Methamphetamine Use Disorder, Mental Health Sequela, And Treatment In Primary Care

Key "Take-Aways":

1. Primary care is an essential access point to care for people who use stimulants and are experiencing psychiatric symptoms.
2. Understand the psychiatric manifestations secondary to methamphetamine use.
3. Become familiar with the medications to treat psychiatric manifestations secondary to methamphetamine use.

Presentation Transcript:

Hi, my name is Jo Sepulveda. I work as the Chief of Psychiatry and Medical Director for Substance Use Disorder Services at Family Health Centers of San Diego. The title of my talk is "**Methamphetamine Use Disorder, Mental Health Sequelae, and Treatment in Primary Care**." And I plan to cover how a busy clinician can engage patients, gain knowledge on the psychiatric sequelae secondary to methamphetamine use and treatment. We hope the content is useful to you as you care for patients who use substances.

There are three takeaway tips that we'll focus on today:

- Engaging patients with stimulant use disorder in the primary care setting.
- Understanding the psychiatric manifestations secondary to methamphetamine use.
- Treating psychiatric manifestations secondary to methamphetamine use.

Overview of Challenges on Methamphetamines: (00:47)

Methamphetamines has been a growing problem across the nation for a significant period of time, and you can see the growth here as far as overdose deaths due to methamphetamines from 1999 to 2020. Juxtaposed into this slide, you can also see the correlation with methamphetamines mixed with opioids and the relationship with those deaths.

Primarily, much of the mixtures that are causing overdose deaths at the present time are due to fentanyl. And there's challenges with dealing with this patient population in the primary care setting:

The first has to do with **ambivalence on the need to discontinue using** methamphetamines or stimulants. Many patients don't see it as a problem, and that's a major problem or barrier to engaging patients in stopping their substance use.

Cognitive impairment is a growing issue, particularly with the stronger formulations of methamphetamines that are being used. This also causes **poor memory**, **clouded judgment**, and this all leads to **poor treatment retention**, both when you're dealing with just stimulant use disorder or the combination of stimulants and opioids.

Anhedonia also plagues this population. And the more common issues that you're going to be dealing with acutely in the primary care setting are those that are presenting with a **psychotic presentation** or other **psychiatric comorbidity**, which we'll go into more detail.

Key Principles for the Busy Primary Care Physician Treating Stimulant Use Disorder: (02:18)

So what are the key principles or the 30,000-foot view that you really need to keep in mind when you're dealing with these patients in the primary care setting?

Well, the first is **avoid confrontation**. These patients are going to be ambivalent about the need to stop, and confrontation is not going to help build a **therapeutic alliance**. And building a therapeutic alliance is really what you need to focus on, because this is a journey that you're going to be taking with these patients. **Meeting patients where they're at** is key. If they're not ready to discontinue their use but they're ready to decrease their use somewhat, work with them on that and start there.

One of the biggest and strongest evidence-based interviewing techniques that you can use in primary care to really change a patient's motivation toward one of abstinence is **motivational interviewing**. And we're going to go into a little more detail on that. **Use frequent follow-up visits** to engage your patients in the primary care setting and realize that **counseling and medications** can be helpful, which we'll go into more detail.

Lastly, there's evidence showing that **exercise** can help individuals that want to reduce or quit their methamphetamine use.

Psychosocial Treatments for Stimulant Use Disorder: (03:28)

Let us focus on psychosocial treatments for stimulant use disorder. There are four key evidence-based strategies that are used for psychosocial interventions. And you can see them outlined here. On top, **motivational interviewing, contingency management, community reinforcement approach, and cognitive behavioral therapy**.

Contingency management probably has the strongest evidence for having a positive effect at reducing methamphetamine use. But the one I'm going to **focus on is motivational interviewing**. And the reason I am going to focus on motivational interviewing is because it's something that you can easily learn, you can master, and one that makes a significant difference in the primary care setting when you're with the patient.

Motivational Interviewing: (04:10)

So, what does motivational interviewing really do? What it really does, it evokes **change talk**. It's a conversation that you're having with a patient. And this conversation allows individuals to overcome their ambivalence and feelings of insecurity largely through a process in which individuals voice their own language on why they want to stop using a particular substance, and it's through their **ability to verbalize** their want of wanting to reach a certain goal that they then are able to make an effective change.

Now the important thing is motivational interviewing **does not have a prescribed time period**. This can be done over several visits. This can be done over one visit. This can be done over a duration of 30-minute visit or just five minutes within the visit. It really is there as a tool to use to engage the patient when it's appropriate.

There are additional resources where one can learn more about motivational interviewing and master the techniques through PCSS, the California Study of Addiction Medicine, which has a master's course every year and their annual meeting, and other resources that you can access through ASAM.

Acute Effects of Methamphetamines: (05:22)

Let us talk about the acute effects of methamphetamines. Now, the acute effects can be both physical and psychological, and unfortunately, some of these acute effects are seen as beneficial to patients, which is a big part of why individuals don't see it as a problem.

For example, **appetite suppression weight loss** is one of the things that a lot of females view as positive aspects of using methamphetamines.

When it comes to the psychological benefits, you can see here acutely you get an **increase in energy, confidence, alertness, mood, euphoria, sex drive, and talkativeness**, which is not really positive, but the other ones you can see how it could be a positive or it could be viewed positively by individuals that use methamphetamines. It also **decreases boredom, loneliness, and timidness**.

Now these are all acute effects, but when you start talking about chronic methamphetamine use is when you really start getting into trouble.

Chronic Effects of Methamphetamines: (06:18)

This is an example of someone that has **skin excoriations** due to chronic methamphetamine use and someone that's developed **delusional parasitosis**, otherwise known as formication. And you can see what they've done to themselves from the picking behaviors in their arms.

The psychological effects due to chronic methamphetamine use can be quite severe. Many of you have probably seen this in the primary care setting, such as **psychosis**. And the psychosis can be manifesting itself as hallucinations, paranoia, persecutory delusions. And this is really when I start getting involved as psychiatrists and seeing these cases.

Additionally, individuals that have chronic use of methamphetamine suffer from **depression**. Again, we've said this in prior slides, but **poor concentration, poor memory, irritabilit**y is a manifestation. They can have **panic attacks, insomnia, confusion, and fatigue**.

Challenges to Disentangling Symptoms Caused by Methamphetamines V.S Psychiatric Disorders (07:10)

And one of the challenging things when you're dealing with these patients is really having this chicken versus the egg conversation of, what is it? Is it substance-induced? Is it really a primary psychiatric disorder? And how do I treat it according to what it is? The treatment is the same whether it's substance-induced or psychiatric in nature, but it's really a conversation of what happens after you treat it. The long-term effects.

And what we're seeing is that with methamphetamine psychosis approximately **26% to about 46%** of people with a methamphetamine use disorder will manifest **psychosis**. And up to **half** of regular methamphetamine users have **a comorbid psychiatric disorder**. For example, the breakdown is often viewed as approximately 40% will have a major depressive disorder. Approximately 20% will have a primary psychiatric psychotic

disorder. And approximately 30% of those that develop methamphetamine-induced psychosis will be re-diagnosed with a schizophrenia spectrum disorder diagnosis within eight years. So there's a need for follow up with these individuals.

When you look at the psychiatric symptoms that are exacerbated by methamphetamines, they primarily will cluster into three regions. And this is a study that looked at the various psychiatric symptoms that are produced with methamphetamine use. An easier way of looking at that slide is the three clusters will be **affective** symptoms, **positive psychotic** symptoms, and **stimulant** effects.

And when we focus on affective symptoms, you'll see that the vast majority of those are going to cluster around **depression and suicidality followed by self-neglect**. When we look at positive psychotic symptoms the vast majority of those one is going to cluster around **suspiciousness, hallucinations, unusual thought content**. And when you look at stimulant effects there are going to be **motor hyperactivity, excitement, and distractibility**, of course, which many of us have already seen clinically.

Methamphetamine-Induced Psychosis (MAP): (09:17)

Let us talk a little more about methamphetamine-induced psychosis.

