Key Points:
1. The newer α-2 agonists medetomidine and its dextro-rotatory isomer, dexmedetomidine, have several advantages over xylazine for use as a sedative/analgesics in small animals patients.
2. Cardiovascular effects of α-2 agonists include a profound increase in systemic arterial pressures and a reduction in heart rate and cardiac output. Co-administration of anticholinergics with α-2 agonists is not recommended, as they do not improve overall cardiovascular performance.
3. Respiratory effects of the α-2 agents are minimal however when they are combined with opioid analgesics respiratory depression can be clinically significant when a patient is not receiving supplemental oxygen.
4. When α-2 agonists are used as preanesthetic sedatives at currently recommended doses, the subsequent amount of anesthetic used for induction and maintenance of anesthesia is reduced by 50-75%.

The α-2 agonists are popular sedative and preanesthetic agents in small animal practice due to the consistent and reliable CNS depression, analgesia and muscle relaxation they produce when administered via either the IV or IM route. Medetomidine and its dextro-rotatory isomer, dexmedetomidine, are more selective α-2 agonists compared to xylazine and as such have greater analgesic properties with fewer undesirable effects as a consequence of α-1 receptor stimulation. Dexmedetomidine, the newest α-2 agonist currently on the market, is licensed for use as both a sedative in the dog and cat and as a preanesthetic agent in the dog in North America.

In general, the sedative effects of α-2 agonists are dose dependant; however, there is a ceiling effect where any further increase in the dose is not associated with a clinically detectable increase in the level of sedation.1 At doses of 2.5-20 ug/kg, dexmedetomidine has a duration of effect ranging from 30-120 minutes. To maximize the reliability of the sedation and degree of analgesia in a patient with a pre-existing painful condition or when a surgical procedure is planned, the α-2 agonist can be combined with an opioid analgesic, such as hydromorphone, morphine, buprenorphine or fentanyl.2

While producing an excellent quality of sedation, α-2 agonists are unfortunately associated with profound cardiovascular side effects, including marked peripheral vasoconstriction and a profound reduction in heart rate and cardiac output.3 Importantly, the duration but not the degree of cardiovascular change produced with the α-2 agonist administration is not strictly dose-dependent.4 As such, reducing the administered dose will not necessarily minimize their impact on the cardiovascular system. Although the co-administration of an anticholinergic will reduce the incidence and severity of the bradycardia produced with α-2 agonists, they result in an increase incidence of arrhythmias, an exacerbation of the increase in systemic arterial pressures, an increase in myocardial workload and a decrease in measures of myocardial contractility compared to animals receiving an α-2 agonist alone. Anticholinergics are therefore not recommended...
for concurrent administration with α-2 agonists.\textsuperscript{5} Experimentally, peripheral α-2 antagonists have been shown to minimize the adverse cardiovascular effects of agents within this class without affecting the quality of sedation however to date, no commercial peripheral α-2 antagonists are currently available.\textsuperscript{5} At this point in time, the alpha-2 agonists should therefore be limited for use in patients with significant cardiovascular reserve.

When administered alone, the respiratory effects of the α-2 are minimal however when used in combination with opioid analgesics, as is recommended prior to diagnostic or therapeutic procedures, significant depression of alveolar ventilation and oxygen can occur.\textsuperscript{6} Clinically, the decrease in oxygenation and hemoglobin oxygen saturation can be difficult to detect with a pulse oximeter due to the vasoconstrictive properties of the α-2 agonist and the resulting poor accuracy of this monitoring modality. Oxygen supplementation is therefore recommended as a precautionary measure in patients heavily sedated with an α-2 agonist-opioid combination.

The α-2 agonists, medetomidine and dexmedetomidine are potent MAC reducing agents. When used as a premedication agent, one should not only reduce the quantity of inhalant used to maintain anesthesia, but also dramatically reduce the quantity of injectable anesthetic used to induce anesthesia. In a study evaluating preanesthetic medication of dogs with medetomidine and hydromorphone prior to induction of anesthesia with ketamine-diazepam, propofol or thiopental, ¼ of the normally recommended dose was used to achieve a depth of anesthesia adequate to achieve orotracheal intubation.\textsuperscript{6} Interestingly, the cardiovascular function in the dogs post induction was similar with all of the latter regimes and not markedly different from the immediate pre-induction time frame. Inhalant anesthetic requirements can be dramatically reduced by incorporating an infusion of an α-2 agonist during the maintenance of anesthesia, however, the potential benefits and risks of such an approach relative to other options such as opioid analgesics require further investigation.\textsuperscript{7,8}

To improve the quality of recovery and minimize the potential risk of self-inflicted injury associated with dysphoria or disorientation during the recovery phase of anesthesia, a low dose of dexmedetomidine (0.5-2.5 ug/kg) can be used as an adjunct during anesthesia recovery. Despite the low doses, the cardiovascular effects of the α-2 agonist are still present, and again, patient selection, monitoring and oxygen supplementation are important considerations to optimize the patients safety.

References: