NEW ALPHA 2 AGONISTS: MUCH MORE THAN JUST SEDATION
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Xylazine, medetomidine (Domitor) and most recently dexmedetomidine (Dexdomitor) are alpha 2 agonists widely used in veterinary medicine. Dexdomitor is a potent and selective alpha₂ (α₂) agonist that is used as a sedative for short procedures such as radiographs. In addition Dexdomitor is labeled for and playing an ever increasing role in premedication providing both pain management and sedation. The new label indications make Dexdomitor very appealing. The principle difference between Dexdomitor and Domitor other than the new label indications is the absence of the inactive molecule, levomedetomide. Domitor contained both the active molecule, medetomidine and the inactive levomebetomidine. Removal of this molecule allows for a purified product with less stress on the liver for clearance. Physiologically and therapeutically the products behave in very similar ways and patient response is expected to be the same.

Although α₂-agonists have been used extensively in veterinary medicine for more than 30 years, veterinary professionals have gained a new appreciation of the unique analgesic and sedative properties of this class during the past decade. Alpha₂-agonists, which are non-narcotic and non-scheduled agents, can be very useful as adjuncts in a balanced analgesic protocol. Their predominant effect is to produce significant sedation accompanied by visceral and somatic analgesia.

There are a variety of new ways to use this drug class as a pre-med, rough recovery rescue and ongoing management of in-hospital pain and anxiety. Dexdomitor combinations are also extremely effective in cats for a variety of surgical and non surgical procedures.

How Alpha₂-Agonists Work
Dexdomitor (dexmedetomidine) specifically binds to alpha₂ adrenaline receptors in the central nervous system and the peripheral nervous system. This inhibits the release of norepinephrine and impedes transmission of further nerve impulses, which provides the dual effect of sedation and analgesia. Alpha-2 agonists cause vasoconstriction and, like kinking a water hose, the narrowed vessels result in increased blood pressure or hypertension. Heart rate goes up when pressure is low and down when pressure is high.
so the slowed heart rate occurs in response to the increased blood pressure and is a very normal response. Bradycardia and vomiting are the most common side effects with \( \alpha_2 \)-agonists.

**The Advantages of Alpha 2s over Other Sedatives**

The provision of analgesia is a component of alpha-2 agonists that is often overlooked. Other commonly used sedatives (e.g., acepromazine and diazepam) do not provide pain relief. The analgesia achieved with alpha-2 agonists is of moderate intensity and moderate duration, much like the analgesia achieved with butorphanol. Obviously, this analgesia is not potent enough for major pain but is appropriate for control of mild pain. Even more importantly, alpha-2 agonists work synergistically with opioids (like butorphanol or morphine) and improve both the intensity and the duration of pain relief.

**When to use Dexdomitor**

Alpha\(_2\)-agonists are short-duration analgesics and can be rapidly reversed with \( \alpha_2 \)-antagonists. This characteristic makes these drugs suitable for procedures requiring short-term restraint and analgesia. Dexdomitor is labeled to be used as a sole agent to facilitate clinical examinations, clinical procedures and minor surgical procedures. A list of minor procedures that require sedation might include radiographs, bandage changes, cleaning ears that are not extremely painful, suturing of minor lacerations, removal of foreign bodies from noses or ears. It is labeled similarly for use as a sedative in cats. Dexdomitor is also labeled as a premedicant as a sole agent but is frequently used off label in combination with opioids. One of the great advantages of using Dexdomitor as a premedicant is the lowering of required induction agent and gas inhalants that results.

Another common use of Dexdomitor® is as a 'rescue' drug for patients that are experiencing bad recoveries following anesthesia. Excitement in recovery (sometimes called 'emergence delirium') is not appropriate whether it is caused by pain or by residual effects of anesthesia. Excitement and pain both cause tremendous physiological stress and side effects that include tachycardia (high heart rate), hypertension (high blood pressure), cardiac arrhythmias (abnormal electrical activity of the heart), ventilation abnormalities (e.g., increased respiratory rate [i.e., tachypnea] with decreased volume of breaths [i.e., tidal volume]), cortisol release (which impairs proper healing), a predisposition for gastrointestinal (GI) ileus and ulceration, etc... This level of stress can cause severe problems in patients with cardiovascular or respiratory compromise. Thus, excitement should be treated regardless of the
cause. Dexdomitor® is an excellent choice (in heart-healthy patients) for treatment since it provides both sedation and analgesia so the patient will be calmed AND will receive some pain relief.

Patients who require repeated rescue doses of Dexdomitor can be placed on a low dose constant rate infusion (CRI) for continued sedation and analgesia. CRIs of dexmedetomidine are commonly used in human patients including children who are agitated in hospital, resistant to ventilators or in narcotic withdrawal. Similar success is reported in veterinary patients particularly in anxious breeds.