What increases one's risk for developing psychosis due to methamphetamines? Earlier **onset** of use, longer **duration** of use, higher **quantity** of use, **polydrug** use, and the **nature** of methamphetamine use, for example, crystal methamphetamine.

Transient psychosis is almost indistinguishable from what one would see in paranoid schizophrenia. And this is what makes it diagnostically difficult to tell early on what is it in the beginning. Is it primarily a psychiatric condition, a substance use condition, or a manifestation of both?

Usually the transitory psychosis, for those that are just starting their methamphetamine journey, and will subside within two weeks to one month from the moment that they abstain from using. But there's a **persistent psychosis** that we're seeing with individuals, particularly with the purer forms of crystal methamphetamine that we're currently seeing. And persistent psychosis is defined as greater than one month after abstinence, and this usually has the greatest concern with cognitive issues.

Long-term treatment and follow-up, again, is important because remember there is a portion of those individuals that will develop a schizophreniform spectrum disorder, either due to their methamphetamine use or it already was there and was manifested, uncloaked because of their methamphetamine use. So about **a third** of those with methamphetamine induced psychosis really need to be treated and followed up over a period of time. And many guidelines are currently saying that you should probably treat them and see them for at least **a minimum of six months** in order to really see how they're doing.

Medications for Methamphetamine-Induced Psychosis (MAP): (11:08)

Let us talk about medications for methamphetamine induced psychosis. The key is **second-generation antipsychotics**. Now first-generation antipsychotics also work but second generation antipsychotics have less of a side effect profile and are the preferred agents to use.

Effective antipsychotics for methamphetamine-induced psychosis: A few that I've listed here are aripiprazole, olanzapine, quetiapine, Risperdal, and haloperidol, or haloperidol. However, they have side effects associated with them. And the one that has the **greatest side effect profile is haloperidol**. It has the highest rate of EPS symptoms of all the antipsychotics that I've listed here. And I've also put the typical dosing range that you're going to dose someone at in the primary care setting, which is going to be one to **40 milligrams** per day for haloperidol.

Olanzapine, its main side effect is weight **gain and sedation**. And, of course, sedation may not be necessarily a bad thing when someone is acutely suffering from methamphetamines, methamphetamine use, and has been up for several nights. The typical dosing range for that is going to be **five to 20 milligrams** per day.

Quetiapine is also going to have sedation and weight gain. That's going to be typically dosed from **50 to 800 milligrams** per day.

And then we get into the ones that are least likely to cause side effects, which is primarily going to be **aripiprazole** dosed at **five to 30 milligrams** per day. The primary side effect with that is typically going to be seen as **akathisia**.

And then we have **Risperdal** from **two to eight milligrams** per day. And the side effect profile for that is going to be **weight gain, sedation, and dose-dependent EPS**. So, as you go higher on the dose of Risperdal, it starts acting more like a first-generation antipsychotic, particularly when you get on the higher end of the dose range, about nine to 10 milligrams. But below that it acts as a second-generation antipsychotic.

(13:04) This is a study that highlighted the retention in treatment between Risperdal and Abilify due to side effect profile. And what you can see here is that the **retention is highest with Risperdal as opposed to aripiprazole**. And it was primarily **due to three areas of in the side effect** profile range, which was akathisia, agitation, and anxiety, where Risperdal outperformed Abilify.

Medication for Stimulant Use Disorder, Depression, and Anxiety: (13:30)

Additionally, **depression and anxiety** are also areas that need to be addressed with individuals that use methamphetamines. And this is a condition that will often **trigger relapse** for individuals, meaning that they will start to feel depression and anxiety, and they will want to self-medicate themselves with methamphetamines in order to elevate their mood.

Now there's two medications primarily that we focus on in this cohort, which is **Mirtazapine** and **Wellbutrin**. And the reason we focus on these two medications is because one, they work for depression. Mirtazapine can help with anxiety, but largely because these two medications also show or have studies that show a **benefit with decreasing methamphetamine use and cravings**.

So, the first medication I'd like to highlight of **Mirtazapine**, and there's two studies that highlighted the effect of methamphetamines and decreasing methamphetamine use. The first one is one by Colfax. And what you can see here on the left-hand slide is that there's a **decrease in methamphetamine use or urine samples** that are positive for methamphetamines with using Mirtazapine. And this was recreated by Coffin as well.

