



*ASHPOfficial - Buprenorphine for opioid use disorder
Transcription*

Speaker 1:

Welcome to the ASHPOfficial podcast, your guide to issues related to medication use, public health, and the profession of pharmacy.

Raniah A.:

Thank you for joining us for Therapeutics Thursdays podcast. This podcast provides an opportunity to listen in as a member to sit down to discuss what's new and ongoing in the world of therapeutics. My name is [Raniah Aljadeed 00:00:27], an emergency medicine pharmacist at King Saud University Medical City in Saudi Arabia. And I'll be your host today for the ASHP Therapeutic Thursdays podcast. With me today is Dr. Rachel Schult, a toxicology clinical pharmacy specialist and assistant professor at the University of Rochester Medical Center in Rochester, New York. Thanks for joining us today, Rachel.

Raniah A.:

Let's get started talking about today's topics, buprenorphine for opioid use disorder. So Rachel, in the past, when our patients suffer from opioid withdrawal, we would normally manage those patients with clonidine and gabapentin. Why is buprenorphine now being used instead?

Dr. Rachel Schult:

Yeah, that's a great question. So buprenorphine for, hopefully most people understand what buprenorphine is, but for those that don't, it is a partial mu opioid receptor agonist, which means that it works at the opioid receptors like most other opioids do. What's different about buprenorphine compared to other opioid agonists is that it is a partial agonist. So with partial agonism, what we see is that it actually sort of has a ceiling effect. So whereas a medication like morphine, when you give higher and higher doses, there's no ceiling to the effects that we see from it, including analgesia, respiratory depression, most importantly.

Dr. Rachel Schult:

Buprenorphine actually usually does hit a ceiling, especially for respiratory depression. So for most patients who are tolerant on opioids, administering something like buprenorphine is very unlikely to cause respiratory depression in those patients, even at very high doses. Obviously there are certain things that may contribute to that. So if a patient had other sedating medications on board, that may cause more respiratory depression. And there's certainly people who are not opioid tolerant, like young children, where we might see more of a risk for



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respiratory depression. But in general, buprenorphine is inherently a safer opioid because of this partial agonist effect.

Raniah A.:

Can you give us a brief overview of the evidence behind the effectiveness of the buprenorphine?

Dr. Rachel Schult:

Absolutely. So there is actually a great Cochrane review about this that looks at buprenorphine for the use of treating opioid withdrawal in particular. And for opioid withdrawal, when compared specifically to clonidine and lofexidine, which are both central alpha-2 agonists, and so really traditionally what was used for symptomatic control of opioid withdrawal, buprenorphine is superior to clonidine or lofexidine. The other medication that it has been compared to in several studies is methadone, which we know that methadone is another medication very commonly used for treatment of opioid use disorder and withdrawal. And what we see when comparing it to methadone is that it appears to work similarly, so has similar efficacy to methadone.

Dr. Rachel Schult:

There was some mention in that Cochrane review that sort of suggests that potentially buprenorphine may resolve symptoms quicker or may produce a different pattern of withdrawal, but they're not really able to use the data that we have to say that it is actually superior to methadone in that regard. So really when you're looking at medications to treat opioid withdrawal, it appears that buprenorphine or methadone really should be the treatment of choice for management of opioid withdrawal and do better than sort of our traditional symptomatic agents for control.

Raniah A.:

So it seems like buprenorphine can be even more effective option for managing acute opioid withdrawal in the ED. Now, Rachel, which patient would you say are the strongest candidates for buprenorphine [inaudible 00:04:00] induction in the ED?

Dr. Rachel Schult:

Well, I really think that we need to think about the use of buprenorphine in the ED in a couple of different ways. So I think patients that are presenting to the emergency department in opioid withdrawal, the most effective agent to manage that would be something like buprenorphine or



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methadone. Now in the US when we're thinking about sort of the legality of this, buprenorphine and methadone, when you're using something, an opioid in particular for the management of opioid withdrawal, those are really only the two agents that would be available legally to treat that.

Dr. Rachel Schult:

Most patients will have other complaints such as pain or other things like that where you may be able to get away with using another indication for a full opioid agonist. But really technically when we're thinking about the legality of this, using a medication that is approved for the use of opioid use disorder, like buprenorphine or methadone is preferred. So usually when I'm thinking about this or explaining this to other people, I like to try and get the point across that a patient is presenting to the emergency department with a medical complication and that we should be treating that with the most effective agents that we can for that medical disorder.

Dr. Rachel Schult:

And so opioid withdrawal is absolutely a medical complaint that patients will present to the emergency department for. And the most effective things that we have to treat that is Buprenorphine or Methadone. I think where things kind of get different is when you actually are looking through the evidence for using buprenorphine in the ED. Most of the studies that are out there are really describing programs that are buprenorphine induction programs. So essentially using the ED as a point of access to further treatment, which is fantastic. So using the emergency department as a frontline area where you can get patients started on buprenorphine and then refer them for more permanent follow-up care thereafter.

Dr. Rachel Schult:

I think what is challenging with a lot of those studies is that they're not necessarily generalizable to the everyday emergency departments out there. So most of these studies are done in large academic centers that have direct affiliation with a substance abuse treatment program where they can directly refer their patients to afterwards. So a lot of these patients will come to the ED, they can be started on buprenorphine and then they will have direct access, either pretty quick follow-up within a day. But most of these studies suggest that they are following up with these programs within 72 hours to be continued for treatment.

Dr. Rachel Schult:



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In a lot of those different studies, they'll report different numbers such as treatment retention at 30 days or 60 days, which are great outcomes to show that if you are able to establish a program like this, that this appears to be highly effective to give buprenorphine in the emergency department and link patients to a program for follow-up. I think that that is the ideal, but it's also hard to do in especially some of these smaller community emergency departments that may not have direct access to one of these programs. So I really think that the bottom line is if a patient presents to the emergency department in withdrawal, the best way to treat them is with buprenorphine.

Dr. Rachel Schult:

And then while taking into consideration the resources that are available in the community of that particular emergency department, it is also probably ideal if there is some way to get these patients into formal treatment for their substance use disorder.

Raniah A.:

What about the dose, Rachel for buprenorphine?

Dr. Rachel Schult:

There's a lot of different ways that this has been dosed in studies. I guess I will sort of speak to our experience here at our emergency department because I feel that's what I'm most comfortable with. Typically what we do, so because buprenorphine is a partial agonist, there is the potential that it can actually precipitate withdrawal in patients who still have full opioid agonists onboard. So what that means is essentially if you have a full opioid agonist onboard, let's say their treatment, the level of their opioid effect is at 100, if you administer something like buprenorphine that's giving, say an opioid effect of 50 you're bringing that patient down to a 50 because Buprenorphine has very high receptor affinity for that mu opioid receptor, and typically we'll kick off most other opioids that we use or see therapeutically.

Dr. Rachel Schult:



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So the potential for precipitating opioid withdrawal is a concern. Typically our practice tends to be pretty conservative in that we try to avoid this. I mean, a lot of times patients who experience precipitated withdrawal really have a bad taste in their mouth for buprenorphine afterwards. And while we oftentimes discuss how opioid withdrawal in general is not a life threatening condition, precipitated opioid withdrawal absolutely can be because if you give a big catecholamine surge to a group of patients who have medical comorbidities that put them at higher risk, this is essentially the concern that we will have in these patients.

Dr. Rachel Schult:

There are certainly case reports out there of patients with precipitated myocardial infarction or different complications like that associated with this catecholamine surge of precipitated withdrawal. So typically what we do at our practice is to start with a low test dose and we usually will start with 2 mg sublingual and then if the patient doesn't have any signs of precipitated withdrawal after that, about one hour later we will administer an 8 mg dose. Another option that we also use in our practice and is mostly reported out of California is this option for providing additional higher doses of Buprenorphine for patients.

Dr. Rachel Schult:

So in our practice, we usually recommend up to a 16 mg dose thereafter so that the patient would be receiving about a total dose of 24 mg. But there are reports of patients getting 32 mg or even higher potentially, which we think is really just going to have the added benefit of providing a patient with a longer duration of withdrawal treatment so that they could potentially have that longer period of time to get into a chemical dependency treatment program. What's also great about that is that having that much buprenorphine on board is very protective for patients. So even if they were to leave the hospital and use heroin, it's likely that they would not overdose on that.

Raniah A.:

Interesting. Who can prescribe buprenorphine?

Dr. Rachel Schult:

Great question. And so this is really one of the ways that we kind of get hung up on how to start some of these programs in the US. In the United States we have something that's called the Data 2000 or X waiver. I think everybody speaks of it in lay terminology as an X waiver. The X waiver is essentially meaning that the provider that can write that prescription has gone through



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a course that teaches them about buprenorphine and allows them to be able to prescribe it in the United States for the indication of opioid use disorder. So what that means is that unfortunately not every provider in the US is able to prescribe buprenorphine to patients for opioid use disorder.

Dr. Rachel Schult:

So one thing that is important is that when patients come to the emergency department, you do not need to have an X waiver to administer it in the emergency department. We have this thing called a 72-hour rule, which essentially means that a patient can come to the ED for no more than three days and receive buprenorphine for their treatment of opioid use disorder. This doesn't necessarily mean an emergency department either, it just means that somebody without an X waiver can administer buprenorphine to a patient, not prescribe but administer to a patient for up to a period of 72 hours. The other sort of caveat here is that patients presenting to the hospital for other medical reasons can also receive buprenorphine or methadone for the management of their opioid use disorder.

Dr. Rachel Schult:

So we for instance, have a lot of patients that get admitted to the hospital for infectious complications related to IV drug use and these patients can also receive buprenorphine or methadone while they're in the emergency department and while they're in the hospital, even beyond that 72 hour duration because we are primarily treating other medical complications.

Dr. Rachel Schult:

So unfortunately most ED, well, I don't know about that, but I would say a lot of ED providers do not have a formal X waiver so they would not be able to prescribe buprenorphine on discharge. What that means is that if there isn't somebody in the emergency department that has that X waiver and can give a prescription to a patient at the time of discharge after induction, then the patient wouldn't go home with any buprenorphine and we'd be hoping that they could get into a treatment program pretty quickly.

Raniah A.:

I was wondering if you can give us a brief overview about buprenorphine induction in the ED and also with MAT at your institution?

Dr. Rachel Schult:



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Sure. So I work on a busy medical toxicology consult service and so our service sees not only the traditional drug overdose patients that a lot of toxicology services will see, but we also do a lot with addiction and withdrawal. So I did talk about previously how we see a lot of patients in our institution that are admitted for sort of infectious complications of IV drug use and we will follow them and get them started on buprenorphine and try to refer them to treatment after the hospital stay.

Dr. Rachel Schult:

Our service also does get consulted on patients that are in the emergency department and will see those that are in acute withdrawal and sort of help them get set up with treatment if we are available. Unfortunately this is sort of a time permitting service because obviously the emergency department will be concerned with how long the patient needs to be in the ED and how long until we are able to see that patient. And so some of those barriers may mean that we don't see every patient.

Dr. Rachel Schult:

So what we ended up doing a few years ago, we rolled out a smart ED opioid program, which really was our goal with that program was to reduce overall opioid use in the emergency department, but we also had formal documents and recommendations for the management of opioid withdrawal in the ED. And so for that we recommended the use of a buprenorphine induction in patients that were presenting in opioid withdrawal. So by providing that 2 mg dose and then if tolerated, giving an 8 mg dose and if both of those were tolerated, we also added the additional option of giving a higher dose load to hopefully provide patients with longer duration of withdrawal relief to allow them to sort of get into other clinics.

Dr. Rachel Schult:

Unfortunately, we don't have a program that is formally set up with our chemical dependency treatment program to kind of get patients in quickly. But a nice thing that's available in our community is that a lot of treatment programs in the area actually offer walk-in hours. So every day of the week there is a program that will offer walking hours for immediate access to buprenorphine, meaning that you can go to that clinic that day without an appointment, walk in, get an intake and get buprenorphine at that time.

Dr. Rachel Schult:



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And so that's been the way that we've been trying sort of refer patients to treatment. We will start them in the emergency department on buprenorphine, give them enough doses in the emergency department to hopefully take care of their withdrawal for an extended period of time and then provide them with information and resources about how to get into a next day walk-in hours at a buprenorphine clinic.

Raniah A.:

So what would you say is our role as a pharmacist, when we have a patient [inaudible 00:15:18] about to initiate buprenorphine in the ED?

Dr. Rachel Schult:

As a pharmacist, there's a lot of different things that we can do. While it might be challenging to really formally set up some of these agreements with, if you have a medication assisted treatment provider that is affiliated with your institution, it may be hard to sort of as a pharmacist set up those agreements. But I think being a champion for that and finding sort of physician colleagues that can also be champions for that is a great way to get started.

Dr. Rachel Schult:

If a patient is presenting to the emergency department in acute opioid withdrawal, I think the first step again is going to be really showing the evidence that the use of buprenorphine is superior to that of symptomatic treatment alone and that this is a patient presenting with a medical condition that we can treat effectively in the ED, whether or not you have a formal program set up to get patients into a treatment program. People that are looking for a great project to work on with this, it's absolutely reasonable to call around to different treatment programs in the area and see what kind of services they provide.

Dr. Rachel Schult:

If any of them provide rapid access to treatment or if any of them provide walk-in hours such as we see here, and then getting together some sort of document that you can give out to patients with that information. I think the most important thing is that we're able to provide patients with symptomatic relief when they come to the emergency department and also give them enough resources that they're able to follow up if they're interested in treatment.

Raniah A.:



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Awesome. One last question before we wrap up. I've heard some talk about buprenorphine being used as a substitute for naloxone in opioid overdose patients. Can you tell us your thoughts about that?

Dr. Rachel Schult:

Yeah. So there was recently a paper that looked at comparing the use of naloxone versus a couple of different doses of buprenorphine for reversal of opioid overdose. I think it is a very interesting idea. Now the idea here is that we're probably giving this to patients who are dependent on opioids. So it's actually pretty rare that we're going to see patients presenting with an opioid overdose who aren't dependent on opioids. It happens probably more likely in kids, but it's pretty rare.

Dr. Rachel Schult:

And so this study is essentially going off of the idea that this will be probably a more gentle reversal. So instead of naloxone, which is a pure antagonist and taking their opioid effect down to zero, we would potentially be giving them something that might just bring their opioid activity down just enough to kind of wake them up. So the study was super interesting in that they compared the naloxone and randomized patients to either naloxone or two different doses of buprenorphine.

Dr. Rachel Schult:

And really what they were reporting is that the patients that received the buprenorphine did really well, had very good responses to it and actually had less precipitated withdrawal than what we saw in the naloxone arm. One of the things that I caution readers in that paper is that one of the ways that they described how they were administering naloxone was referring to the Goldfrank's chapter on it. And they also said that they would administer 2 mg IV to a person who is apneic. Now, in my opinion, that dose is too high, even if a patient is apneic.

Dr. Rachel Schult:

Now typically our recommendation in the emergency department is for a patient that is not breathing, we would still provide assisted ventilation via a bag valve mask and then also provide low doses of naloxone to sort of gradually reverse that opioid overdose. If you provide a patient with a really large dose of naloxone, you're very likely to see precipitated withdrawal symptoms, and I am sort of cautious in interpreting that data that I feel like the high levels of withdrawal that



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they saw in those patients may potentially have just been related to the high doses of naloxone they were potentially using.

Dr. Rachel Schult:

Now they don't give us a lot of data about how much they actually used in the patients that receive naloxone, but just in the way they discussed their protocol, I was concerned about how much naloxone those patients could be receiving. But super interesting that a lot of the patients in the buprenorphine arm seemed to get really great reversal while also not having that much withdrawal symptoms. I think obviously there's some bias risks there because this was not a blinded study, but certainly something that warrants more investigation. Another thing, there's been a lot of different case reports out there talking about how do we get patients started on buprenorphine earlier? So a lot of these things that we're talking about today is a patient presents to the emergency department in opioid withdrawal, but what do we do for patients who are coming in with overdose?

Dr. Rachel Schult:

And in that population it's going to be a lot different trying to get them on to buprenorphine. So if a patient presents in overdose, they receive naloxone, is there a way to seamlessly get them onto buprenorphine while they're in the ED? So there are some case reports out there that look at patients who have withdrawal that is induced on naloxone, so have a COWS score or a clinical opiate withdrawal scale score that is high enough that means that we're seeing some withdrawal symptoms in the patient, and then at that point administering buprenorphine to them.

Dr. Rachel Schult:

I could find about two case reports on it. I think there are probably more people out there doing it than those two case reports. But that's also an interesting idea. So just kind of thinking about how we can quickly get patients that are interested on it, even after an opioid overdose. Because the alternative there is really another potential program which admitted patients to a clinical decision unit or emergency observation unit so that there could be enough time that passes from their last use of an opioid to get them started on buprenorphine.

Raniah A.:

That's all the time we have today. I want to thank Rachel for joining us today to discuss buprenorphine for opioid use disorder. Join us here every Thursday where we will be talking with ASHP member contact matter experts on variety of clinical topics. Thank you, everyone.



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Speaker 1:

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