Update on Medications in Behavioral Medicine

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The use of psychopharmacology in behavioral medicine is an evolving discipline. At the present time, in the United States only three medications are approved for the treatment of behavioral disorders (Reconcile®, Clomicalm® and Anipryl®). While medication can be useful in the treatment of phobic, panic and anxiety disorders, and disorders with impulse control issues the level of strong evidence for certain interventions may be lacking. When considering the use of medication in a specific case it is essential to determine your diagnosis, which cases and patients are good candidates for drug therapy and what medication to utilize, the dosage and length of therapy. Finally, medication alone is rarely if ever appropriate as a sole treatment modality because it is unlikely to change the relationship to the stimulus or learned responses therefore concurrent behavior therapy is always recommended.

Diagnosis

Many texts are available that detail how to take a history and diagnose behavior problems in companion animals (see reading list at the end of the paper). Without a proper diagnosis using medication at best may not be helpful and in the worst case harmful. The conditions that benefit from the addition of medication include anxieties (separation anxiety , global anxiety), fears, phobia (noise and storm phobia), urine marking in cats , and selected cases of aggression in dogs and cats (extremely impulsive, explosive aggression). It is essential to have some way to measure treatment response before you begin, either by recording the frequency, duration or intensity of the behavior or behavioral bouts. Once medication has been administered and a therapeutic level reached, changes in those parameters will allow monitoring of behavioral change and medication efficacy.

Determining if medication is appropriate

Once a diagnosis has been established, which cases and patients make good candidates for medication? It is essential to initially rule out any medical causes of the unwanted behavior by a good physical examination, laboratory testing (for baseline values prior to medication) and perhaps imaging studies. Make sure your diagnosis is established, and a behavior modification plan is in place and being implemented by the owner. Ascertain if there are any contraindications for drug usage including; poor safety measures in place, high risk of injury to humans or other animals, or the home shows poor compliance for following recommendations. Be familiar with the potential side effects of the chosen medication. Always inquire if the pet is on other concurrent medications, nutraceutical or homeopathies that might make your drug choice inappropriate or contraindicated.

Medication is indicated when the animals welfare is compromised which may occur in severe fears, anxieties and phobias and when the addition of medication will enhance the behavioral modification process.

It is also appropriate to inform clients when medication is being used in an “off label” or in a non approved manner and perhaps have signed consent and release forms. Additionally it is always best to try medication when the owner will be home to observe the pet and begin at the low end of the dosage range and observe for signs of change in the targeted signs or side effects.

Medication for acute situations

Certain medications work relatively quickly and are well suited in situations where immediate effect is needed. These medications can be used concurrently to provide immediate short-term relief with a chronic medication that may take longer to reach efficacy. Alternately these medications may only be used in acute situations that are intermittent, situational and predictable. Some situations that fit this description include car or airline travel anxiety, specific episodic noise events for noise phobic pets, separation anxiety when the dog must be alone and chronic medication is not active or not strong enough and visits to the veterinary hospital.

Benzodiazepines

These are the most commonly utilized class of drug in this category. They work by enhancing GABA, an inhibitory neurotransmitter. An additional benefit is that not only do they diminish anxiety, but are safe with animals that have seizure disorders. Benzodiazepines have a short duration of action of 4-6 hours and must be administered 30-60 minutes prior to the trigger event. Approximately 10% of animals show excitement rather than a diminished anxiety when given a benzodiazepine, switching to another medication within the same class may help. Caution is advised when using this class of drug in animals showing fear based aggression because disinhibition of the aggression is possible. Over time tolerance may develop and higher dosages needed for the same effect. Generally this class of drug is given orally but other preparations exist. Benzodiazepines are a controlled class of medication that also has the potential for human abuse.

Trazadone (not labeled for use in dogs or cats)

This is an atypical antidepressant that has recently been utilized as an event drug for additional control for anxious animals that are also on other serotonin enhancing medications. It is usually administered one hour before the onset of the event. Limited information is available on potential side effects and long-term usage. A recent open label trial evaluated the usefulness of trazadone to facilitate

post surgical confinement in dogs. Initial dosage was 3.5 mg/kg every 8-12 hours although some dogs needed higher dosages. The onset of action was 31-45 minutes and median duration of effect was ≥4 hours. Eighty nine percent of owners felt their pet improved moderately or extremely in tolerance of confinement and calmness. Because no placebo group was utilized it is unknown what the placebo effect may have been in this study.

