VETERINARY TEACHING HOSPITAL

VIRGINIA VETERINARY NOTES

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WHAT'S INSIDE!

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This newsletter is published quarterly in support of the outreach program of the Veterinary Teaching Hospital VMRCVM, Blacksburg, VA and is prepared for and distributed to veterinarians in the Mid Atlantic Region.

HOW TO USE MEDETOMIDINE (DOMITOR®) IN DOGS

A new alpha-2 agonist (Domitor®, medetomidine) and antagonist (Antisedan®, atipamezole) have been recently approved for use in the dog and are available through Pfizer. This the first of a series of two articles regarding the use of medetomidine, covering general indications, dosage and other attributes of medetomidine. In the second article, the use of the antagonist atipamezole in dogs will be discussed.

Medetomidine is a potent a-2 agonist designed for use in dogs and cats. It is approved for use in European countries in both dogs and cats, but in the U.S. it is only approved for use in dogs. Within recommended dose ranges in dogs and cats (dogs: 10-40 µg/kg, IM; cats: 40-80 µg/kg, IM), medetomidine induces dose-dependent sedative, analgesic and muscle relaxant actions. In dogs, the sedation and analgesia of 30 µg/kg, IM is equivalent to 2.2 mg/kg of xylazine. Higher doses of medetomidine do not result in more sedation, but the duration of effect is increased.

Medetomidine is approved for both IV and IM routes of administration. Medetomidine is absorbed rapidly following IM injection. Sedation developed within 1 minute following IV administration and within 5 minutes following IM injection. Medetomidine is primarily used as chemical restraint for non-invasive or minor surgical procedures. Medetomidine alone is not suitable for profound painful procedures or major surgical procedures. If painful procedures must be performed, a local anesthetic or other anesthetic adjuncts (ketamine, propofol, opioids, or inhalants) should be used to provide better analgesia and muscle relaxation.

As with other anesthetics, several precautions should be considered before medetomidine is used in dogs. Medetomidine, at the recommended doses, is only suitable for use in young, exercise tolerant dogs, because following medetomidine administration, bradycardia and hypertension occur. Heart rate following medetomidine injection may be as low as 32 beats per minute. The bradycardia is a result of a baroreceptor reflex to hypertension. Medetomidine-induced bradycardia may be prevented or treated with anticholinergics (atropine or glycopyrrolate). Preventing bradycardia with preemptive anticholinergic administration may be more effective than attempting to reverse bradycardia after it has occurred. To prevent medetomidine-induced bradycardia, the current recommendation is to administer atropine at 0.02 mg/kg, IM or glycopyrrolate at 0.005 mg/kg, IM 10 minutes prior to medetomidine administration (IM or IV). To treat medetomidine-induced bradycardia without inducing profound tachycardia, the current recommendation is to administer atropine at 0.01 mg/kg, IV or glycopyrrolate at 0.0025 mg/kg, IV. Mean arterial blood pressure may increase to 120 mmHg 90-100 minutes following medetomidine administration. This is primarily due to a vasopressor effect from the medetomidine. Respiratory function remains within acceptable ranges following medetomidine administration. Cyanosis may be present in up to 33% of dogs breathing room air and sedated with medetomidine. These animals showed insignificant changes to arterial blood oxygen tension and their hemoglobin oxygen saturation often greater than 95%. It has been suggested that the cyanotic mucous membranes result from a low heart rate, accompanied by slower blood flow through the tissues, leading to increased oxygen extraction and venous desaturation and is a non-harmful effect of medetomidine. Because medetomidine induces dramatic cardiovascular changes, the use of medetomidine in debilitated dogs or those with cardiopulmonary dysfunctions is not advised.

Medetomidine may be used to produce sedation for non-invasive procedures (radiography, oral, and ear examinations, nail clipping, diagnostic procedures, etc.) or minor surgical procedures (suture removal, minor laceration repair, joint taps, etc). Medetomidine, at the recommended doses produces a rapid and reliable sedation which can be shortened, at any time during the procedure, with atipamezole. At 30 µg/kg, IM, medetomidine induces a duration of sedation that is approximately 70-90 minutes. Up to 50% of dogs receiving 30-40 µg/kg medetomidine may be intubated. The remaining dogs may not tolerate the endotracheal tube despite relaxed jaw tone and may have dramatic reactions to the endotracheal intubation procedure. If intubation is desired following medetomidine sedation, several methods can be used to ensure successful endotracheal intubation in all dogs. The dog can be masked with a low percentage (2%) of isoflurane or halothane for a short period of time (1-2 minutes) or induced with thiopental, propofol or diazepam/ketamine.

