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https://reachmd.com/programs/cme/shelter-from-the-storm-the-role-and-impact-of-pharmacological-treatment-approaches-for-the-management-of-acute-agitation-in-an-emergency-medicine-setting/15413/

Time needed to complete: 1h 15m

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Shelter from the Storm: The Role and Impact of Pharmacological Treatment Approaches? for the Management of Acute Agitation in an Emergency Medicine Setting

Announcer:
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Dr. Gooch:
Hello, I'm Dr. Michael Gooch, and welcome to Shelter from the Storm: The Role and Impact of Pharmacological Treatment Approaches for the Management of Acute Agitation in the Emergency Medicine Setting. I'm an emergency nurse practitioner, and I also do flight and teach emergency nurse practitioner students.

This is a common patient interaction we encounter in the ED. So let's talk about some of our options. So first, we have our first-generation drugs, sometimes typically referred to as our atypicals or our neuroleptics. And we have several options available for us here. Probably haloperidol is the one that we see used the most, it's talked about a lot in the literature. But there are several other categories that fit in here. And the big thing to remember about these agents is they tend to be very nonspecific. As you can see, they interact with dopamine, some with alpha, some with histamine as well. And this tends to play a role with their side effect profile. So some of us probably have our one that we prefer to use the most, typically haloperidol. But it has some side effects we need to be aware of and think about its role in our practice setting.

One of the biggest things we have to worry about with these agents is their risk for extrapyramidal symptoms. And this can be seen with both our second and our first-generation drugs, and definitely something to watch for and maybe even educate our patients or even our coworkers about, that if this patient may develop some acute dystonias, they may have some of those akathisias that go along with this. This also may be why some patients tend to become noncompliant, because they develop these acute dystonias, they don't want other people to see these side effects, and it may give them some negative impact as well. One thing we may do there in the ED is go ahead and administer some of antihistamine or anticholinergic with that medication to kind of prevent that from happening, or sometimes just wait and see if it happens, and then treat that patient after the development. In regular practice, the goal here is to either lower that dose, or maybe try a different agent that may have less of those effects.

Some of the other side effects we have to worry about with these neuroleptics is going to be our risk for tardive dyskinesias. Unfortunately, like the EPS symptoms, which usually are reversible, especially if we stopped the medication, or lower the dose, where TDs tend not to be reversible. Those usually happen for long-term therapy. So not a big concern when we're dosing that patient in the ED, but something we need to be aware of. All of these agents had the risk for seizures because they lower the seizure threshold. They can all cause some other problems, especially cardiac. Most of these do tend to prolong the QT interval, and have to worry about that risk for arrhythmias. And that's a big risk, especially for patients on other medications that may alter the QT, or they have some deficiencies such as B12 or maybe magnesium that may play a role there as well.

And now, probably most of us are more familiar with our atypicals, or our second-generation agents. These tend to have a little bit better

safety profile. They tend not to be as sedating as my first-generation drugs. And we have several options here. Some of these are injectable and oral, some may only be oral. They have several indications, as you can see. But definitely maybe they're preferred in your practice setting in that patient who we want to control their agitation, but definitely don't want to cause as much sedation. And if that patient is cooperative, they realize they need to get some medication on board, this may be a great chance for one of those oral drugs. But definitely in that patient that's acutely agitated, they're are risk to themselves or others, we may have to go with an injectable.

Very similar to our first-generation drugs, these are going to have very similar side effects. They tend not to be as bad in the second-generation drugs, but they may still have that risk for the QT prolongation, the seizure problem. One of the things do see with atypicals that we don't see with the first-generation drugs is this risk for hyperglycemia. And that tends to be exacerbated in the patient who already has a risk for that, such as the patient with diabetes. But if your patient's on corticosteroids or other things that may influence the blood sugar, we need to watch that a little closer.

All these atypicals and typical antipsychotics have a box warning now for their use and agitation in the dementia patient. We really should avoid that because it does tend to increase mortality. And some of these also have a box warning about the increased risk of suicidality. And that varies depending on the class of the medication. This is something of course to be aware of. And definitely just aware of if we are using this for acute agitation in that patient with dementia, there is a box warning out there about that. So understand the risk, but also sometimes the benefits this may play.