Now, when we looked at **bupropion** and methamphetamine use, this is one study that highlighted its effectiveness for those individuals that use it less than daily. Now what you can see here is that there's a separation from placebo as far as abstinence goes, but when you really separate the group into adherence, so those that it **really adheres to taking the buprenorphine** as prescribed, what you saw is a clear separation between those that were nonadherent to those that were adhering as far as having less methamphetamine use.

(15:22) So, when we're looking at mirtazapine and when we're looking at dosing this medication, we typically start the medication at **15 milligrams every night**. And the reason we started every night is because it can have a **sedating effect and help with sleep**. We then increase it to **30 milligrams after approximately seven days.** And again, this is focused on methamphetamine use, and we may increase it up to the **maximum 45 milligrams nightly**. It treats depression and anxiety. It helps with insomnia, and the common side effects for mirtazapine are going to be weight gain and sedation as possible side effects.

Now when we look at bupropion, you can start bupropion the XL formulation at **150 milligrams daily**. You can then increase it to **300 milligrams daily after seven days** and then increase it then further **to 450 milligrams** daily. Now I'll highlight a study where they were much more aggressive with the dosing, but in general, this is a typical dosing that you will do. It's fairly aggressive.

Treatments: What does it treat? It treats depression. It can also be used for a **smoking cessation**, particularly the SR formulation.

Things to consider avoiding: When to prescribe this is those individuals are abusing **alcohol or sedatives** or undergoing abrupt discontinuation of these substances largely because it will lower your seizure threshold, and in combination with **buprenorphine** may cause you to have a seizure. Additionally, **bulimia and anorexia nervosa**. We also want to avoid it for the same reasons that I just said are those that actually have a seizure disorder.

Common side effects are **dry mouth, anxiety, and insomnia**.

Bupropion and Naltrexone: (16:57)

This is a study that highlighted its effectiveness of bupropion, but specifically, paired with long-acting injectable naltrexone. It's a two-stage study and I like to bring your attention to the bottom part of this slide. And what you'll see is when you use this combination there's a separation from placebo as far as individuals that had less methamphetamine use really through urine toxicology analysis. But what they did is they took it a step further from the study and they took it into a second stage. And what they did is they took this placebo group, and they stratified them into those that were receiving the treatment versus placebo again. And you could see that there's a **separation even among the individuals that were in the placebo group**.

So, when we talk about naltrexone, naltrexone comes in two formulations, an oral formulation and a long-acting injectable formulation. You can use naltrexone for methamphetamine use, and if you're going to use naltrexone the very important thing to realize is **that they have to be opioid free**. Now that's very important because a lot of times what we're seeing now is that methamphetamines will be laced with fentanyl and if

they are and you give them naltrexone, you will **precipitate withdrawal**. So, you would have to make sure that they're not taking an opioid. But if they're not taking an opioid, you can start this medication once they're opioid-free for a **minimum of seven to 10 days** before you start naltrexone treatment orally. And then long-acting injectable as well.

Then what you do, if you're going to give the **oral** formulation you give **50-milligram dose daily**. The extended-release formulation is an **injectable** suspension of **380 milligrams given IM every month**.

Now, in the study I highlighted previously there's a difference between what they did in the study and what we typically do in the real world. And what I mean by that is the long-acting injectable naltrexone is typically given every four weeks or monthly. In the study they gave it every three weeks. In combination with the Bupropion XL. Now remember I said they were much more aggressive at titrating than what I had recommended in previous slides. In this study, they titrated the Bupropion XL to 150 milligrams on day one, 300 milligrams on day two, and 450 milligrams beginning on day three. One of the things I highlight in the study if patients were having a difficult time initiating that dose that aggressively, they would hold a dose at a lower end and then increase it. But the goal was really to aggressively increase a dose.

I hope this lecture was helpful and beneficial. Again, this is a quick 15-minute overview of what you can do in the primary care setting to treat individuals that suffer from methamphetamine use. And if you have any questions, please feel free to reach out.