

## **Dr. Jose Lança: Effective Alternative Treatments to Opioids**

**Dr. O'Keefe:** The federal government has recently introduced legislation about cannabis and also the government takes a great interest in managing the opioid crisis. These two issues, opioids and cannabis are generating quite a lot of questions from dentists and I've caught up today with Dr. Jose Lança, who's a medical doctor who teaches pharmacology to both medical students and dental students at the University of Toronto to ask him one of those questions. Jose, I'm a very conscientious dentist, I don't want to contribute to the opioid crisis, but I've got patients who are in pain. Are there any alternatives for me to use to reduce the pain of my patients that are on opioids?

**Dr. Lança:** Pain management is very important, and I fully share your concerns about opioid prescription. The good news is that we do have answers, we do have alternatives that will allow us to manage pain without prescribing opioids. Let's take a look.

**Dr. Lança:** So, let's look at pain management in dentistry and effective alternatives to opioid prescription. I would like to look at the way that dentists in the United Kingdom have been managing pain, using the typical standard pain management for analgesia of impacted third molar extraction. These are the numbers and they are quite clear. In the United Kingdom, where patients have pain just as much as in America, we tend to prescribe under those situations, Ibuprofen in 73 percent of all the analgesic prescriptions. The only opioid that dentists prescribe in the UK is codeine and that is only used in less than 20 percent of all analgesic prescriptions. Let's compare this scenario with one that we have in North America. In small print, you'll see the references of the work that I have just presented. So, again, this is not based on personal opinion. In the United States, in the University of Alabama Faculty of Dentistry, the same condition was treated by the administration of either Oxycodone or Hydrocodone, either one in combination of Acetaminophen in 80 percent of the patients. If you were to compare this with Canada, you would say that probably the number could be replaced by codeine and Acetaminophen in 80 percent of the patients. Again, the question that we should ask before we proceed is why is it that we are prescribing opioids in conjunction with Acetaminophen, if the same effect in terms of analgesia are provided by colleagues in the UK in almost three out of four cases by single administration of Ibuprofen.

Dr. Lança: That is the first question for which clearly, we know the answer by looking at the numbers. The second one is that there are situations where it has been tested that if you were to give, either Ibuprofen alone or paracetamol, which is Acetaminophen and a dosage of 400 milligrams Ibuprofen or 1000 milligrams of Acetaminophen and compare the in compare the mean pain relief one hour after administration of the drug. Again, in cases of moderate to severe post-operative dental pain, uh, and specifically pain management. After third molar extraction, we will see that there is a very strong analgesic effect reaching a peak at approximately 60 to 90 minutes after administration of either Acetaminophen 1000 milligrams or Ibuprofen, 400 milligrams. Either of them alone, much more effective than the placebo. Where there is basically no pain relief. So now the important point is what happens if we combine these two analgesics? If we combine, Ibuprofen with Acetaminophen and when we refer to combining, that doesn't mean that that they are given to the patient exactly at the same time all the time. You can give them a in an alternate mode. Ibuprofen, then later on Acetaminophen et cetera. So, if you give them together 400 milligrams of Ibuprofen with 1000 milligrams of Acetaminophen, you can see that the recent increase in analgesia, in pain relief, and the curve is very similar to what we have in the beginning when the drugs were administered, uh, in isolated manners. However, it proceeds for a higher and longer period of time with the combination of these two drugs. If you now ask the following question: what happens if I lower the dose of both Ibuprofen and Acetaminophen by 50 percent i just give half of what I gave when they were given in an isolated manner as the only analgesic?

Dr. Lança: So, we'd say about 400 here. Or 1,000 for Acetaminophen, what happens if I give just 200 milligrams of Ibuprofen in 500 of Acetaminophen? We have the red line and we can see that difference at one hour and two hours between half the dose of the combined drugs we the full dose is not statistically significant. However, the red line is still significantly higher than the one that we'll obtain two hours after administration of the drug. Although at when our administration of a single drug provides a similar effect. Overall, the analgesia remains much more effectively for a long period of time of several hours.

Dr. Lança: We can see now that we should address in the question we may ask before I proceeded to following these new and the answer is no. This is not new. This is from the Journal of the American Dental Association from 2013 in situation that are used in medical practice. Many more

publications have shown in corroborated identical effectiveness for much longer periods of time for many years. So, bottom line, this is effective. This is not even new. There are no opioids being used in the management of this painful third molar extraction, the very same one that was just a, um, controlled by Ibuprofen management by three out of four prescriptions in the United Kingdom. So, the question that we now should address is a question that was addressed in uh, by Moore and colleagues in 2015 and it gives a study, a Cochran review that included 39 separate Cochran reviews with an incredibly large number of 50,000 patients and included, 416 individual studies. The conclusion was that Ibuprofen 200 milligrams in conjunction with Acetaminophen 500 milligrams was efficacious. The fast-acting formulations use good in often long-lasting analgesia at relatively low doses of 200 plus 500 milligrams.

Dr. Lança: This has been corroborated by other studies including Aminoshariae and colleagues in 2014. In addition to the issue of efficacy, the next question that must be asked and answered is: is it safe? And the answer is not new either. The answer is that a conjunction of 39 separate Cochran reviews--this is a study by again Moore and colleagues in 2015 in another Cochran review--that instead of using 50,000 patients as the previous study, used still an incredibly large number of 35,000 patients from 350 individual studies, were given different doses of Ibuprofen and Acetaminophen in conjunction with other groups of drugs and they showed that specifically in terms of the co-administration of Ibuprofen 200 with Acetaminophen, 500 milligrams these combinations and the adverse effects caused by these combination of low dose or Ibuprofen and Acetaminophen is generally similar to placebo in the low dose combinations. Adverse effect only occur at higher combination doses like for example, 400 versus 1000 milligrams of fan or in combination such as Acetaminophen 500 or 1,000 in conjunction with opioids. So, clearly the conclusion is that not only low dose of the combination of Acetaminophen with Ibuprofen is efficacious, but it is safe as well.

Dr. Lança: So, the conclusion that we clearly can draw from these studies that have been around for a number of years is that there is no scientific medical valid reason to prescribe combinations of Acetaminophen with codeine or any other opioid as often as it is done in North America by physicians, some physicians, and dentists.

Dr. Lança: I should just finally point out there are two groups of healthcare professionals that prescribe opioids either alone or in conjunction with

other analgesic drugs, are dentists and family physicians. That is quite startling when you look at other specialties such as emergency physicians where pain is so prevalent and such an important symptom presented by the patients that they prescribe opioids in about one third of the situations--one-third to half of the times that dentists in family physicians prescribe. These certainly as uncomfortable as they might be, have been significant contributors to the opioid crisis that we have in our hands, particularly in North America. Thank you.

Dr. O'Keefe: Dr. Jose Lança, thank you very much for your very important insights about our role in the management of the opioid crisis.

Dr. Lança: Thank you for the opportunity.