Week 6 - Alcohol & Sedatives

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00:02

All right. Hello, and welcome, everyone. Good morning. Thank you all for attending. I see a lot of familiar names. So thanks for coming back. If you haven't been with us, my name is Giulia Demello. And I work here at ASAM. And the way that this this office hours works is we'll go through a couple of practice questions that we've prepared. But as we go, you'll have a chance to respond to the questions that are coming and submit any additional questions. So if you have questions, or follow up questions about the practice questions that we're covering, or if you just thought of things as you were reviewing the lectures, feel free to, to share them. And you can do that either by unmuting yourselves and coming on, or by typing it into the chat. And I'll also be monitoring that. So for today we'll be covering and focusing on alcohol and sedatives. And we have here Dr. Ricardo Restrepo with us, so I'll turn it over to him to introduce himself and then get us started.

00:52

Hello, everyone, good morning in the Pacific coast, Eastern Time, almost lunchtime, in the middle of the country, maybe a little bit of breakfast-lunch. I'm really pleased to be here, always trying that together, we will navigate these two topics that are essential. My name is Ricardo. My last name is Restrepo. I work at the VA hospital in Long Beach. And I have been committed to education in different levels with residents, fellows and of course with colleagues in different settings here in in Southern California. And part of my purpose to be honest in with you is like, is kind of be in mutual participation and how we can learn, how we can improve. And I really hope that today with this exercise of questions, we will understand even more, probably some things that you already know, but we will review them in detail. My thank you, Giulia, for putting all your efforts and ASAM to make this journey go in this year, and hopefully in the next year is coming. Good. Let me reduce my screen here that I can read to you. Please feel free to interrupt me during the session.

02:21

We are going to start with the first case, you are seeing a 16-year-old male patient who presents to your primary care clinic because he drank a couple of beers with some friends the other day and quickly- that's very important when we read these in- let's say if you're gonna take the test or not but a little line that hits you right away- and "quickly" developed headache, dizziness, flushing, nausea, and vomiting. What do you believe is happening in his system at this point? Let's take a few minutes.

03:02

And as a reminder, please feel free to put your answers into the chat and seeing some C's and B's.

03:21

So quite a range of answers here.

03:26

And this is really important. Okay, perfect. Let's see the rationale because this is kind of a question that- those questions that make you think twice and makes you have doubts. What we are seeing here is actually what we are almost seeing when someone takes disulfiram actually, that's kind of a case but in this case, it is a genetic component that we know that part of our population has that is certain alleles that basically interfere with the metabolism of alcohol. And going backwards remember that from alcohol to acetaldehyde, it is the activation of alcohol dehydrogenase. But after that, it is that enzyme that the disulfiram inhibits. I'm not saying that this person is taking disulfiram but just to give you that symptomatology that indicates that actually that person has normal activity of the alcohol dehydrogenase but low activity of aldehyde dehydrogenase means almost it inhibits not totally but it is almost ... it is low and that is the reason that the aldehyde increases and creates those symptoms to a person.

04:49

Again, please feel free to come up with ideas, thoughts, or questions in case that you have one but that's the main reason and the main percentage. Okay. Please, Giulia, you help me also if you see in the chat questions or something, right, we pay attention to them. Thanks. I will shout them out. Yes, thank you so much.

05:13

Well, look how interesting this is. During the lecture, we talked about how genetic components and precise medicine broadly is going to be part of our career, just the beginning of it. But we need to pay attention in what is happening in that aspect of precise and genetic components in our field. And this is a question related with that. Always try to go with the most obvious, and from there, you make the conclusions to see if it is something else that gets your attention.

05:49

The efficacy of naltrexone for the treatment of alcohol use disorder is significantly better in patients with the A355G allele polymorphism on exon one, for which of the following genes?

06:09

We have quite a few C's in the chat already.

06:12

It's good to know. Let's see, we have our possibilities there.

06:20

Looks like pretty much consensus on C so far.