And as we close out the atypicals and the typical antipsychotics, we have to worry about the risk for neuroleptic malignant syndrome. This is a rare but serious side effect we see with these medications. One of the big things here is this doesn't have to be a medication error, it doesn't have to be an overdose, it's just a side effect that happens. This patient also developed significant muscle rigidity and hyperthermia, they become altered. Our big focus here is making sure this patient maintains their airway. We can use benzodiazepines for muscle relaxants, to treat their seizures if they're having those, get their temperature under control, either with cooling measures or using things like dantrolene. And just be aware of this is a rare but serious side effect that we've seen with these medications.

Benzodiazepines still play a role here. Sometimes these are given in conjunction with an antipsychotic or maybe separately. These are going to have great anxiolysis. They're going to enhance GABA. They have the GABA receptors that have that calming effect. Several options out there. Some of these may be great for all if the patient is cooperative. If I had to choose an injectable, I like midazolam because it can be given I.V. or I.M. It's the preferred agent for I.M. because it's water soluble, where diazepam and lorazepam tend to be more lipid soluble, and they don't absorb as well. And midazolam could even give an intranasally. Not sure that's a good option in our acutely agitated patients, but something to have in your toolbox just in case.

There is that new box warning out there we should be aware of if we're using benzos regularly, and definitely if that patient is a chronic benzodiazepine user, they have a significant risk for withdrawal seizures if those are stopped abruptly or tapered too rapidly.

As we wind down, thinking about ketamine. This is not a first-line agent, but definitely if that patient is refractory to other therapy, ketamine may be a very good option. The use here is off label but definitely can be great for providing sedation. One of the benefits of ketamine is it tends not to have any negative effect on the respiratory drive are the cardiovascular system. So we may dose it at 2 to 4 milligrams per kilogram I.M., some may use higher dose or use a standard dose across the board. But as you can see, a rapid onset and pretty decent duration to get that patient under control. These can cause hypersalivation. So we'll probably use in somebody that may go ahead and pre drug with an anticholinergic. They can stimulate the GI tract, so nausea and vomiting sometimes happens. And these are contraindicated if the patient's having a hypertensive emergency, or they're having ischemic event. And this is in that catecholamine release that we sometimes see, that's enhanced by ketamine. So definitely a great option. But definitely probably not my first line, especially if this patient is refractory. And I might want to go ahead and add a little benzodiazepine if we haven't yet, to kind of blunt some those psychedelic effects we might see with ketamine so it is chemically very similar to PCP.

And lastly, we have dexmedetomidine. Dexmedetomidine has been around for a while, it's used a lot in the ICU setting for sedation, but definitely has some utility here in the acutely agitated patient as well. If this patient is refractory to other therapies, I cannot get their agitation under control, this may be a good option. Like ketamine, it tends not to have any negative effects on the cardiovascular or respiratory system, it tends to not have that catecholamine effect, so we don't have to worry about the hypertension. It actually may cause hypotension and bradycardia. It's use here is also off label, but definitely something to think about if something else is not an option.

And we now do have a sublingual formulation available for dexmedetomidine. This just got approved last year in 2022. And definitely maybe something we can use in that patient who's cooperative. In that patient realizes they need to get their mood under control, and they can still do some things themselves, this might be good options available so that patients can do their sublingual film and have that autonomy to do it themselves, versus to have to go for something that's going to be as a parenteral agent. As you can see here, it can be repeated in 2 hours. It does have a max dose there in 24 hours but definitely something that we may consider. It tends not to cause

some of those other effects we might see with ketamine, and definitely may be useful in that patient who's a little bit cooperative. It doesn't have the risk for QT prolongation. And one of the nice things about it, it doesn't have any renal adjustment concerns that we could think about.

So there's several options we talked about for controlling the acutely agitated patient. Maybe we can go with an oral agent, or maybe this sublingual film, or maybe that patient has not cooperative and we may have to go with an injectable. But just think about the more medications we give or if we're combining a benzo and an antipsychotic, we're going to have more longer sedation, and that may prolong their stay and they get more thorough evaluation by mental health provider.

Hope you found this beneficial. Thank you for your time.

Announcer:
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