If medetomidine is used as premedicant prior to inhalant anesthesia, several routine procedures must be adjusted. Since medetomidine is a potent sedative and has profound sparing effects on other anesthetics, the induction dose of thiopental, propofol, diazepam/ketamine, Telazol® or inhalants should be dramatically (up to 80%) reduced and a conservative "titrate to effect" for induction should be used. Following endotracheal intubation, the inhalant anesthetic for maintenance must also be reduced. We suggest that the dog begin on a 1% vaporizer setting on either halothane or isoflurane, until the dog reacts to surgical stimulation. When the dog reacts to surgical stimulation, the vaporizer should be adjusted to approximately 1.5-2%. If further reaction to surgical stimulation occurs, the percentage of the inhalant should be increased accordingly, Following subcutaneous or IM administration of medetomidine, vomiting may occur with the earliest signs of sedation. Even with doses as low as 10 µg/kg, diuresis is observed, and large volumes of dilute urine are produced approximately 60 minutes after medetomidine administration.

In summary, medetomidine is an effective and reliable sedative for chemical restraint in dogs. Coupled with atipamezole, the duration of sedation can be precisely controlled, Selective use of medetomidine, with knowledge of cardiopulmonary changes and medetomidine sparing effects on other anesthetics, improves the safety of this drug. **--Jeff C.H. Ko, DVM, University of Florida; and Charles J. McGrath, DVM, VMRCVM, Virginia Tech.**

HOW TO USE THE NEW ALPHA-2 ANTAGONIST, ATIPAMEZOLE (ANTISEDAN®) TO REVERSE MEDETOMIDINE (DOMITOR®) IN THE DOG

Both the new alpha-2 agonist, medetomidine (Domitor®), and antagonist, atipamezole (Antisedan®) have recently been approved for use in the dog and are available through Pfizer Animal Health. This is the second of two articles regarding the use of medetomidine. The first article covered general indications, dosage and other attributes of medetomidine. In this article, we hope to accomplish the same objectives for atipamezole.

Several questions should be addressed before atipamezole is used. The first question is: what is the purpose of the reversal? Some reasons may be a) to shorten the duration of sedation, allowing the patient to be completely mobilized, following a non-invasive or minor surgical procedure; and b) to reverse adverse cardiovascular side effects induced by medetomidine, allowing the patient to return to the hemodynamic stage prior to medetomidine administration. Another question to consider is: following reversal, will the patient experience pain? These questions should be considered carefully.

The use of atipamezole to shorten medetomidine induced sedation following a noninvasive procedure or minor surgical procedure is appropriate and may provide several advantages. A shortened recovery time for both in- and out-patients allows the patient to be conscious, not requiring full supervision, or ready for discharge from the hospital. Reduced recovery time also allows the patient to regain thermoregulatory ability, which may prevent hypothermia. Although atipamezole can be used to counteract the bradycardia induced by medetomidine, one should realize that once atipamezole is administered to the patient, the sedation, analgesia and muscle relaxation induced by medetomidine are also gone, and, therefore, the initial purpose of using medetomidine is diminished. Consequently, we prefer to prevent or treat medetomidine induced bradycardia, should it occur. If a painful procedure is performed on the patient, one should consider supplementing an analgesic before the medetomidine is reversed. This is because atipamezole will reverse all the actions induced by medetomidine, including analgesia. The most commonly used supplemental analgesics include butorphanol or a similar opioid.

When using atipamezole, we suggest a dose that is 5 times (mg for mg) the medetomidine dose. Therefore, given the formulation of atipamezole, the volume of the injected dose should equal to the volume of medetomidine injected. The route of administration indicated on the label is IM injection, but we have not encountered any problems with IV injections of atipamezole using an equal-volume dose. Results from some clinical experiences indicate that a reasonably complete reversal can be obtained using a dose of atipamezole that is half the volume of medetomidine given, if the atipamezole is given IV and it has been more than 45 minutes since the medetomidine injection. We found no benefit to increasing the dose of atipamezole to more than 5 times the medetomidine dose.

An equal-volume IM injection of atipamezole produced complete reversal of medetomidine within 8 to 10 minutes of injection, even if the atipamezole was given as short as 15 minutes after medetomidine. In some dogs, because of the vasoconstriction in skeletal muscle following medetomidine, reversal might be better achieved by using atipamezole IV.

We also found that a dose of atipamezole that was 10-20 times the medetomidine dose (2-4 times the volume of medetomidine), while not improving reversal, did not have any adverse effects. Therefore, if a dog given an IM dose of atipamezole does not seem to respond in 10-15 minutes, a second dose of atipamezole, equal to one half of the volume of the medetomidine dose, could be given. The clinician should be mindful that there are residual effects of other CNS depressing drugs, such as opioids or anesthetics, that may account for persistent sedation and appropriate action should be taken to reverse or enhance the elimination of these agents, as desired. Inadvertent injection of atipamezole in the absence of medetomidine is not a concern. It has been shown that healthy dogs tolerated treatment with 10-times the recommended dose of atipamezole and repeated doses of 1, 3- and 5-times the recommended dose of atipamezole in the absence of medetomidine. Excitement, panting, trembling, vomiting, soft or liquid feces or vasodilation of sclera are reported signs of atipamezole overdose. **--Charles J. McGrath, Professor of Anesthesiology, VMRCVM, Virginia Tech and Jeff C. Ko, Assistant Professor of Anesthesiology, University of Florida**

PARALYSIS AFTER VACCINATION

Cervical intramuscular vaccination caused granulomatous inflammation that resulted in spinal cord compression and paralysis in a group of 3-5 month old dairy heifers. Seven of fifty heifers (14%) in this group developed a progressive neurologic deficit. Three affected heifers were evaluated clinically, but results were nondiagnostic. Symptomatic therapy did not slow progressive worsening of the clinical picture. Five heifers died (10%) or were euthanized after becoming tetraplegic, and three were necropsied. Gross and histopathologic changes were similar in all three cases.

Epaxial muscle on the right side of the neck between C4 and C6 was pale, firm, and friable; with extension of the soft tissue reaction through intervertebral foramina at either C4-5 or C5-6. Grossly visible compression of the spinal cord by the resultant granuloma was evident in one calf at the time of necropsy.

Histopathology in all cases showed focal, segmentally severe, wallerian degeneration of spinal cord segments immediately beneath the epidural granulomas. Affected muscle was necrotic and expanded by numerous granulomas surrounding variable sized optically clear spaces. One granuloma contained a hair shaft.

Aerobic and anaerobic cultures of affected muscle were negative. Stains for fungi, mycobacteria, and bacteria were negative. The combination of the histologic appearance, localization of the gross lesions, the presence of the hair shaft deep within epaxial muscle, and negative culture and stain results led to the conclusion that these granulomas were the result of an injection site (foreign body) reaction.

Questioning of the owner revealed that all 50 heifers in this group had been vaccinated in the cervical musculature fifteen days prior to the onset of clinical signs. Each calf received three different oil adjuvanted bacterins totaling nine mls of vaccinal product.

Recently it has been recommended that the neck be used for intramuscular injections in cattle in response to consumer concerns about injection site granulomas in preferred cuts of meat. While this procedure has significant positive economic impact, this case illustrates the risk of losing individual animals if a large volume of an irritating solution is administered in close proximity to the cervical spine. **--DVM News, South Dakota State University, Extension Service, Vol. 10, No. 4, July/Aug 1996, as reported in Animal Health Beat, Volume 12, Issue 10, October 1996, University of Nevada - Reno.**

JUVENILE BLINDNESS IN THE SHAR PEI LINKED TO HERITABLE LENS LUXATION

A study is underway at the Virginia-Maryland Regional College of Veterinary Medicine to investigate the incidence and etiology of a syndrome seen in the Shar Pei involving lens luxation and glaucoma. Preliminary results show that this condition arises as anterior lens luxation (or subluxation), secondary glaucoma, and subsequent blindness. In the VMRCVM study, this condition has been documented in a closely related, but not inbred, family of Shar Peis, lending strength to the hypothesis that the condition is indeed heritable. An autosomal recessive mode of inheritance is proposed, based on phenotypic analysis.

