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Medical Management of Behavioral Problems

Behavioral problems are prevalent in our veterinary patients. The more common canine issues include separation anxiety, storm phobia, and aggression directed at people or other dogs. In cats, the common problems include inappropriate elimination, urine marking, and aggression directed at people or other cats. Those of us who work with birds know that screaming and feather-picking (with or without resulting self-mutilation) are not uncommon.

INDICATIONS

The core of any behavioral treatment plan consists of teaching the pet to “relearn” a variety of appropriate behaviors. For example, a dog with separation anxiety will need to learn that it can be left alone without panicking. The dog with fear-motivated aggression directed at tall men in hats needs to learn that it does not need to react anxiously to those men.

However, if the dog is too anxious during a training session, it will have difficulty processing the information it needs to learn. Therefore, most of the medications used in behavioral cases help decrease pets’ overall level of anxiety and reactivity so they can learn new things and change their behaviors.

CONSIDERATIONS

The more commonly used classes of behavioral medications include benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), azapirones, and monoamine oxidase inhibitors (MAOIs). The use of these medications—unless specifically indicated through FDA approval—is considered to be “off-label” and their use must be discussed with your clients (see **Box**).

Before starting any behavioral medications, baseline blood analysis and urinalysis should be done as part of the general medical workup. As the prescribing veterinarian, you should remember that the patient is in your care and therefore your responsibility. Medication should only be prescribed for patients you have seen and diagnosed or under the instruction of a board-certified veterinary behaviorist who is treating the patient.

DRUG CLASSES

Benzodiazepines

Mode of Action. Benzodiazepines facilitate the effect of gamma aminobutyric acid (GABA)—the major inhibitory transmitter in the brain. Benzodiazepines specifically bind to GABA-A receptors and act on the hypothalamus and limbic system, resulting in an anxiolytic effect.¹

OFF-LABEL DRUGS: WHAT TO DO



Discuss use of the medication with your client and provide an informed consent form that outlines the reason the medication is being prescribed (including a behavioral diagnosis), what the medication is expected to do, and what the potential side effects are. Both the veterinarian and client should sign this document. A copy should go to the client, and the other should remain with the patient’s record.

Indications. Benzodiazepines are potentially useful for any behavioral problems that manifest with anxiety, fear, or phobia (especially if rapid action and as-needed dosing are desirable) associated with such events as owner departures, storms, or visits to the groomer.

Considerations. Potential side effects include sedation, ataxia, hyperphagia, and weight gain.² Tolerance can also be seen with these drugs—the more the pet takes, the more the pet may need to attain the same effects.

Another thing to watch for is “paradoxical excitement,” a situation where the pet gets more agitated after taking the drug instead of becoming more relaxed. Therefore, owners should give the first dose when they are present so they can observe the effects.

Interactions. Benzodiazepines can be used in combination with SSRIs, TCAs, and MAOIs.

Dosing. Table 1 outlines the more common benzodiazepines used in dogs and cats, and their doses.

Indications. The more common uses in veterinary medicine include treatment of anxiety disorders (separation anxiety, urine marking), compulsive disorders (overgrooming in cats, acral lick granulomas), aggression (especially anxiety and fear-motivated), and phobias (storm phobia). SSRIs have also been recommended for birds who pluck their feathers. One SSRI, fluoxetine (Reconcile, elanco.com), has been FDA-approved for the treatment of separation anxiety in dogs.

Considerations. The effects of SSRIs may be seen in as little as a few days but typically take 4 to 8 weeks to reach peak effects. Potential side effects include gastrointestinal manifestations (decreased appetite, diarrhea) and nervous system effects, including sedation and agitation.³ These effects can vary with the drug, dose, and patient. Some cats, particularly males, may experience urine retention when treated with an SSRI, so care should be taken to ensure that owners know their cat’s litter box habits.

Interactions. In general, SSRIs shouldn’t be used in combination with one another or with any of the TCAs or MAOIs to prevent the possibility of serotonin syndrome, which results from too much serotonin in the pet’s system. Signs of this potentially serious adverse effect include mental, neuromuscular, and autonomic changes. In addition to withdrawing the offending medication, treatment should include thermoregulation and fluid therapy. Anticonvulsant therapy may be needed to decrease agitation.¹

Dosing. Tables 2 and 3 outline the doses for the most common SSRIs used in dogs, cats, and birds.

