Separation Anxiety in a Dog with Fear-Based Behavior

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A 6-year-old spayed terrier crossbreed is presented for a 2-month history of crying and barking when left at home alone. The behavior began 2 weeks after the patient was adopted from a local animal shelter. She becomes increasingly agitated (eg, panting, whining, following her owners) when her owners prepare to leave the home; when the owners return, she exuberantly greets them, engaging in marked attention-seeking behaviors (eg, standing on hindlimbs, frantically pawing at the owners) and requiring at least 15 minutes to settle.

The owners provide a video of the patient vocalizing when crated (see ***Video***, page 74) and report that she pants, paces, vocalizes, and chews and paws at doors and window frames when not crated. These behaviors continue for the duration of the owners' absence. The owners have crated the dog, offered long-lasting chews before departures, and used verbal reprimands, none of which have impacted her behavior. The dog does not have a history of aggression toward humans or other animals.

No abnormalities are observed on physical examination. CBC, serum chemistry profile, total thyroxine, and urinalysis are unremarkable. On examination, the patient is visibly trembling, refuses food, and remains crouched on the owner's lap with ears down, tail tucked, and eyes averted. To avoid exacerbating her fearful response to handling, temperature is not obtained.

Diagnoses of separation anxiety and fear-based behaviors in the veterinary setting are made.

Which of the following drugs would be appropriate for this patient's separation anxiety?

Based on the information provided, how would you grade the following drugs and why?

RED = do not use YELLOW = proceed with caution GREEN = safe

Alprazolam	RED	YELLOW	GREEN
Acepromazine	RED	YELLOW	GREEN
Trazodone	RED	YELLOW	GREEN
Gabapentin	RED	YELLOW	GREEN
Clonidine	RED	YELLOW	GREEN
Fluoxetine	RED	YELLOW	GREEN
Clomipramine	RED	YELLOW	GREEN
Dog-Appeasing Pheromone	RED	YELLOW	GREEN
L-Theanine	RED	YELLOW	GREEN
Rescue Remedy	RED	YELLOW	GREEN
α-Casozepine	RED	YELLOW	GREEN

TURN THE PAGE TO COMPARE YOUR RESULTS

Did you answer?

The following represents the best responses based on drug metabolism, pharmacokinetics, species, diagnostic differentials, clinical and laboratory data, and other pertinent findings.

Alprazolam

CORRECT RESPONSE 

Alprazolam is a short-acting benzodiazepine that exerts anxiolysis by enhancing the effect of the inhibitory neurotransmitter γ-aminobutyric acid (GABA). Alprazolam should be administered 30 to 60 minutes prior to the stressful event (eg, departure of pet owners, arrival to the veterinary clinic).[1,2] Because time to onset is variable and paradoxical reactions (eg, increased restlessness, hyperactivity) may be observed, the owners should be advised to administer a test dose prior to using this medication in a stressful situation. Because alprazolam is short-acting (ie, 4-6 hours), a longer-lasting maintenance medication will also be needed to treat this patient's separation anxiety.

Acepromazine

CORRECT RESPONSE 

Acepromazine is a phenothiazine tranquilizer that blocks dopamine receptors and increases the dopamine turnover rate. It is a CNS depressant that induces sedation and muscle relaxation. Acepromazine has poor anxiolytic properties and should never be used as a sole agent when treating anxiety disorders. The only exception is when the drug is used in conjunction with an anxiolytic to prevent self-injury or trauma.

Trazodone

CORRECT RESPONSE 

Trazodone is a serotonin antagonist and reuptake inhibitor that functions by enhancing serotonin, dopamine, and norepinephrine, resulting in antidepressant, hypnotic, and anxiolytic effects. This drug has been demonstrated to be an efficacious adjunctive medication for the treatment of separation anxiety.[3] Trazodone has a mild sedative effect, which can be highly advantageous in animals that panic and/or are destructive.[3] Occasionally, paradoxical reactions (eg, restlessness, hyperactivity) are observed; owners should be advised to administer a test dose before using trazodone in a stressful situation. Trazodone should be administered 2 hours prior to departures or veterinary visits. Because trazodone is short-acting, a longer-lasting maintenance medication will also be needed to treat this dog's separation anxiety.

