Sedation and Management of Behaviorally Challenging Patients
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Introduction
• Most pet behavior problems will NOT be successfully treated with drugs alone!
• "I have a _____ dog or cat who is doing X. What medication do I use to treat it?"

Setting the Stage = Low Stress Environment
1 • Visual
   • Auditory
   • Olfactory
   • Tactile
2 • Pre-test medications
   • Pet should be hungry
   • Reception facilitates
   • Cater to preferences
   • Cell phone check in
   • Wait outside
   • Prepay
   • Last or first appointment
   • Set up exam room prior to
   • Treat outside
   • Use alternative methods?

This...

So what do I do about “aggression”?
• Aggression is a clinical sign not a diagnosis!
• Diagnosis is required for treatment
• Treatment varies with diagnosis
• Approximately 30% of the cats and dogs that walk into your practice are aggressive.
• Fear-based behaviors

• What pharmaceuticals can you use to facilitate handling, decrease stress and improve safety for your patients and staff?
•
7. **Use Chemical Restraint (CR)**
   - Decrease patient anxiety and emotional distress
   - Prevent fear memories from being established and to prevent increased future aggression
   - Increase handler safety through decreased fractious behavior
   - Prior to any painful or socially invasive procedure
   - Marked fear at any point
   - Moderate fear in response to minimal handling
   - Severely fractious behavior at any point
   - Moderately fractious behavior in response to minimal handling
   - Start with oral premeds-trazodone, benzodiazepines, gabapentin, acepromazine (NOT as sole agent)

8. **Treating Behavior Problems With Drugs...**
   - Should only be done in 3 circumstances
     1) To prevent harm to the patient until it can be seen by a specialist
     2) As a part of a complete treatment program that includes a diagnosis and plans for behavior modification in addition to drug therapy
     3) On an occasional “as needed” basis to prevent harm or extreme distress when stimuli are predictable such as visits to the veterinary hospital

9. **Consider two types of psychotropics:**
   - Event medications
   - Daily medications

10. **Before Beginning Drug Therapy**
    - Start with a detailed behavior history and a proper medical work up
    - Establish a working diagnosis first
    - “Fear-based aggression in a veterinary setting”
    - Educate your clients!
      - Almost all of these drugs will be used extra-label
      - Ideally don’t use without blood work
      - Behavior problems are rarely cured, they are managed
      - Equivalent to any other chronic disease condition
      - Likely to recur with withdrawal of the drug or when drugs are used alone without behavior modification

11. **Consider this approach:**
    - Step 1: Begin treatment with the event medication.
    - Step 2: Titrate the dose to the needed effect.
    - Step 3: Refer OR pursue a more detailed work-up and initiate treatment with maintenance medication.
12 **Classes of Psychotropic Medications**
- Different classes affect different neurotransmitters
- This explains how they work and...
- What their side effects might be

13 **Drugs in your toolbox**
- Benzodiazepines
- Serotonin antagonist reuptake inhibitors (SARI)
- α2adrenergic agonists
- Beta-adrenergic receptor antagonists
- α2δ1 ligand binders
- Neurokinin (NK1) receptor antagonists
- Antipsychotics
- Selective serotonin reuptake inhibitors (SSRIs)
- Tricyclic antidepressants (TCAs)

14 **Benzodiazepine Effects**
- May affect memory
- Low doses - calming, anti-anxiety
- High doses - sedating
- Paradoxical excitation can occur - try a slightly higher dose or switch BZs
- May increase impulsivity
- Use with caution in aggression

15 **Benzodiazepine Side Effects**
1. Sedation
   - Ataxia
   - Muscle relaxation
   - Increased appetite
   - Increased friendliness
   - Anxiety
2. Hallucinations
   - Muscle spasticity
   - Insomnia
   - Idiopathic hepatic necrosis in cats (diazepam)
Clinical Guidelines for Use

1. Use caution when prescribing - addictive
   • Withdraw gradually - 25%/week
   • Tolerance may develop
   • Most useful when combined with longer lasting agents for treatment of separation anxiety and noise phobias

2. Contraindications
   • Concurrent liver and kidney disease
   • Glaucoma
   • Pregnant or lactating females
   • Overdose
     • Treat symptomatically
     • Flumazenil (Mazicon) - BZ receptor agonist

Commonly Used Benzodiazepines

• Alprazolam (Xanax) - minimal active metabolites
  • Rapid onset
• Oxazepam - no active metabolites
  • Slower onset but longer duration of action
  • Wide separation between effective dose and sedating dose

Trazodone

• Categorized as a SARI
• Use similar to clonidine or benzos for anxiety
• Don’t use w/ clonidine
• Can potentiate CNS depressants
• Multiple studies in dogs and cats but mixed results

Alpha-2 adrenergic agonists

1. Bind to presynaptic α2 receptors (negative feedback receptors)
   • Causing a decrease in calcium levels
   • Inhibiting the release of norepinephrine (NE)
   • Resulting in a subsequent decrease in sympathetic tone, sedation, analgesia and anesthesia

2. Clonidine
   • Detomidine
   • Dexmedetomidine

Clonidine

• It is a relatively non-selective alpha-2 adrenergic agonist acting on α2A, α2B and α2C adrenergic receptors as well as the I1 receptor (imidazoline receptor)
• Used for treatment of fear or anxiety
• Can be given BID or PRN 2 hours prior to event
• Single study in dogs (Ogata 2011)

