

## **Dr. Mark Donaldson - Naloxone – The Eighth Drug in the Dental Emergency Kit?**

Chiraz Guessaier: Hello and welcome to CDA Oasis. My name is Chiraz Guessaier. I have the pleasure to welcome Dr. Mark Donaldson to CDA Oasis. He is our expert in pharmacology and the senior executive director at Vizient. He is here today to talk to us about the antidote to another pandemic, the opioid crisis, which we seem to have put at the back burner for this time, but which is still boiling. We are of course referring to the drug Naloxone. Dr. Donaldson, it's always a pleasure to see you and host you on Oasis. Welcome.

Dr. Donaldson: Thank you so much, Chiraz. Nice to see you.

Chiraz Guessaier: So, in a very recent article that you published with your friend, Dr. Jason Goodchild, you spoke about Naloxone as the eighth drug in the dental emergency kit, my question is how does Naloxone work and why should it be in the emergency kit?

Dr. Donaldson: Yeah, great question. So, I liked your introduction to this because, you know, I think some of us may be suffering a little bit of COVID fatigue, because that's certainly grabbing all the headlines. But, you know, prior to COVID I think that the opioid epidemic had really been something that we were all getting almost a little fatigued over as well. And as you correctly stated, you know, the opioid epidemic really has not gone away. We still see a significant number of overdose deaths associated with opioids, whether those are licit or illicit. And so one of the challenges out there is how can we as oral healthcare professionals, you know, be part of the solution here. Now, Naloxone is a very interesting medication. It actually goes back or has its history back to 1961.

Dr. Donaldson: So, there was a physician, Dr. Jack Fishman, who was looking to create a medication that would combat the side effects of narcotics, in particular constipation. And so what he did, recognizing that, you know, the molecules themselves, the opioids attach to a very specific opioid receptor, if you could create something that looks exactly like an opioid, but when it attaches to the receptor, rather than giving the good effects of the opioids, it actually just blocked that receptor. In other words, it reversed the effects of opioids. Then that would be, you know, something to consider. And in fact, that's exactly what he sorts of stumbled upon. He replaced the methyl group with an allyl group from the nitrogen atom in oxymorphone, which was a precursor to morphine.

Dr. Donaldson: And so by almost tricking the body, giving it something that looked exactly like an opioid and therefore it attached to the exact same opioid receptor, but instead of causing good effects, it actually acted as an antagonist he created this drug Naloxone. So, Naloxone has been around since at least 1961. And it, in fact received a number of accolades, if you will. 1983, the World Health Organization added it to its list of, essential medications. And so, this is a drug that, you know, we've had in the hospital environment, that our EMTs carry. A

lot of ambulances as well as fireman carry this. And given the high incidents of opioid use as well as overdoses and unfortunately deaths, I think Naloxone's almost become a household word. Not too many patients or even family members that have not heard of Naloxone.

Chiraz Guessaier: So, I mean you're talking about something that has been around since 1961 and it's only now coming to the light. Any reason why?

Dr. Donaldson: Well, you know, it's multifold and I think really what is sort of driving this this resurgence or interest in Naloxone is unfortunately the opioid epidemic. And I'll give you a great example. Naloxone is a prescription medication. It comes as an injectable drug. And so, we use it in the hospital environment if we have somebody that comes in, that's brought in with a potential opioid or narcotic overdose. It's very effective in reversing those effects. We also use it routinely in the hospital because you know, when patients go for surgery or they're recovering from surgery, we do use a lot of narcotics for pain management.

Dr. Donaldson: And if we accidentally narcotize a patient, meaning that we give them a little bit too much morphine postoperatively, then we want to be able to, you know, kind of control those side effects with a reversal agent. Again, that's Naloxone. So, we've been using it clinically in the hospital for a lot of years. But now that the cat is out of the bag, if you will, we're seeing a lot more opioid use—again, legal and illegal opioids—outside of the hospital environment. It's becoming very important for people to have access to that reversal agent and hopefully limit the number of overdose deaths that we're seeing. The nice part about Naloxone is in general it really doesn't have any side effects. It does one thing which is to reverse the effects, typically the over sedation caused by opioids.