Table 1. Doses for Commonly Used Benzodiazepines¹

| Medication | Dogs | Cats |
|------------|------------------------|-------------------------|
| Alprazolam | 0.02–0.1 mg/kg Q 4 H | 0.0125–0.25 mg/kg Q 8 H |
| Clonazepam | 0.1–0.5 mg/kg Q 8–12 H | 0.015–0.2 mg/kg Q 8 H |
| Diazepam | 0.5–2 mg/kg Q 4 H | 0.1–1 mg/kg Q 4 H |

Selective Serotonin Reuptake Inhibitors

Mode of Action. SSRIs are a class of antidepressants that have anxiolytic effects in addition to anticomulsive and antiaggressive effects. SSRIs block the reuptake of serotonin, making more available in the synapse and thereby optimizing transmission. Serotonin, also called 5-HT, is involved in modulation of mood, anxiety, satiety, cognition, aggression, and sexual drive.³

Tricyclic Antidepressants

Mode of Action. TCAs act very much like SSRIs except that they are less selective for serotonin and have effects on other neurotransmitters, such as norepinephrine.

Indications. Uses for TCAs are very similar to those of SSRIs, as are the onset of action and side effects. Clomipramine (Clomicalm, novartis.us) has been FDA-approved for the treatment of separation anxiety in dogs.

MAOI = monoamine oxidase inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant

Dosing. Tables 4 and 5 outline the doses for the most common TCAs used in dogs, cats, and birds.

Azapirones

One medication used in the treatment of anxiety in dogs and cats is buspirone, which belongs to a class of drugs called azapirones.¹

Mode of Action. Buspirone is a partial serotonin agonist, so its effects and uses are similar to those of SSRIs and TCAs.

Indications. Due to its very few side effects, buspirone is a good choice for older patients and those with other medical conditions.

Interactions. Buspirone can be used in combination with benzodiazepines as well as with SSRIs and TCAs because it seems to have a synergistic effect. However, buspirone should be used cautiously with MAOIs.¹

Dosing. The typical dose for dogs is 0.5 to 2 mg/kg Q 8 to 24 H; for cats, the typical dose is 2.5 to 7.5 mg Q 12 H or 0.5 to 1 mg/kg Q 12 H. If you're using buspirone in combination with an SSRI or TCA, use a lower dose of each than you typically would.

Monoamine Oxidase Inhibitors

Mode of Action. Monoamine oxidase (MAO) is an enzyme that catabolizes the oxidative deamination of catecholamines, including dopamine, norepinephrine, epinephrine, and serotonin.

There are 2 types of MAOIs—those that prevent the action of MAO-A, and those that prevent the action of MAO-B. By preventing the action of these enzymes, catecholamine levels increase in the central nervous system.

Indications. Of the MAOIs, only selegiline is routinely used in the treatment of behavioral conditions in animals. Selegiline is an irreversible inhibitor of MAO with a greater affinity for MAO-B than MAO-A.

Table 2. Doses for Commonly Used SSRIs in Dogs & Cats¹

| Medication | Dogs | Cats |
|------------|-----------------------|----------------------|
| Fluoxetine | 1–2 mg/kg PO Q 24 H | 0.5–1.5 mg/kg Q 24 H |
| Paroxetine | 1–1.5 mg/kg PO Q 24 H | 0.5–1.5 mg/kg Q 24 H |
| Sertraline | 0.5–4 mg/kg PO Q 24 H | 0.5–1.5 mg/kg Q 24 H |

Table 3. Doses for Commonly Used SSRIs in Birds⁶

| Medication | Dose Options | Forms Available |
|------------|--|---|
| Fluoxetine | 2 mg/kg PO Q 12 H 1–5 mg/kg PO Q 24 H 2–3 mg/kg PO Q 12–24 H | <ul style="list-style-type: none"> • Capsules (10-, 20-, 40-mg) • Tablets (10-, 20-mg) • Solution (20 mg/5 mL) |
| Paroxetine | 1–2 mg/kg PO Q 12–24 H | <ul style="list-style-type: none"> • Tablets (10-, 20, 30-, 40-mg) • Solution (10 mg/5 mL) |