06:23

Perfect. I like the consensus. And yes, you are right. And here we go. This is a very interesting thing. Because as you're gonna see more articles coming and actually, in the lecture that we had a few weeks or months ago, we were reviewing the importance of the OPRM1 gene that is on the mu receptor, the opioid receptor, right? What has happened is initially, some articles were pointed out that these was the gene, some other articles are questioning that. But definitely, we need to continue paying attention to this gene. And if you remember, I'm trying to put certain points in perspective, remember that naltrexone helps a lot with this polymorphism also with family member, sorry with family history, and male sex, supposedly on the studies. But again, those things has been back and forth reevaluated and we don't have a consolidated answer that this is just for sure, it is our theory. And it is there. And studies have been shown that we're going in that direction, but you're completely right. And that is the best answer for this question.

07:51

Let's go for another one. Compared- look how interesting this is- Compared with younger persons, older persons are more likely to have alcohol related complications due to: higher overall alcohol intake, higher blood alcohol concentration with same alcohol dose ingested, lower burden of co-occuring illnesses or d- less overall medication use?

08:23

We also have a lot of confidence in B in the chat. Good,

08:28

good, good confi-, good confidence, I like to be confident in many different aspects. Definitely. And, again, this shows that we are definitely in this field actively pulling what we know. Because these are questions that probably some of us will have doubts to, "Hey what in reality is the complication due to", but right away, you catch it. And here we go. Trying to add more into the perspective of this answer is remember that these days, let's say when we are in detoxification with the elderly population due to the changes of the metabolism. That's the reason that many people use I- let's say,

benzodiazepines that goes right away to the conjugation stage and doesn't have metabolites to avoid that effort in the liver and to avoid complications. And this is kind of related with with your with your answer. Good.

09:45

Okay, here we go. Another important topic here. A patient denies recent alcohol use. His blood- his blood alcohol concentration is negative. Which of the following laboratory values is a relatively specific indicator of alcohol consumption, even after the blood alcohol level is negative? Keep in mind and we reviewed this, when we have the lecture, certain changes on, on the enzymes occur. And this is something that probably also will be related with indirect or direct causes or consequences of alcohol in your system and how you can detect. Some people are marking D, which is ethyl glucuronide. But the other answers are something that you are aware: the serum sodium, the GGT and the AST.

10:54

We have consensus on D on the chat.

10:58

Perfect. Well, that's the answer. And remember that as clear as for you this answer is, for many people, maybe not. And keep in mind in addition to the ethyl glucuronide, if we will give you an opportunity to mark the CDT that we will talk later about it. That similar kind of answer that will probably derail you from what you need to think about, but in this case is what is the relative specific indicator for alcohol consumption, in this case, when the alcohol blood levels are negative. Remember that ethyl glucuronide is a real tool that you can use because it captures pretty much between three and five days prior the time that you see the person. And moreso, I hope that I answered, Jennifer, with my brief sentence that between three and five days is when you- great- when you capture the ethyl glucuronide component in the blood.

12:14

What I was going to tell you is this, this is also an opportunity that we will use the laboratory test not to blame or accuse a person of not telling us or telling us the truth. Just to use the tools of laboratory tests as a way of connecting the person, their motivation, changes, and the possibilities to improve the outcome of the three. Okay.

12:44

Very important question these days, especially with the importance of women health, I think it's key that we connect with that aspect. And that we try to educate our population about it. A 20-year-old female college student gets a positive pregnancy test after missing two menstrual cycles. She

presents to your office one week later and is concerned because she reports partying with ethanol heavily over the past several months. Which of the following physical examinations findings will be anticipated in fetal alcohol syndrome?

13:29
It looks like you have a lot of confidence in D as in David.

13:35
Good. And here we go. I know. Now these questions- These are easy questions. Right? I don't think that they are easy questions. These are questions that demonstrate that clinically, and basically, through your experience, you are able to, to catch and develop, you know and evaluate. But remember that in this case, what is really important is everything tends to be micro, right? And it's a narrow nasal bridge. The thin upper lip is kind of the answer as you pointed out. And I'm glad that you captured it right away. This shows one more time how clinically-oriented you are but more than that, how all these years of experience has been leading you to go in this direction right away, but good. And just before we move to these questions, yes to put redundancy into our answers, remember that in the lecture we review, basically the fetal alcohol syndrome- it is the most preventive component of rent- mental retardation in our population and if we catch these on time, we will avoid that kids will go in that direction. And it's so important to use preventive medicine in our practice, really key component.