Gabapentin

CORRECT RESPONSE 

Gabapentin functions by inhibiting calcium channels. It is used to treat pain and epilepsy in humans and has anxiolytic and sedative properties. Sleepiness is a common adverse effect and may be advantageous in the treatment of separation anxiety. Gabapentin should be administered 1 to 2 hours prior to veterinary visits or departures. Because gabapentin is short-acting, a longer-lasting maintenance medication will also be needed to treat this patient's separation anxiety. Of note, gabapentin remains a frequent choice as a short-acting departure medication used in the treatment of separation anxiety despite little research supporting its use.

Clonidine

CORRECT RESPONSE 

Clonidine is a selective α_2-receptor agonist that blocks norepinephrine release in the locus coeruleus, which induces noradrenergic stimulation. It is short-acting and requires 1 to 2 hours to reach full effect. Clonidine has been shown to be an effective adjunctive medication for treatment of canine separation anxiety.[4] Because it is a hypotensive agent, clonidine should be used with caution (ie, not as a first-choice drug) in older patients and patients with cardiovascular disease. Adverse effects may include increased water intake, incoordination, sedation, and constipation.[4] Owners should be advised to administer a test dose before using this drug in a stressful situation. Because clonidine is short-acting, a longer-lasting maintenance medication will also be needed to treat this patient's separation anxiety.

Fluoxetine

CORRECT RESPONSE 

Fluoxetine is a selective serotonin reuptake inhibitor that provides anxiolysis by increasing serotonin levels in the neurosynaptic cleft. Common adverse effects include drowsiness, loss of appetite, and occasional diarrhea. Fluoxetine is FDA-approved for the treatment of separation anxiety in dogs in conjunction with behavior modification. Although improvement may be seen as soon as the first week, in most cases, the medication must be administered daily for 4 to 6 weeks to be effective.[5] Thus, a short-acting medication should be used prior to departures to provide additional needed support. Some dogs can tolerate separation once the maintenance medication is initiated, whereas others require lifelong departure drugs and maintenance medication.

Clomipramine

CORRECT RESPONSE 

Clomipramine is a tricyclic antidepressant that helps reduce anxiety by the selective inhibition of neuronal reuptake of serotonin and has lesser effects on neuronal reuptake of norepinephrine. It must be administered daily as a maintenance medication. Common adverse effects include drowsiness, loss of appetite, urine retention, and occasional diarrhea. Clomipramine is FDA-approved for the treatment of separation anxiety in dogs in conjunction with behavior modification. Improvement can be seen as quickly as 1 week, but maximum effectiveness in most cases takes 8 to 12 weeks[6]; a short-acting medication should therefore be used prior to departures to provide needed support. Some dogs can tolerate separation once the maintenance medication is initiated, whereas others require lifelong departure drugs and maintenance medication.

Dog-Appeasing Pheromone

CORRECT RESPONSE 

Dog-appeasing pheromone is a mimic of the pheromone released from nursing dams that provides a sense of reassurance and calm to help dogs adjust to stressful situations (eg, triggering noises, travel) and new environments. The efficacy of dog-appeasing pheromone for treatment of separation anxiety has been demonstrated.[7] This product is appropriate for mild cases of separation anxiety and fear-based behaviors and when used as a component of a comprehensive treatment plan.

L-Theanine

CORRECT RESPONSE 

The available research on L-theanine is limited but appears promising.[8,9]

Theanine is an amino acid found in green tea that binds to glutamate receptors in the brain, countering neural stimulation at these sites. This effect causes a subsequent rise in GABA, thereby inhibiting neural transmission and excessive firing associated with anxiety.[8] Although it can be used as a sole agent to help address mild distress due to separation, theanine is best used as part of a comprehensive treatment plan with other psychoactive medications when clinical signs of separation anxiety are escalated.

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Rescue Remedy

CORRECT RESPONSE 

Rescue Remedy contains extracts of rockrose, impatiens, clematis, Star of Bethlehem, and cherry plum. No research is available regarding its efficacy in animals. A double-blind, placebo-controlled study in humans demonstrated no effect.[10] When discussing this product with owners, the clinician should keep in mind that the placebo effect can be as high as 45%.[11]

α–Casozepine

CORRECT RESPONSE 

α–Casozepine is a supplement derived from milk protein. It affects GABA receptors and has benzodiazepine-like properties, resulting in an anxiolytic effect. α–Casozepine can be used as a sole agent to help address mild fear and anxiety or as part of a comprehensive treatment plan in conjunction with other psychoactive medications.[12,13] Although it can be used as a sole agent to help address mild distress due to separation, α–casozepine is best used as part of a comprehensive treatment plan with other psychoactive medications when clinical signs of separation anxiety are marked.