Often the afflicted dogs present blind due to irreversible glaucomatous optic nerve and retinal damage. The affliction is usually first noted at 4 to 5 years of age. Although most animals first present with a complaint of blindness, other clinical signs may be seen prior to endstage disease. Iridodonesis (a wavering motion of the iris, due to a lack of lens support, seen with ocular movement), increased intraocular pressure, buphthalmic (globe enlargement), corneal edema (either focal or generalized), and/or subluxation of the lens (aphakic crescent) or luxation of the lens into the anterior chamber may be seen early by the observant owner or the astute veterinary practitioner. Once identified, medical and/or surgical therapy is recommended to try to prolong vision. Neutering afflicted animals (and potentially their close relatives) is recommended to prevent perpetuation of this painful, blinding disorder. **--Jarrod A. Lazarus, BS, DVM, and J. Phillip Pickett, DVM, Diplomate ACVO, VMRCVM, Virginia Tech, Blacksburg, VA.**

MAMMARY NEOPLASIA IN MALE DOGS

The purpose of this retrospective study was 1) to investigate the incidence and clinicopathological features of mammary neoplasms in male dogs, and 2) to compare findings from cases in male dogs to literature reports of mammary neoplasms in male and female dogs.

The criteria for selection of cases was as follows: male dogs in which mammary neoplasia was diagnosed by histopathological examination of biopsy specimens submitted to the Animal Disease Diagnostic Laboratory at Purdue University between July 1991 and December 1995.

Data collected and evaluated were age and breed of dog, gland(s) affected, evidence of metastasis, and histopathological diagnosis. Telephone interviews with practitioners were conducted in order to assess local recurrence, metastasis, and patient survival.

Of 997 cases in dogs with a histopathological diagnosis of male dogs, mean age at diagnosis was 9.5 years. Forty percent (8/20) of male dogs with mammary neoplasms were mixed breed; 20% (4/20) were cocker spaniels, and 15% (3/20) were poodles. Fifty percent of mammary neoplasms in males occurred in the fourth of fifth glands; 25% (5/20) had neoplasms in multiple glands. Histologically benign neoplasms were diagnosed in 65% (13/20) of male dogs with mammary neoplasms; the most common histopathological type was mammary adenoma. Of seven males with histologically malignant mammary neoplasms, local recurrence was diagnosed in two (29%).

Most mammary neoplasms in male dogs occur in the third, fourth, or fifth gland. Although approximately one-third of mammary neoplasms in male dogs were histologically malignant, 90% of all mammary neoplasms in male dogs did not recur locally or metastasize. **--DVM News, South Dakota State University Extension Service, Vol. 10, No. 4, July/Aug 1996, as reported in Animal Health Beat, Volume 12, Issue 10, October 1996, University of Nevada - Reno.**

OPPORTUNITY

In the middle of difficulty lies opportunity **--Albert Einstein**

Problems are opportunities in work clothes. **--Henry Kaiser**

FIRST IMPRESSIONS

"Coffee stains on flip-down trays in airplanes make passengers think the engines don't work." That's what an airline executive told Jeffrey Nugent, vice president for Johnson and Johnson.

The comment shows how quickly people connect one aspect of an operation with another. That's why it's important to look at the little things that mean a lot in terms of impressions. Here's a checklist of questions you might ask about your operation:

- How are phones being answered? Does someone pick up a call by the third ring? Do employees give their names when answering, so that callers feel they're dealing with a person instead of an institution?
- How are visitors greeted when they enter your building? Are they acknowledged promptly - or are they made to wait until someone gets good and ready to approach them? If a receptionist is on the phone, does he or she tell a visitor, "I'll be with you in a minute?"
- Have you coached your employees to use nonsexist communication? For example, do some of your male workers sill call women "girls?"
- When greeting visitors or customers, do your people convey positive body language? Do they smile, for example? Studies show that the most important thing in determining whether you impress others favorably is how often you smile.
- Have you selected typefaces, for both your letterheads and fax cover sheets, that convey the image you want to have represent your organization?
- Do you return reporters' calls as soon as possible? Or do you give the impression that you're indifferent about media relations?
- Is your company's logo current? Does it represent today's culture - or does it give the impression that your organization is behind the times?
- Have you checked the appearance of your building and grounds recently? Does the building look in need of repairs? Are the rugs starting to show wear? Do you keep the shrubs and lawn manicured?
- If you have vehicles on the road, do they look clean and well-maintained? Are the drivers courteous and do they follow all traffic laws?
- Have you provided choice parking spots for visitors - and are they clearly marked? Do employees often claim the best spots, causing visitors to walk a long distance?

--Animal Health Spectrum, Mississippi State University Cooperative Extension Service, Vol. 7, No. 3, September 1996, as reported in Animal Health Beat, Volume 12, Issue 10, October 1996, University of Nevada - Reno.

TEACHING HOSPITAL DIRECTOR INJURED

Dr. Robert Martin, Director of the Teaching Hospital, College of Veterinary Medicine at Virginia Tech, fell from a tree on his farm near Blacksburg while deer hunting on November 11. He suffered a fracture of T7 which severely damaged his spine, causing paralysis posterior to the injury. Dr. Martin is recuperating following surgery at the University of Virginia Medical Center in Charlottesville. He will receive an extended period of rehabilitation before returning home, hopefully before Christmas. His spirit is excellent.

Dr. Martin appreciates the expressions of concern from his many friends, colleagues, and former students. He has assured us he will be back at work before long. Dr. Greg Troy has assumed the role of Hospital Director until Bob is back in the Teaching Hospital.

LETTER TO THE EDITOR

Dear VVN Editor:

I am deeply concerned over the blurb about unwanted pregnancies in the dog. The dog is exquisitely sensitive to estrogen. The sensitivity is often unpredictable, idiosyncratic, but can be dose related. This is especially true of estradiol cypionate. The veterinary literature is rife with manuscripts describing permanent, irrevocable aplastic pancytopenia...and death, associated with the use of this drug. Therefore the choices for a veterinarian and the client are three when there is an unwanted pregnancy:

1. let the bitch have pups
2. spay the bitch
3. abort the bitch using prostaglandins and bromocriptine

It is quackery to use estradiol cypionate in this clinical setting. Veterinary clinicians I know refuse to use this drug for treatment of unwanted pregnancy. Although the article did state, "All of these (estradiol, prostaglandins, bromocriptine, dexamethasone - the drugs mentioned in the article) have side effects, some of which may be potentially life-threatening.", the use of estradiol cypionate carries even greater risks and should never be thus used. **--Bernard F. Feldman, DVM, PhD, Professor of Veterinary Clinical Hematology and Biochemistry, Chief of Service, Clinical Diagnostic Laboratories, President, American Society for Veterinary Clinical Pathology, VMRCVM, Blacksburg, VA.**

NEW DERMATOLOGIST

Dr. Rosanna Marsella has joined the veterinary college faculty and Teaching Hospital staff as a board-certified dermatologist. She earned her DVM at Universita' degli Studi di Milano in Milano, Italy; spent time in private practice and completed her residency in dermatology at the University of Florida in Gainesville. She has special training in pharmacology.

CONTINUING EDUCATION OPPORTUNITIES WINTER-SPRING 1997

Date	Topic	Location	Contact Hours
January 24-25	Orthopedic Surgery of Canine Hindlimb	Blacksburg	10
February 28 - March 1	Diagnostic Clinical Cytology	Blacksburg	10
March 14-15	Canine and Feline Reproduction	Blacksburg	10
March 21-22	Practical Eye Surgery	Blacksburg	10
March 29	Equine Reproduction	Leesburg	8
April 11-12	Gastrointestinal Endoscopy	Blacksburg	10
April 19	Anesthesia for Technicians	Blacksburg	6
May 16-17	Diagnostic Ultrasonography	Blacksburg	10
May 23-24	Aquatic Medicine	Blacksburg	10

Please note: The courses listed above are limited enrollment and feature a hands-on laboratory experience. Program brochures will provide course details. For registration or more information, please contact:

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