15:14
Okay, let's move on with the next one. A 22-year-old patient presents for the first time to your practice as a referral for- from his primary medical doctor for evaluation and advice regarding treatment for binge drinking behavior- remember that we reviewed what is binge drinking- with increasing ethanol ingest, ingestion. The most sensitive and first test among liver enzymes to change is likely to be? Here we go. Here is a tricky question, but really important, what is the most sensitive and the first test among liver enzymes to change? Between ALT, GGT, LDH. And AST?

16:10
Looks like we have a mixture between D and B. And definitely a lot more hesitation.

16:15
Yes, yes, I know. I know. These are the questions that always wonder, Where are we going? What is this- affected first? Yeah. But let's move with the answer and see exactly, you put B, some of you put a different one. But remember, prior the ALT or AST, or AST/ALT changes. The first one that is very sensitive and most sensitive. The first test to change is the GGT. It is kind of almost close to the same time. But the GGT is the first one that changes just to to keep that in mind.

17:02

And remember, here we go again, I don't want to be repetitive. But remember the consequences of in the biomarkers that we review and other occasions, biomarkers that are affected indirectly. Biomarkers that are affected directly. We already talked about the EtG- indirectly in that family are all of these and it's important to know when they showed up and maybe when they go down and when when they normalize if we are able to stop drinking.

17:33

Okay. Next one. Why are recently abstinent individuals with a severe alcohol use disorder who have a history of chronic daily alcohol consumption frequently less sensitive to the general depressant effects of barbiturates than nondrinkers? The reason of this question I want to mix benzos, alcohol with kind of a complex situation that we will capture, points here that sometimes if we understand well, we will be able to really figure out options with our patients or possibilities of treatment or understanding.

18:19

But let's review the answers: A- individuals with a severe alcohol disorder absorb barbiturates poorly in the absence of ethanol. B- In the absence of ethanol, barbiturates binding to the central nervous system is depressed. C- enzymes responsible for barbiturate hydroxylation are inhibited in individuals with a severe alcohol use disorder. D- Enzymes responsible for barbiturate hydroxylation are induced in individuals with a severe alcohol use disorder.

19:01

Seeing a lot more hesitation in the chat, but we have a D so far.

19:15

Right... and it's great that we don't know. We don't need to know everything. And sometimes we have questions. But look, some of you were put in your mind in order to choose between not the four of them between two of them and some of you just catch the D, but just to put in the context is which is really important. Many times when we talk about alcohol we talk about the alcohol dehydrogenase and the aldehyde dehydrogenase, but remember that the CYP450 also has some component into how we are metabolizing the different components- in this case alcohol or barbiturates. More interesting enough, when I am drinking heavily, alcohol goes into the path of CYP450 and more specifically, the CYP2E1 and controls that. And in other words, the barbiturate at that point, basically are not capable to really have what they need to do. Suddenly I stop drinking and the CYP2E1 right away- because alcohol is not there- It is able to go there and have the mechanism of action of the barbiturate hydro-hydroxylation. That's what is interesting here in this kind of dynamic of how things work. And I'm so glad that that based on your answer, it seems that you you know this in depth. And that's great that we we are able to recognize this. Excellent.

21:14

Which one of the following tests is the most accurate biomarker of recent alcohol use: GGT, CDT, AST, ALT?

21:35

Some B's in the chat.