21  □  Detomidine
• Similar to clonidine but is more selective for the α-2 receptor subset
• Commercially available in an oral transmucosal (OTM) formulation used for restraint and sedation in horses Dormosedan® (Zoetis)
• Two studies looking at its efficacy in dogs (Hopfensperger 2013, Messenger 2016)
• Single study in cats (Smith 2017)

22  □  Dexmedetomidine
• Highly selective α2-adrenergic agonist
• Binds to presynaptic α2-adrenergic neurons in the locus ceruleus (LC) in the brain stem inhibiting voltage gated Ca2+ channels, decreasing the firing rate of LC neurons and causing presynaptic inhibition
• The end result is a decrease in norepinephrine (NE) release
• Reduced level of NE lead to reduced fear and anxiety

23  □  Beta-adrenergic receptor antagonists
  1. β blockers were developed in the 1950's for the treatment of cardiac and circulatory diseases in humans
• β blockers have also been used in the treatment of post-traumatic stress disorder and panic disorders in people and canine post-traumatic stress disorder (C-PTSD)
• Work centrally and peripherally to inhibit the actions of norepinephrine

  2. Propranolol
• Pindolol

24  □  Propranolol
• Is a β1, 2-adrenoreceptor antagonist that works centrally and peripherally to inhibit the actions of norepinephrine
• Has a centrally acting inhibitory effect on the protein synthesis needed to consolidate recent events into long-term memory
• No published studies on the use of this medication in dogs or cats

25  □  α2β1 ligands
  1. Bind to the α2β1 presynaptic voltage-sensitive calcium channels blocking release of excitatory neurotransmitters (glutamate, substance P, norepinephrine)
• They have been used as anxiolytics for the treatment of social anxiety and panic disorder in people
  2. Gabapentin
• Pregabalin

26  □  Gabapentin
• is a structural analog of gamma amino butyric acid (GABA) but it does not alter GABA binding
• Its anxiolytic effect is believed to be due to the binding of voltage-sensitive calcium channels in the amygdala preventing the release of glutamate and the associated fear response
• Two studies in cats (Pankratz 2017; van Haften 2017)

27 Neurokinin (NK1) receptor antagonists
• Substance P and NK1 receptors are widely distributed and are found in areas associated with the regulation of emotions including the amygdala, the periaqueductal gray and the hypothalamus
• Substance P has been linked with aggressive behavior in some mammalian species
• NK1 receptors and substance P are also involved in stress and pain responses

28 Maropitant (Cerenia®-Zoetis)
• Acts both centrally and peripherally by inhibiting substance P, the neurotransmitter associated with vomiting
• Used for the treatment of motion sickness and other causes of nausea in dogs and cats
• Potential for many additional uses including as an adjunct medication for the treatment of pain and as a mediator of the stress response during handling and hospitalization

29 Antipsychotics
• Phenothiazine neuroleptic most commonly used in vet med (acepromazine)
• Blocks post-synaptic dopaminergic receptors
• Anticholinergic, antihistaminic and alpha adrenergic blocking effects

30 Neuroleptic Side Effects
1 • Hypotension
• Bradycardia
• Cardiovascular collapse
• Syncope
• Apnea
• Hypothermia
• Ataxia
2 • Paradoxical excitation
• Reaction to noise
• May aggression

31 Neuroleptic Uses
1 • Pre-anesthetic agent
• Chemical restraint
• For short term of motor activity
• Antiemetic
2. Not an anxiolytic!
   - Not for phobias
   - Not for long term use
   - Not for aggression

32. **Tricyclic Antidepressants (TCA's)**
   - Block norepinephrine reuptake
   - Block serotonin reuptake
   - Anticholinergic and antihistaminic effects
   - Alpha adrenergic antagonists
   - Initially may cause some stimulation or anxiety
   - Very bitter tasting so may require compounding
   - Amitriptyline and clomipramine (Clomicalm) most commonly used
   - Several weeks to take effect - do not use prn

33. **TCA Uses**
   - Urine marking in cats (clomipramine)
   - Anxiety disorders in dogs and cats
   - Compulsive disorders
   - Psychogenic alopecia
   - Hyper vocalization in cats
   - Canine aggression?

34. **Selective Serotonin Reuptake Inhibitors (SSRI)**
   - Increases 5HT levels in the synaptic cleft
   - Mood-elevation, calming, sedation without learning impairment
   - Minimal effects on other neurotransmitters
   - Weeks to take effect - do not use prn

35. **SSRI Uses**
   - Urine marking in cats
   - Fear and anxiety related conditions
   - Compulsive disorders
   - Some anti-aggressive and anti-impulsivity effects

36. **Summary**
   - Drugs don't modify behavior, we do
   - Drugs are just one tool in our tool box
   - Inappropriate use of psychotropics may decrease client compliance with behavior modification protocols thus decreasing overall efficacy of treatment
   - The sooner you treat, the better your chances of success
Recommended Texts

- Veterinary Psychopharmacology by Sharon Crowell-Davis and Thomas Murray, Blackwell Publishing 2006
- Blackwell's Five Minute Veterinary Companion- Canine and Feline Behavior 2nd ed. by Debra Horwitz, Blackwell Publishing, 2018

Finally a book you can recommend with confidence!

Questions?

www.behaviorsolutions.guru