References

1. Crowell-Davis SL, Seibert LM, Sung W, Parthasarathy V, Curtis TM. Use of clomipramine, alprazolam, and behavior modification for treatment of storm phobia in dogs. *J Am Vet Med Assoc*. 2003;222(6):744-748.
2. Wismer TA. Accidental ingestion of alprazolam in 415 dogs. *Vet Hum Toxicol*. 2002;44(1):22-23.
3. Gruen ME, Sherman BL. Use of trazodone as an adjunctive agent in the treatment of canine anxiety disorders: 56 cases (1995-2007).*J Am Vet Med Assoc*. 2007;233(12):1902-1907.
4. Ogata N, Dodman NH. The use of clonidine in the treatment of fear-based behavior problems in dogs: an open trial. *J Vet Behav*. 2011;6(2):130-137.
5. Landsberg GM, Melese P, Sherman BL, Neilson JC, Zimmerman A, Clarke TP. Effectiveness of fluoxetine chewable tablets in the treatment of canine separation anxiety. *J Vet Behav*. 2008;3(1):12-19.
6. King JN, Simpson BS, Overall KL, et al. Treatment of separation anxiety in dogs with clomipramine: results from a prospective, randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial. *Appl Anim Behav Sci*. 2000;67(4):255-275.
7. Gaultier E, Bonnafous L, Bougrat L, Lafont C, Pageat P. Comparison of the efficacy of a synthetic dog-appeasing pheromone with clomipramine for the treatment of separation-related disorders in dogs. *Vet Rec*. 2005;156(17):533-538.
8. Araujo JA, de Rivera C, Ethier JL, et al. ANXITANE tablets reduce fear of human beings in a laboratory model of anxiety-related behavior. *J Vet Behav*. 2010;5(5):268-275.
9. Pike AL, Horwitz DF, Lobprise H. An open-label prospective study of the use of L-theanine (Anxitane) in storm-sensitive client-owned dogs. *J Vet Behav*. 2015;10(4):324-331.
10. Armstrong NC, Ernst E. A randomized, double-blind, placebo-controlled trial of a Bach Flower Remedy. *Complement Ther Nurs Midwifery*. 2001;7(4):215-221.
11. Conzemius MG, Evans RB. Caregiver placebo effect for dogs with lameness from osteoarthritis. *J Am Vet Med Assoc*. 2012;241(10):1314-1319.
12. Beata C, Beaumont-Graff E, Diaz C, et al. Effects of alpha-casozepine (Zylkene) versus selegiline hydrochloride (Selgian, Anipryl) on anxiety disorders in dogs. *J Vet Behav*. 2007;2(5):175-183.
13. Palestrini C, Minero M, Cannas S, et al. Efficacy of a diet containing caseinate hydrolysate on signs of stress in dogs. *J Vet Behav*. 2010;5(6):309-317.

Suggested Reading

Crowell-Davis SL, Murray TF, de Souza Dantas LM. *Veterinary Psychopharmacology*. 2nd ed. Hoboken, NJ: John Wiley & Sons; 2019.

Horwitz DF, ed. *Blackwell's Five-Minute Veterinary Consult Clinical Companion: Canine and Feline Behavior*. 2nd ed. Hoboken, NJ: John Wiley & Sons; 2018.

Ogata N. Separation anxiety in dogs: what progress has been made in our understanding of the most common behavioral problems in dogs? *J Vet Behav*. 2016;16:28-35.

VIDEO

To watch a video of the patient's behavior when crated, scan the QR code or go to **cliniciansbrief.com/article/separation-anxiety-dog-fear-based-behavior**

Using QR codes from your mobile device is easy and quick!

Simply focus your phone's camera on the QR code as if taking a picture (but don't click!). A notification banner will pop up at the top of your screen; tap the banner to view the linked content.