21:39

Perfect. And I think we we we can definitely- said- you are right. Initially in another question, I kind of put some words into what we were going to see later. But it's so important that when it's necessary, we see that these biomarkers is extremely useful. When it's not necessary. We don't need to order an expensive test for our patients independent and what is the condition that the patient has, we will use the clinical component, the assessment and if necessary to clarify things we move in this direction. Remember that actually the CDT, you can capture CDT almost three weeks prior three to four weeks prior that the person goes to your office if they have been drinking. And kind of the analogy that I use for the CDT as our accurate biomarker is almost what we do when we have patients with diabetes and the H1AC component of the hemoglobin. Gives us certain lecture and certain parameters to determine if the person had been in good control or not. But here we go. These is a great tool. And you identify that it's one of the most accurate biomarkers. Many people use the GGT. As as the sensitivity and specificity- specificity of the GGT is good too. But remember that this is the FDA-approved biomarker for alcohol use disorder that can can be tracked down in the past if the patient has been drinking.

23:24

Okay. Next one. Very long. I know. I'm going to try to read fast. And let's see what we can come up with. A 26-year-old man is brought to the emergency department by his roommates two hours after he became agitated and confused. They report that he was not drinking alcohol or using illicit drugs prior to the change in behavior. For the past six months, he has been taking a liquid supplement obtained from a trainer at his gym. He had used the supplement every two to four hours daily, but stopped six hours ago because he had begun to need more of it to achieve its calming effect, and he was unable to fall asleep without using it. He has no history of serious illnesses and takes no other medications. The patient is agitated and restless. He says he hears voices he doesn't recognize and sees things moving that are not moving. His- his pulse is 104 and blood pressure is 170 over 100. Physical examination shows vertical nystagmus and a fine tremor in both of upper extremities. He is unable to sit through the examination and paces around the room. Which of the following is the most appropriate next step in the management of this patient condition: Ivania says A and the A

24:54

A great, Eliza- A- perfect, Jenny for A and you are right, you are right, a very extensive description. But here we go. It is part of our reality. In our clinical settings, we need to put all the pieces in order. And right away, you basically capture the the need of diazepam. I wonder if in the chat, you, you kind

of detect probably what this patient is getting at it from from the trainer at the gym? I don't know if you probably catch it already. But I just want to see what do you think he was taking?

25:50

Also as a reminder, feel free to unmute and share it or put it into the chat as well.

25:56

Exactly, what the trainer was giving to this young person? What do you think? What was the- GHB? Perfect. Perfect. Thank you, Michael for for saying it. Yes, GHB. And remember that GHB is part of that sedative component that initially, GHB is a neurotransmitter. GHB has an interesting behavior in our system, because initially activates the GHB neurotransmitter if you take it when higher dosages activate a dopaminergic system. And that's the reason that people feel that pleasure versus activation of the system with the GHB component. And basically the treatment is like when you treat, let's say barbiturates withdrawal, or benzos withdrawal. You can use in this case, benzodiazepine to really try to access this patient with the GABA system. But remember that GHB goes to the GABA-B. And remember that the benzos go to the GABA-A, but helps with the GABA component. And that's the reason that diazepam is kind of the answer for this question. Thank you so much.

27:30

Of the following instruments, which instrument assesses alcohol withdrawal severity?

27:42

We don't need to go around and around, I think it's a question that if we pay attention, what in reality is is alcohol withdrawal, is the CIWA. The other ones assess the possibility of a person at risk, or starting to have difficulties with alcohol use disorder, even mild and that's when using the AUDIT or the CAGE, we can start the preventive measures that this will escalate to difficulties and change behaviors and actions in our patients. But the CIWA- it is the answer here. And we are always familiar with it, taking the opportunity of the CIWA. Remember, that it's not written in stone. But we have a person with certain numbers of the CIWA- that's when we're going to start the treatment and we have a person in the 15 range of the CIWA is something that definitely we need to move in that direction. If we have person on eight, we can observe the dependent of the symptomatology. But it is key that all of us are familiar with it. And of course the COWS you know, with the opioid use disorder component, a tool, probably a tool to help us with the buprenorphine induction or buprenorphine initiation as we know.

29:09

Okay, next, very important component in our field sometimes. We talk a lot about AA, but it is key to really put in perspective, aspects of it. Which of the following form the primary basis for the underlying philosophy of Alcoholics Anonymous, espoused by its founders?

29:35

You already have some D's in the chat.

29:37

Yeah. Yeah. Perfect. And that's what it is. And interesting stories. When the founders, let's say, start to integrate their- their potential of changes, Bill, actually, maybe you know this anecdote, but Bill was having such a strong difficulty with maintaining his sobriety, suddenly, and I don't know how he was able to connect with his partner, Doctor..., I forget his last name, to be honest with you, the doctor of AA. But he was able to talk with the wife of the doctor. And in that moment, the wife was seeing her husband lying on the floor drunk. But she woke up the doctor and said, "Hey, there's a person coming to visit you." And the doctor said, "Okay, tell him that I'm going to be here, but I don't have much time." Well, guess what? That meeting ended up a three to five hours meeting between them. And that was the beginning of the AA conceptualization as you reviewed. It was an individual in recovery, an individual component of working together to help each other. And that's kind of the story behind the AA initiation.

31:10

Okay, next. When, when asked about changing his or her drinking related behavior, the patient replies, quote, "I know, I shouldn't drink so much, because it's causing me a lot of problems." Based on this statement, you will infer that the patient is in which stage of change: precontemplation, contemplation, preparation, action?

31:50

I see some B's coming through.

32:01

Perfect. Excellent. Well, you're right. And key enough is motivational interviewing is such a big component of our intervention and recognizing what stage the person is- to see we can resonate on that level of what it is called sometimes as the dancing with the person. Instead of clashing with the patient, let's try to dance- to see if I can lead this person to dance with us and between, between the person and us as the clinicians. And definitely this person is definitely in the process of considering, but he hasn't done yet the move to make the change. And that's the main reason that he's in the contemplation stage. And many of you as primary care clinicians that when sometimes our time is so valuable in our clinic, and we need these days to move so quick in our appointments and 50 minutes appointment, again, is related with with the MI component, but remember the SBIRT- a Screening, Brief Intervention and Referral. That's actually a key element that in the 50 minutes can make a difference in our population. And I know that I'm mixing things here by trying to, to kind of make these these dialogue more open to remember certain points that are key in our practice.

33:38

Okay. Here we go with another question that is important here. The main difference among benzo- benzodiazepines relates to which of the following? Pharmacokinetics, sedative properties, anxiolytic effect, psychomotor performance effects?

34:01

I already see some A's in the chat.

34:10

And you're completely right. The pharmacokinetics is actually the main component and the main difference in terms of the benzos and is key because it's not what is the anxiolytic effect. It is not the psychomotor effects. It is not the sedative properties. It is the pharmacokinetics- how as soon as that medication goes in our system, how the metabolism is, how the absorption is, etc. I thank you.

34:42

Which of the following statements regarding benzodiazepine use disorder is true? A- benzodiazepines are remarkably unsafe when taking in overdose alone. B- the combination of buprenorphine and therapeutic benzodiazepine is unsafe. Benzodiazepines attach to the GABA-B receptor subunit to exert their effect. D- alcohol dependent patients and their offspring are more likely to experience mood elevation with benzodiazepines.

35:30

Great, you are moving with the D and this is a good opportunity to review as we were reviewing genetic precise medicine. Now through studies, basically, we see this component of patient's offspring, likely to have mood elevation instead of sedation with benzodiazepines. And this is a good opportunity to kind of put in perspective what what we review earlier- benzodiazepines attach to the GABA-A receptor. Remember that? Benzodiazepines need GABA.

36:25

Oh, oh, it looks like you're muted.

36:29

Yes, I don't know what happened with the system and it kind of stopped for one second, my apologies to all of you. And as we were talking, I was kind of reviewing with you the importance to remember that benzodiazepines need GABA to open the gate and the receptor. But remember that barbiturates by themselves, they are able to open the receptor. The frequency, it is the key element that benzodiazepines have to open the receptor, then duration goes in alliance with the barbiturates. And

those are little things that are key elements here. If you remember what parts of what we review in the lectures- these days pretty much is so difficult to see just sedative use disorder by itself. But it's so key to really pay attention that many times behind the sedative use disorder is another drug or alcohol behind. And it's important to keep these in consideration when we assess these populations.

