

# Using Alpha-2 Drugs for Pain in the Perioperative Setting

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There are several alpha 2 drugs on the market including dexmedetomidine, medetomidine, clonidine, romifidine, detomidine and xylazine. This lecture is about their use in small animal medicine and is aimed at dexmedetomidine. However, most of what is going to be said will be true for medetomidine as well.

When xylazine first came on the market it was widely used in small animal medicine, but lots of problems occurred. With the advent of medetomidine, there really was no longer any place for xylazine in small animals. Both medetomidine and dexmedetomidine are much safer products and much more is known about them in their use in small animal medicine than there is with xylazine.

Dexmedetomidine is the positive isomer of medetomidine, which means that it is all active ingredient compared to medetomidine which is half active and half inactive. In order to avoid dosing confusion, when Pfizer Animal Health came out with DexDomitor, they “diluted” it 1:1 so that there would be no difference in the volume used compared to the old product. This is still true today. There is some anecdotal evidence that dexmedetomidine does not cause the length of sedation that medetomidine does. Some people perceive this as being less effective, but in reality, it is the sedation not the alpha 2 action of the drug.

Yohimbine is a drug that was made to reverse the action of xylazine. It is not effective for use with medetomidine or dexmedetomidine. The drug use for reversing these two is atepamizole hcl which goes under the trade name of Antisedan.

There are several pharmacological considerations that need to be considered. Alpha 2 agonists effect the cardiovascular system, the CNS, and the renal system. I will discuss each in turn.

## Cardiovascular effects

Anyone who has used dexmedetomidine has probably seen the disconcerting effect that it has on the heart rate. Dexmedetomidine increased the cardiac afterload and this causes an increase in blood pressure resulting in a reflex bradycardia. This is not dose dependent, in other words, it happens at any dose. It is not unusual to have heart rates around 30 bpm. However, keep in mind, this does not translate into increased cardiac output. This is detrimental to the vast majority of cardiac diseases.

## CNS effects

There is an overall drop in the peripheral perfusion, however the blood flow to the brain is maintained adequately for normal function. It additionally has the benefit of preventing high frequency EEG activity when used together with ketamine, thereby preventing seizure activity. Overall it is neuroprotective with one known exception. If there is an ischemic brain injury, the slight decrease in perfusion to the brain could be enough to tip the scales in the direction of hypoperfusion, enough so to cause an exacerbation of the ischemia. It should not be used in cases of suspected brain injury.

## Renal effects

There are mixed renal effects. Although there is a drop in the renal blood flow, it has a “somewhat” balancing effect by preserving renin release, preserving the glomerular filtration rate and reducing ischemic injury. It is best not to use in acute renal disease.

## Use of alpha 2 in the emergency setting

Alpha 2's have several benefits in the ER setting. They are anxiolytic, analgesic, you can incrementally reverse them, and they result in a reduction of the use of other drugs like opioids and gas anesthetics. Common uses are for any anxious ER patient, treating fractures, lacerations and in calming fractious patients. When used for lacerations, they decrease cutaneous blood flow which makes suturing easier. There is no adverse effect of using dexmedetomidine on skin healing if it is given as a single injection or as part of a short term CRI. However, consistently low cutaneous blood flow secondary to prolonged CRI use can cause delay or failure in healing. If an animal is in shock, you should not use alpha 2's as they depress the sympathetic response, which hypovolemic animals need. The exception is septic shock, where an animal that is endotoxic can benefit from alpha 2's: it reduces pro-inflammatory cytokines, promotes macrophage phagocytosis and has an anti-apoptosis (naturally programmed cell death) effect. Use it at a dose of 0.1 to 5 mcg IV over 15 minutes. Finally, in the ER setting, data shows that using dexmedetomidine can be beneficial in CPR. The data is preliminary but it shows an improvement of coronary perfusion pressure and oxygen consumption by the cardiac tissue. There are no doses for this at this time.

## Anesthesia

There are four phases of anesthesia, premedication, induction, maintenance and recovery. Using dexmedetomidine in anesthesia is part of a multimodal strategy with the resulting decrease in anesthetic and analgesic drugs. It has the effect of inhibiting the perception of

pain in the brain, modulation of the spinal pathway, inhibition of transmission at the level of the nerve and it limits transduction by the nociceptor at the periphery.

I will discuss three protocols to use for three classes of animals; Healthy calm, healthy excitable and healthy geriatric, that will fit most of your patients. The patient that I will not discuss is the cardiac patient in which dexmedetomidine should not be used.

As a premedication, dexmedetomidine should be used in combination with an opioid. In healthy calm dogs, give a dose of 10 mcg/kg dexmedetomidine (0.02 ml/kg) IM. In healthy excitable dogs give a dose of 15 mcg/kg dexmedetomidine (0.03 ml/kg) IM. In healthy geriatric dogs give a dose of 2.5 mcg/kg dexmedetomidine IM. To any of these three classes of dogs, add an opioid, I usually use morphine or hydromorphone, and give 0.02 ml/kg IM. Although you can give this in two syringes, I usually combine them in one syringe.

Induction becomes easier once you have used the above premedication protocol. Lower doses of what you normally use increases the safety profile plus it reduces the cost of induction. If you use propofol, give at a dose of 1-2 mg/kg IV. If you prefer diazepam/ketamine, give at a dose of 0.5-1 mg/kg IV.

Maintenance with either isoflurane or sevoflurane can be done at about 1-2% lower than you are accustomed to. Again, increasing margin of safety and saving money on inhalants.

Recovery is great with this combination. No hangover from ketamine if it was used and dysphoria is a rare occurrence. If recovery is too prolonged (especially cats) consider partial reversal of the dexmedetomidine but don't forget you will lose some of the analgesia it provides.

### **Sedation**

When general anesthesia is not needed for very short surgical procedures or slightly painful procedures, then I like to use the "kitty and doggy magic" combination for sedation and mild pain control. Although butorphanol is not my first choice as an opioid for very painful procedures, it is perfectly adequate for some of the shorter and less painful procedures you might perform because of its superior sedation compared to other opioids. When used in this combination it is best to calculate the dose out in meters squared instead of weight. See the chart that follows.

### **Rescue medication/dysphoria**

Dexmedetomidine is a great drug to give post operatively when you feel that either an animal is in pain or if you feel that there is some dysphoria. A single micro dose of dexmedetomidine given IV will usually give positive results within a few minutes. For either case, give 0.25-1 mcg/kg as an IV bolus. Even in a large dog, you are only talking about a few hundredths of an ml of medication. This same dose per hour can be added to a CRI for continued pain control