Dr. Donaldson: So very, very safe drug. It's not a controlled substance. And in fact, I started off this answer telling you that Naloxone is a prescription drug. While that's true, new formulations of Naloxone, let's say a patient- or public-friendly formulations have actually been deregulated such that it's not a prescription medication anymore in certain formulations. Now, the United States is an interesting place. I'm sure as a Canadian we can all appreciate that. But believe it or not, it was California that was the first state to deregulate Naloxone. And it wasn't a physician or medical group that got together and, you know, petitioned the health lawmakers to deregulated it, it was actually a group of parents. So, you know, they had been so concerned that a number of their loved ones, these kids who were experimenting with drugs, were suffering unintended overdoses and many of them were dying, that they had petitioned the government to deregulate Naloxone and give it a non-prescription status so that anybody could access it.

Dr. Donaldson: And hopefully somebody would have Naloxone available in case, let's say at a party, some kid, you know, took the wrong medication or too much of a narcotic

and got into an overdose situation. And if nobody is thinking about calling 911 at that moment or not doing it fast enough, you know, that life saving medication Naloxone would be available.

Chiraz Guessaier: So, how is it administered? How does a dentist use it?

Dr. Donaldson: Perfect. So, let me answer your question in two ways. First of all, when I said that it was a prescription medication, I meant in the original IV formulation. So, it's an injectable drug. It's given intravenously, intramuscularly. You can give it subcutaneously. It's an injectable drug that gets into the body very, very easily. On the backdrop of the opioid epidemic though, from a public standpoint, you know, our expectation is not for somebody to carry around a needle, a syringe and a vial of Naloxone and be skilled to inject it if, you know, one of their colleagues suddenly overdoses. And so, a lot of pharmaceutical companies have now done the research and development and created an intranasal formulation. And so, this is a single one-time nasal spray that if somebody was to overdose, you can simply just take this, push it up the patient's nose, hit the actuator and it releases Naloxone intranasally. The drug, again, is absorbed very, very rapidly and that over sedation, that overdose reverses very quickly. But there's also a new product out called Evzio.

Dr. Donaldson: Evzio is a little bit like an auto-injector, similar to an EpiPen, but instead of epinephrine it actually injects Naloxone into a patient. So again, if a patient suddenly, you know, succumbs to an overdose of an opioid, hopefully somebody in the room has this Evzio, this auto-injector and can simply, you know, hit the patient with it, inject it right through clothing. Again, very similar to an EpiPen auto-injector. And as soon as they push on it, it actually gives you positive feedback, meaning it talks you through it. As soon as you take the cap off of it, it tells you how and where to inject and then it counts down as you inject. And then it also reminds you of course, to call 911.

Dr. Donaldson: Now, from a dental perspective, you know, we're healthcare professionals. We're used to pulling drugs with a needle and a syringe out of a vial and injecting it. And so, for my dental colleagues, I would still sort of encourage you to think about having a vial of Naloxone, and of course a needle and syringe available, in case you have that patient that requires this life saving medication. The reason I encourage that formulation is because it's very inexpensive and I'm talking, you know, less than a few dollars for Naloxone. Some of those more patient friendly formulations that I spoke about, in the United States anyway, that single one-time intranasal dose costs about \$150. That auto-injector that I talked about is several hundred dollars. In fact, the average wholesale price for that is over \$4,500.

Dr. Donaldson: So, some of the patient friendly devices, you are paying a lot of money for convenience and I think in a dental office, we're used to pulling up drug and

injecting it into patients and that certainly is the most economical way to do it. And you know, I think in our hands it's at least as fast.

Chiraz Guessaier: So, is it prescription free everywhere or is it still limited in certain areas? Like, do you know what's happening in Canada?

Dr. Donaldson: Yeah, so Canada is very similar to the U S in that, through what we call a collaborative practice agreement, pharmacists are in fact able to dispense to patients, without a prescription, the different Naloxone formulations. Now, your corner neighborhood pharmacy is probably not going to have the injectable formulation. So, they are going to have those more convenient to patient-friendly or public-friendly formulations available.

Dr. Donaldson: There have been some additional changes in the United States, which I think too will start to influence Canada, and the first state I'm thinking of is Washington state. So, dentists in Washington state, if they do want to prescribe opioids or narcotics for postoperative dental pain, it is now written into the Washington State Board of Dentistry guidelines that you must consider either co-prescribing Naloxone with that narcotic prescription or at least direct the patient to discuss with the pharmacist whether or not they need to have access to Naloxone, if they're going to have that opioid prescription filled. And so, it's not going to surprise me if the colleges in Canada, the Dental Colleges start to take a look at the change in regulations here in the States and consider that same opportunity.

Dr. Donaldson: Now it's going to do one of two things, which as a prescriber I think is great. It's going to create an additional hurdle for dentists who prescribe opioids. And I think that that's a good thing because I think we still need to take that gentle time out, that pause, and really ask ourselves, should we be prescribing opioids for this patient? So, it's going to cause you to take that pause and in some cases, you know, maybe that additional prescription, which you know, is not an undue financial burden on the patient is perhaps even going to make the patients sort of push back a little bit. At the end of the day our goal is always appropriate prescribing and if really that patient does require narcotic then we want to do what's best for the patient and also keep them safe and create a conduit for them to have access to that reversal agent, if that's going to be required. And you know, maybe like I said, it causes us to take pause and decide perhaps we really don't need to order an opioid here. And for that reason, we have the nonsteroidal anti-inflammatory drugs and acetaminophen which are probably better indicated for postoperative dental pain.

Chiraz Guessaier: So, if I conclude, from what you're saying is that they have to have it in the dental emergency kit. At least we have an antidote. And the conversation continues about whether dentists should or should not prescribe.

- Dr. Donaldson: Yeah. And I, you know, I thank you very much for bringing me back to that because I think, you know, some of your listeners out there might be looking and saying, well, you know, I never use narcotics in my dental office. Why would I need a reversal agent for narcotics? And of course, the challenge here is that — and this primarily affects those dental offices where sedation is done — so you have a patient, a very nervous individual who comes into your office and maybe you offer them something like a Valium or a triazolam, some type of benzodiazepine medication to get them to relax. And then you do that, you know, normally patients relax very easily, and they are able to accept dentistry. In the odd case, you might give them this tablet and all of a sudden, they might go out and lose consciousness.
- Dr. Donaldson: So, the automatic reaction is, well, they came into your office upright on room air. The only thing you did different was give them a sedative agent. So, you will reverse that sedative agent with flumazenil. And you know, 9 times out of 10, those patients will perk right back up. But if the reversal agent for the sedative does not work, not only are you calling 911 but you probably want to be giving that patient Naloxone because more than likely that patient being so nervous, you know, might've taken some type of narcotic to calm their nerves and they didn't tell the dentist about that. So, the combination of this narcotic, whether that's licit or illicit, in addition to the sedative that the dentist gave caused this unintended overdose. And that truly is a medical emergency. So, we have seven drugs in the minimal dental emergency kit. If you do sedation dentistry, you definitely have to add one more, that's flumazenil the reversal agent for benzodiazepines. But I think just due to the fact that our patients don't always tell us the truth and certainly on the backdrop of the opioid epidemic, it makes great sense for dental offices to also consider the addition of Naloxone into the dental emergency kit.
- Chiraz Guessaier: Perfect. As always, thank you for the very valuable information Mark. It's a pleasure to see you and host you on Oasis. I wish you all the best and hopefully see you again soon.
- Dr. Donaldson: Absolutely. Stay healthy.