37:48

Next one, please. Evidence exists for the involvement of which neurotransmitter in the mechanism of action of the benzodiazepine at the receptor site?

38:06

A- norepinephrine. B- serotonin. C- GABA. D- aspartate.

38:17

I'm seeing a mix of C's and A's.

38:39

Perfect, as I was mentioning earlier, remember what we just reviewed. That benzodiazepine to really get inside and allow that that channel will be open. The receptor channel will be open and chloride will be able to get in. It needs GABA. That's pretty much the component that we were reviewing earlier but this is a question confirming basically, the- the need of benzos for the GABA at the receptor site to open.

39:19

Very long, you can listen to my voice or some of you read faster than I do, but I'm going to try to read as fast as I can. A 23-year-old Army veteran of Operation Enduring Freedom is referred for an evaluation of prolonged and heavy use of benzodiazepines over the past two years. While in Afghanistan, he was in an armored vehicle that was hit by an improvised explosive device, leading to the death of two of the members of his platoon. Soon after he returned home he developed symptoms of PTSD. Despite the urging of his wife and friends, he didn't seek treatment at the VA. He was given an alprazolam tablet by a friend, that he experienced significant temporary relief from his anxiety and physiologic arousal. He began seeking out alprazolam and other sedating medications, and will buy them of the street and obtain prescriptions after presenting with complaints of acute anxiety to various urgent cares clinics and emergency rooms. He was able to obtain a steady supply of alprazolam and clonazepam and was taking an average of eight milligrams of alprazolam, and four milligrams of clonazepam daily by the time he was referred for treatment.

40:43

He has been unable to maintain any employment, and he's on the verge of a divorce, and his wife

demanded that he seek treatment to get off the pills. During an intake assessment in the substance use clinic, he acknowledged that he used benzos and problematic and says that he's motivated for treatment. He also reports being scared of stopping the medication as previous attempts to quit on his own have led to intolerable side effects such as nausea, with vomiting, severe shaking, extreme anxiety and inability to stay- to sleep. And one episode of blacking out according to his wife. He has not able to go for more than 36 hours without using benzos in the past six months. Given the above description of this patient's use of benzos, what will be the most effective pharmacological strategy for managing withdrawal symptoms, and some of you already started to answer.

41:52

Would you mind reading the options just for the-

41:55

-for the recording purposes. A- discontinue alprazolam and clonazepam, initiate divalproex. B- discontinue alprazolam and rapidly taper- three to five days- clonazepam. C- rapidly taper- three to five days- clonazepam. D- slowly taper alprazolam and clonazepam at 10% per month?

42:16

Quite a few Ds in the chat.

42:19

Yes, complex story. And right away, you right away find the answer. But what is key here is that one, we talk about the systems and possibilities of tapering. Some of you are from the school that you feel comfortable managing a taper with two benzodiazepines. I am coming from a school that I learned or we learned to consolidate with a long-acting benzo all the benzos that the person takes. And of course with the scale and equivalents, we try to match that. And then we start to taper down and slowly by 10, or 15% per month.

43:07

Something that you know, and we know is that when we do benzo tapers drastically and quickly, they rebound- the withdrawal symptoms are going to be on our face and more complications are going to come up and showed up. Some of you are from the school of probably using clonazepam to consolidate all the benzos that the patient takes. Some of us use diazepam or clonazepam. In this case, the clinician felt comfortable doing the taper with two and that's it. That's the answer.

43:46

Now. Remember, that strategies for benzo withdrawal are different. And I encourage you to explore other lectures that probably you're gonna get more data about. Some people when they say, let's say that the first month or two months didn't, didn't go as well as we expected. Some people use

that the first month or two months didn't, didn't go as well as we expected. Some people use clonidine patch, for example, in addition to the taper, and of course, other prm medication let's name it- trazodone for sleep, or gabapentin, right? But just to give you kind of tools outside of what is FDA approved, but importantly those tools for you to keep in mind. And many of you also maybe have been using anticonvulsants. Some people use carbamazepine. Some people use depakote or some some people use oxcarbazepine because it is better tolerated in the system of the person. But those are the strategies.