Table 4. Doses for Commonly Used TCAs in Dogs & Cats¹

| Medication | Dogs | Cats |
|---------------|---------------------|-----------------------|
| Amitriptyline | 1–6 mg/kg PO Q 12 H | 0.5–2 mg/kg Q 12–24 H |
| Clomipramine | 1–3 mg/kg PO Q 12 H | 0.25–1.3 mg/kg Q 24 H |

Table 5. Doses for Commonly Used TCAs in Birds⁶

| Medication | Dose Options | Forms Available |
|---------------|--|---|
| Amitriptyline | 1–5 mg/kg PO Q 12–24 H | <ul style="list-style-type: none"> • Tablets (10-, 25-, 50-, 75-, 100-, 150-mg) • Injectable (10 mg/mL) |
| Clomipramine | 0.5–1 mg/kg PO Q 12–24 H 3 mg/kg PO Q 12 H 4.5–9 mg/kg PO Q 12 H | <ul style="list-style-type: none"> • Capsules (25-, 50-, 75-mg) • Tablets (20-, 40-, 80-mg) |
| Doxepin | 1–2 mg/kg PO Q 12 H 0.5–1 mg/kg PO Q 12 H 1–5 mg/kg PO Q 24 H | <ul style="list-style-type: none"> • Capsules (10-, 25-, 50-, 75-, 100-, 150-mg) • Solution (10 mg/mL) |

CONTINUES

One formulation, Anipryl (pfizerah.com), is FDA-approved for use in dogs with cognitive dysfunction syndrome (CDS). Selegiline should be reserved for treatment of dogs with clinical signs of cognitive decline. Because signs of anxiety are often more common in dogs with CDS, treatment with an SSRI or TCA—often in combination with a benzodiazepine, may be more appropriate—especially in the early stages of the disease process.

Although selegiline is not approved for use in cats, geriatric cats treated with selegiline for signs of cognitive decline have shown improvement.⁴

CDS = cognitive dysfunction syndrome; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant

Considerations. In one clinical trial of dogs treated with selegiline, 4% of the study population experienced adverse events, warranting dose reduction or withdrawal from medication. Side effects included restlessness, agitation, vomiting, disorientation, diarrhea, and diminished hearing.⁵

Dosing. The labeled dose of selegiline for dogs with CDS is 0.5 to 1 mg/kg Q₂₄ H, given in the morning. Note that it is also used in dogs for pituitary-dependent hyperadrenocorticism, but at a dose of 1 to 2 mg/kg Q₂₄ H.

See Aids & Resources, back page, for references and suggested reading.

Medical Therapy Q&A

How do I know the medication is working?

If the medication you've chosen is effective, the pet will exhibit the inappropriate behavior less frequently and, when it does surface, it will be less severe and last for a shorter duration.

How long should medical therapy continue?

Medical therapy should be continued for 3 to 6 months to facilitate adequate learning of new behaviors.

How do you wean a pet off the medication?

When it's time to wean your patient from the medication, do so slowly to ensure that the patient can indeed manage with a lower dose; then manage without medication (see **Box**). Even if anxious behaviors resume, a lower dose may be effective.

- A rule of thumb is to decrease the original dose by 50% for 2 to 4 weeks, but this strategy can be varied, depending on the medication formulation and the clinician's personal experience.

- If the patient continues to do well, halve that dose and continue for another 2 to 4 weeks.
- If symptoms do not recur, give the new dose every other day for 2 to 4 weeks and then discontinue the medications.

If at any time the pet exhibits clinical signs, go back to the last dose that controlled those signs. Several attempts may be needed to successfully wean the pet—and with some conditions, such as urine marking, it may not be possible at all.

SAMPLE CASE: **Withdrawing Fluoxetine**

If a dog has been receiving fluoxetine, 20 mg Q₂₄ H, for an anxiety disorder, decrease the dose to 10 mg Q₂₄ H for 2 to 4 weeks. If the dog does well, decrease the dose to 5 mg Q₂₄ H for another 2 to 4 weeks, then every other day for 2 to 4 weeks, then withdraw the medication completely.