Dexdomitor® is used commonly in cats. As with dogs, Dexdomitor® can be used alone or with an opioid for deep sedation or can be used with ketamine for actual anesthesia. The most common use of Dexdomitor® in cats is in a combination called 'kitty magic' that consists of Dexdomitor®, an opioid (most commonly buprenorphine) and ketamine. Because ketamine is a true anesthetic drug the addition of ketamine makes the combination a general anesthetic protocol rather than just a sedative protocol. Minor surgical procedures can be performed under kitty magic or kitty magic can be used prior to gas anesthesia for more advanced procedures. Kitty magic is a very potent combination and the dosage of anesthetic gas will be very, very low. This is a positive effect but is sometimes overlooked by practitioners who may over anesthetize the cat if not warned about the need for low dosages of gas.

**Antisedan (atipamezole) reversal**

One of the primary benefits of alpha-2 agonists is that their effects can be reversed with alpha-2 antagonists. Antisedan® (atipamezole) is most commonly used to reverse Dexdomitor®. Antisedan® is the safest of all of the reversal agents because it works almost exclusively by simply displacing Dexdomitor® from the alpha-2 receptors so that the nerve function can return to normal. Antisedan® has little actual drug effect of its own whereas older reversal agents, like yohimbine and tolazoline, cause both a displacement of the drug at the receptor and CNS stimulation, which causes unwanted side-effects. Furthermore, Antisedan® has a long duration of action (longer than Dexdomitor®) and the animal will not 're-sedate' as often occurs with the older, shorter acting alpha-2 antagonists. Reversibility is extremely important because it not only allows the veterinarian to control the duration of sedation, but it also adds a safety factor since animals that might have previously been sent home sedated or left sedated in a clinic unattended overnight can now rapidly be returned to full consciousness and discharged or left in the clinic without the concern of residual sedation. Also, in the rare case that the
patient isn't responding well to the drug or the veterinarian thinks that the patient is too deeply sedated, the drug effects can be quickly eliminated with the administration of Antisedan.

After administration of Antisedan, patients usually awaken in about 5 to 10 minutes and are able to stand or walk in less than 10 minutes. Antisedan rapidly reverses all physiologic effects of Domitor to 80% of baseline levels within 15 minutes

**Administration**

Dexmedetomidine is a dose-dependent sedative analgesic commonly used as a preanesthetic agent in healthy animals. Onset of effect takes 5 to 15 minutes depending on route of administration (IV or IM) and sedation can last up to 90 minutes. Dexmedetomidine administration results in physiologically normal peripheral vasoconstriction, temporary decreased heart rate, and a transient increase in blood pressure. All cardiovascular parameters smoothly return to pre-sedation levels upon reversal with atipamezole. Candidates for α2-agonist administration should be healthy, have sound cardiovascular systems and be exercise tolerant. α2-agonist should not be administered to animals with compromised cardiovascular and/or respiratory systems

Whether or not an anticholinergic should be administered routinely in conjunction with an α2-agonist has been the subject of considerable scientific debate. Initially, treatment of α2-agonist-induced bradycardia was thought to be beneficial. But today, anticholinergic drugs are generally not recommended, unless bradycardia is profound. Because bradycardia produced by α2-agonists is centrally mediated, it is less affected by anticholinergic action. Excessively high blood pressure, as well as undesirable tachyarrhythmias, has been reported when atropine was combined with dexmedetomidine.

As with any sedative, Dexdomitor works best when administered to an animal that is not overly agitated. For agitated dogs, allow 15 minutes of quiet time to calm down, then administer Dexdomitor and let it take effect. The best-case scenario, however, is to administer Domitor before stress associated with manual restraint occurs. Handling, loud noises, or any other sudden stimuli may cause a startled reaction, even if the animal is sedated. Caution should be used especially when around the animals head and neck.

**Dexdomitor Doses**
**Dogs**

**Premed for routine surgeries**
Combine ¼ label dose with opioid of choice at standard dose and administer IM 15-20 minutes prior to induction. Induction drug volume should be reduced to ½ the usual amount or less. Inhalant anesthesia should be reduced to 0.5-1%

**Protocol for short nonpainful or mildly painful procedures**
Combine ½ label dose Dexdomitor with 0.2mg/kg Torbugesic and administer IM or IV
Can reverse with equal volume Antisedan (to Dexdomitor) IM

**Mini Micro Rescue dose for rough recovery**
Administer 2-5ug/kg IV. (0.2ccs for a 25kg dog) Provides about 30 minutes of sedation to transition smoothly from anesthesia. Can repeat or deliver as a CRI.

**CRI dose for continued dysphoria/anxiety/pain**
Deliver at 2ug/kg/hr. The same dosage can be used in cats. Can be added to other infusions

**Cats “Kitty Magic” for surgical or painful procedures**
In a 5kg cat combine and administer IM:
0.2cc Dexdomitor
0.2cc Ketamine
0.2cc Buprenorphine (or other opioid)
This combination provides 30 minutes of profound sedation and analgesia typically sufficient to perform castration or less painful procedures or intubation. Occasionally small amounts of inhalant anesthesia by mask are required.

**For simple non painful procedures dose can be reduced to**
0.1cc Dexdomitor
0.1cc Ketamine
0.1cc Torbugesic

**Rescue and CRI**
See above dog dosages

References available upon request