44:58

And again this person as veteran with PTSD- definitely is going to be- more than the taper- is how we're going to treat the PTSD. And I'm going to add a line it will go probably a little bit outside of what the main objective is today. Remember that the PTSD, hopefully you will start the treatment with an SSRI. Either sertraline, either paroxetine, and you have other tools in place. If the person has vivid nightmares, you can use prazosin as to as a tool to to to reduce the nightmares. And of course, you have now the possibility to do the taper with this person. But many complex stories. And I know that you found the answer right away. But more than that, we know that we have many different fields to see where where do we need to do first with these complex situations that we face in our practice.

46:00

Okay, next one. Which of the following will be unsafe for a patient with severe hepatitis C and/or liver failure? A- Temazepam. B- Lorazepam. C- Diazepam. D- Oxazepam.

46:17

We have a lot of confidence in C's in the chat.

46:21

Yes, as I said, I love confidence because confidence goes with knowledge. When we are over-confident is when probably we start to make certain steps that are leading us to difficulty but yes, your confidence leads you to the right answer.

46:38

Just to review what you probably already know with these answers is: What are the three benzodiazepines that jump right away to the conjugation- are those three- the LOT. Lorazepam, temazepam, oxazepam. Exactly, Ivania just mentioned the LOT. That's key. Then, as we know diazepam had to go through oxidation, and has a lot of metabolites. And it requires a lot of efforts from the liver. And it's a long acting benzo. It can stay in your system for hours and hours. Remember, something important that when we have a person on diazepam, and we try to conclude the taper, and let's say that we conclude a taper because the pressure from many agencies or from the administration is, "Hey Ricardo, nobody can be on benzos in this hospital for more than two

months." And you, you you let yourself go with that abrupt change and you taper the diazepam quickly. Remember that the diazepam withdrawal is not going to come maybe in the first week, it comes after and then more complications, more difficulties are going to show up.

47:56

In summary, let's be gentle with tapers when it's necessary. Let's be gentle in the approaches, let's be open with the possibilities that we open to our population to really respond better to our measures and our steps. And an additional tool that is again, outside of the scope of FDA approval is still as we know, the the standard of treating detox alcohol detoxification is with benzodiazepines. But as you know, right now, many people are using alpha-2 agonists, you know, for the taper- clonidine for the for the withdrawal. Some people are using phenobarbital- many other components that here we go we need to consider and we need to understand how people are doing it, but important to know how we can practice an exercise good medicine. Okay.

49:07

That was our last prepared practice question. But are there any additional comments that you would like to reemphasize for participants? And then if not, we can also open it up to additional questions.

49:22

I will say as a matter of keeping in mind all epidemiologically it's important and we review these, probably one of the key elements to remember these days is in terms of genders. For long time people thought that males drink more than females and right now these days we're almost equal.

49:46

Keep in mind that that epidemiological component of how key it is, again don't take me wrong with what I'm going to say... These days we are targeting opiates. And we need to target the opioid epidemic. And we need to target the fentanyl. But remember that tobacco, alcohol are in our face. And we need to pay attention to those components and to try to execute preventive measures into not letting that person that in the AUDIT, it is maybe on number five or so on. And we are ready to do the intervention, the AUDIT-C I'm talking about, and we are ready to prevent that that person will escalate to bigger numbers. Let's use the tools, let's use, let's say, evidence based approach. That's kind of what I just want to mention in brief before we open the floor.

50:46

So at this time, if y'all have any additional questions, please feel free to type them into the chat or, or to unmute yourselves and jump into the conversation. It makes it easier if we can have open dialogue.

51:05

51:03

We'll give a minute just in case someone is typing because we can't see the typing bubbles.

51:20

We do have a comment in there- the same for the exam we can answer as the rate being equal between male and female as far as use goes? And that's correct. Right? That would be the correct answer?

51:32

And let's say if you -it can be the correct answer depends of the context of the question because it still is a little difference. It's- it's a little difference in the, in the studies. But if if they give you an answer, if they give you the answer, and you see that that's the most correct one, and they don't give you kind of a little percentage of the difference. You can definitely use that as as the answer of your question. Yes.