Clonidine (not labeled for use in dogs or cats)

Clonidine is an alpha 2 agonist typically used in human medicine as an anti-hypertensive agent and off label by psychiatrists for symptoms associated with hyperarousal, hypervigilance, PTSD, impulsivity and attention deficit-hyperactivity syndrome. Clonidine works by blocking norepinephrine release from the alpha 2 receptors on the presynaptic neurons in the locus ceruleus. An open label trial by Ogata and Dodman examined the use of clonidine for the treatment of fear based behavior problems in dogs. Twenty two dogs were divided into two groups (Group A separation anxiety, noise sensitivities, storm phobias, Group B fear based aggression and/or fear based territorial aggression) given clonidine in addition to their other baseline medications at an initial dose maximum of 0.01 mg/kg once or twice daily with a minimal interval of 6 hours. Clonidine was to be administered 1.5 to 2 hours prior to the fear inducing situation or event. Seventy percent of owners in group A felt their dog was improved and 90% of owners in group B felt there was improvement. No placebo group was included therefore the placebo effect cannot be determined.

Phenothiazines

This class of drug has often been utilized for anxiety situations but is not the most effective at diminishing anxiety. Although they incapacitate the animal, they usually do not affect underlying anxiety and thus are not really a useful adjunct for diminishing the underlying emotion that may be causing the behavioral problem. They may be useful in situations where the animal is at risk of injuring themselves in certain contexts but even then should be used cautiously due to the possibility of paradoxical excitement rather than calming.

Medication for chronic use

Daily medication is indicated in clinical cases where anxiety is underlying the primary diagnosis or is the primary diagnosis. The groups of drugs most commonly utilized are serotonin-enhancing drugs including fluoxetine, paroxetine and sertraline (Selective Serotonin reuptake inhibitors), clomipramine, and amitriptyline (Tricyclic antidepressants). These classes of medication work by enhancing serotonin levels within the brain. Serotonin is a neurotransmitter that has multiple functions and receptor sites in the body. Little real information is available in animals, but in humans, low serotonin levels are associated with irritability, hostility, depression and impulsivity. Enhancing serotonin in humans has been associated with a diminishing of depression, alleviating anxiety and changing temperament. Unfortunately the behavioral effect of these classes of drugs is not immediate; it may take 7-31 days before a behavioral effect is noted. It is important to stress to clients that these are not event medications and they must be given daily for an effect to occur.

Separation anxiety and extreme or self injurious storm and noise phobias respond well to serotonin enhancing medications. Underlying anxiety may be present in animals showing aggression, compulsive disorders and urine marking and serotonin enhancing drugs may be useful in these conditions.

Another syndrome, cognitive dysfunction may present with chronic behavioral changes and may benefit from the use of a MAOI selegiline.

The preferred method of administration of serotonin enhancing drugs is orally. Although the use of transdermal medication has been advocated, current studies have shown only limited absorption and therefore the usefulness of this modality for psychotropic medication appears limited at this time. Although often used as transdermal preparations, especially in feline patients, information on actual dosing levels needed is unknown at the present time.

Side effects

Side effects are possible with any medication and the client should be advised to watch the patient carefully for the first few days of medication administration. In elderly or compromised individuals beginning medication at one third to on half the recommended dosage or at an every other day dosing may be prudent. If no side effects are noted after a few weeks and if no therapeutic effect is seen, the dosage can slowly be increased to recommended levels.

Tricyclic antidepressants

(TCA) may have anticholinergic, antihistaminic and adrenergic side effects including dry mouth, urinary retention or GIT upset. Cardiac problems are possible but not reported in companion animals but care should be exercised in compromised individuals. This class of drug is contraindicated in animals with seizures.

Selective serotonin reuptake inhibitors

Have a lower side effect profile and rare anticholinergic or adrenergic side effects but may cause appetite suppression and have a long half-life of metabolic clearance. SSRI medications may also inhibit cytochrome P450 enzyme pathways and decrease the clearance of other medications utilizing the same pathway. SSRI's are also contraindicated in animals with seizure disorders.

