squeezed out the entire contents. What I did not know about hand sanitizer until this case is that it is 62% ethanol. That's a very high concentration of alcohol.

 24:48

In the usual alcoholic beverages that you may drink, you just don't get to that kind of percent. Beer is about 5% alcohol. Wine usually about 13-14. Jack Daniels 44%. Southern Comfort 50... So, there's a lot of alcohol in hand sanitizer.

 25:05


Listerine 25% alcohol. I think there's an alcohol free Listerine. Vanilla extract 35% alcohol. You know, who knew? A lot of alcohol, and the cough syrup, some of them have alcohol.

 25:18

So, she then said she had a five year history of drinking hand sanitizer in health care facilities. She says it's very much like vodka but stronger, and she would drink sanitizer to alleviate withdrawal when she was hospitalized. No hangovers, she said, I also drink Listerine from time to time. And in the past, she's required ICU admission and intubation after the hand sanitizer ingestion.

 25:42

This is a slide that I only want to make a couple of points about. One point is that there is a literature about hand sanitizer ingestion. This occurs primarily in people with severe alcohol use disorder, and very severe psychiatric problems. You can get the very high blood alcohol levels as a case with 700 milligrams per deciliter. And in this case report of 14 cases, there was one death.

 26:07

Now, as I was doing this hand sanitizer case, anything that related to hand sanitizer became very interesting to me. So this is 2017, subway riders in New York City get in a subway car, which is filled with Nazi graffiti, swastikas all over the place. A whole lot of people pull out their Purell sanitizer, and they have some tissues with them. And they were able to remove all of the Nazi graffiti with the Purell and the tissue. So that was a very positive experience with hand sanitizer, and depending on where you're going next, you really don't need hand sanitizer all the time.

 26:46

And that concludes the interesting cases that I had. And I hope you did find them interesting. And I wish you all good luck on your ASAM exam. Thank you.