52:03

The other context in which it could be honest, is also as a- like change over time. So you know, how has the epidemiology of alcohol use changed over time?

52:14

Yes, it has changed. And definitely. Let's say, let me see quickly. Here, I'm going to try to put in the context. Gender-wise, the 12 month prevalence of alcohol use disorder right now the differences in in studies, and one of the main studies that is done by Grant and collaborators in 2015. It was men around 18%, if I remember correctly, and, and women 10%, 11%. That shows you more or less that little difference that I was talking about. But in the past, supposedly, it was even much bigger than that. But we are seeing the tendency of how, how the trend is changing. And also to take in consideration, the binge drinking in women is something that people are paying attention these days in studies. And as we know, based on the metabolic components of the LDH enzymes, in our, in our system, the gastrointestinal system, the liver system, the women doesn't have too much the capacity to run faster their enzyme, that will kind of filter better the alcohol and that's the reason that people get drunk easier. And of course, the the cell adipose tissue versus water. All of those components lead us to keep in mind the epidemiological, but also how the alcohol is playing a major role right now in our population and our gender that we need to pay attention to and have more studies about, yes.

54:10

Now we have another question that says is there ever a time where it is safe to use benzos for panic in patients with alcohol or sedative use disorder history?

54:20

If I understood the question is, it is okay to use benzodiazepines in an outpatient setting to use them for detoxification... Am I right with...

54:30

So for panic. Is there a time to use it in an outpatient setting for panic in patients that have a history of AUD or sedative use disorder.

54:40

Okay, good question. And these are questions that I will try to put in with the big picture of the clinical component. I will say it is possible to consider a benzodiazepine for a short period of time on a patient with history of alcohol use disorder or benzo use disorder considering the clinical presentation. But it's so key to see if you have other strategies to implement first, prior moving with the benzodiazipine. I'm talking clinically about it, let's say that I have a person with panic disorder that yes responds extremely well to benzos. But just recently got discharged from the hospital after alcohol detoxification. Last dose of benzos a week ago, maybe, maybe that person will be will need an SSRI. And if it is not benzos between- here we go, non FDA approved but all of us use it- a short trial of gabapentin to see if we can control the anxiety. Try to use other strategies first, but the answer is individualize your care. And if you think that it's important to prescribe it for a short period of time, I will be open to that with with good kind of follow up and good, good analysis of of the outcome. Yes.

56:19

And then we have another question that is how is the metabolic behavior of the ADH in the Asian population?

56:26

Great, great question. Yes, in the Asian population, as you know, it is a component that is related with allele number 22. If I remember correctly, probably I'm wrong with it. But in that population pretty much why that is similar to a case that we saw at the beginning with that young person, because it is based on a genetic allele that doesn't have the capacity to make the enzyme work as in other populations. And that's the reason that the flushing comes because the aldehyde starts to increase in in the system with one beer or one shot of of hard liquor. And the aldehyde starts to increase similarly to when the disulfiram arrives and blocks the aldehyde dehydrogenase and it can start to accumulate the aldehyde in our system. But it's pretty much a pure genetic component of our allele. And maybe I'm wrong. Please check it again. It is allele 22 but or allele 222. But check that out. Yes.

57:51

And we are right at time. So I want to be considerate of your time. I know you have a busy schedule. But thanks, everyone, for attending and for being with us here today and for submitting additional questions. And then thank you especially to Dr. Restrepo for being here with us. Is there any final

closing thoughts that you want to share or anything you want to say?

58:11

No, I want to say all the best to all of you. I really appreciate you being here. I know that it's an effort for all of us to take time for all of these. I wish you the best in the future. And I hope to see you soon. And in one way or another just a little addendum that when when I was mentioned in my doubt about the aldehyde acetaldehyde dehydrogenase. It is the A-LDH22 well-known mutation in this population that you were asking me for. Just just to be sure that I answered correctly your lessons. Yes.

58:50

Thank you so much. So with that we will conclude and I hope to see you all again next week. Take care. Thank you so much.

58:58

Bye bye. Thank you