Goal of therapy

The goal of drug therapy is to use medication for a limited time (3-6 months) to enhance the application and administration of a behavioral modification plan. The hope is that the animal will learn appropriate new responses and behavior in the previously problematic situations. Once new behaviors are learned and stable, weaning off medication is advised. Weaning is usually accomplished by diminishing the dosage by 25-50% weekly or semi-weekly and watch for a return of the problematic responses. If the signs return, remaining at the lower dose for several weeks may allow stabilization of the behavior and weaning can commence again. Some patients however may never be able to come off medication either because of the lack of owner compliance with behavior modification plans, genetic predisposition to anxiety or continued exposure to the causative stimuli that is unavoidable. Those patients should be evaluated on a regular basis (1-2 times yearly) for both response to medication and a recheck of laboratory values to assess liver and kidney function.

Serotonin syndrome

This is a potentially fatal side effect that may occur with high doses of serotonin enhancing medications or combinations of serotonin enhancing medications such as MAO inhibitors (amitraz, selegiline), other SSRI's, TCA's, tramadol, tryptophan, buspirone, St. John's Wart, amphetamines, dextromethorphan and bromocriptine. Therefore, combinations of serotonin enhancing drugs must be avoided.

Final word of caution

With the exception of the medications mentioned in the first paragraph, most psychotropic medications are not approved for use in dogs and cats. Dosage recommendations are primarily based on anecdotal reports and are not based on placebo controlled studies. Caution should be exercised when dosing animals and supervision and re-evaluation are important components to psychotropic drug usage.

Acute medications dogs and cats

Drug	Class	Canine	Feline	Freq	route
Diazepam	Benzo	0.55-2.2 mg/kg	0.2-0.4 mg/kg	q 6-24 H	PO
Alprazolam	Benzo	0.01-0.1 mg/kg	0.02-0.1 mg/kg	q 8-12 H	PO
Lorazepam	Benzo	0.1-0.2 mg/kg	0.05 mg/kg	q 12-24 H	PO
Trazadone	SARI	2-5 mg/kg	Not used in cats	q 8-12 H	PO
Clonidine	Alpha 2	0.01-0.05 mg/kg	Not used in cats	Q 12 hr.	PO

Chronic medication dosages in dogs

Drug	Class	Canine	Freq	Route
Amitriptyline	TCA	1-2 mg/kg	Q 12 H	PO
Clomipramine	TCA	1.0-2.0 mg/kg	Q 12 H	PO
Fluoxetine	SSRI	0.5-2.0 mg/kg	Q 24 H	PO
Buspirone	Azapirones	0.5-1.0 mg/kg	Q 8-12 H	PO
Sertraline	SSRI	1-3 mg/kg	Q 24 H	PO
Selegiline	MAOI	0.5-1.0 mg/kg	Q 24 H	PO

Chronic medications and dosages for cats

Drug	Class	Dose Range	Frequency	Route
Fluoxetine	SSRI	0.5-1.0 mg/kg	Q24H	PO
Paroxetine	SSRI	0.25-0.5 mg/kg	Q24H	PO
Clomipramine[5]	TCA	0.25-0.5 mg/kg	Q24H	PO
Amitriptyline	TCA	0.5-1.0 mg/kg	Q12-24H	PO
Buspirone	Azapirone	0.5-1.0 mg/kg	Q 12-24 H	PO
Selegiline	MAOI	0.5-1.0 mg/kg	Q 24 H	PO

Chronic Medications and dosages for cats

Reading list

Horwitz DF, Mills D. (2009) BSAVA Manual of Canine and Feline Behavioral Medicine second edition. British Small Animal Veterinary Association, Gloucester, UK.

Horwitz DF, Neilson J, (2007) Blackwell's 5 Minute Veterinary Consult Clinical Companion: Canine and Feline Behavior, Blackwell Publishing, Ames IA

Landsberg G, Hunthausen W, Ackerman L (2013). Behavior Problems of the Dog and Cat, 3nd edition, Saunders, Edinburgh, UK