

## ESVCE position statement on the use of medications to manage acute phobic states in dogs as an alternative to acepromazine

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- Use of acepromazine

Veterinarians are at the forefront of the decision-making process of selecting and prescribing psychopharmacological agents in dogs presenting with acute phobic states (e.g. those induced by noise/fireworks/transport). Despite considerable literature advising against the use of acepromazine for treating behaviour problems in dogs [1-4], it still persists as one of the psychoactive drugs prescribed to reduce behavioural manifestations of noise phobia and other phobias, which may partly be due to it historically being suggested as a treatment option for managing destructive behaviour and transport fear [5, 6]. ESVCE strongly recommends the choice of an alternative psychopharmacological approach, as acepromazine has no anxiolytic effect and therefore it is not appropriate to manage acute fear/phobic states [1].

Acepromazine is a phenothiazine, producing a therapeutic effect by blocking dopaminergic receptors [2]. This results in the blocking of motor responses without likely altering the sensory experience – whilst at the outset it may appear to reduce an individual's reactivity, it does so in the absence of anxiolytic effect. The dog continues to perceive the phobogenic stimuli (and it may even be amplified) without the ability to move away from it. The misuse of acepromazine in noise phobias can therefore potentially increase sensitization to noise, worsening the severity of the phobic state, which is exactly the opposite of the intended treatment [1, 3]. Acepromazine can potentially lead to paroxysmal arousal and behavioural disinhibition when used to solve aggressive behaviours [3]. Acepromazine should only be used as a premedication drug prior to anaesthesia where there is no expectation or requirement of an anxiolytic effect from it [4]. At such times, acepromazine is used always combined with opioids and other agents to produce a reasonable pain management and sedation [7-13].

The ESVCE recommends that acepromazine is not used to prevent/treat noise phobias, in line with the recommendations of other veterinarian behaviourist and animal behaviour associations from different countries (e.g.: AVEC, AVEPA-GRETCA).

- Alternative medication and treatment options

Phobia can be defined as a “disproportional and irrational response to a stimulus perceived as a danger” [1], so whilst it is important to use psychopharmacological interventions to manage acute events, this should form part of a broader behaviour modification programme. Regarding noise phobia, the recommended behaviour approach should be:

- Use a psychopharmacological agent which is effective in producing an acute anxiolytic effect in the individual;
- Identify the stimuli that triggers the phobic response, and avoid or minimise exposure to such triggers;
- Create a *safe area* - a quiet, pleasant place that has been previously positively conditioned, where the dog has the choice to freely come and go from, and may eventually use as a coping mechanism whilst noise stimuli occur [14];
- Utilise behaviour modification techniques such as desensitization and counterconditioning techniques aiming to change the dog's perspective of the phobogenic stimuli;
- Encourage owners to implement environmental enrichment techniques in order to frequently promote positive emotions and behaviours[1];
- Consider the use of long-term psychopharmacological agents in order to reduce the phobic state and ongoing anxiety/fearful responses[1, 15, 16];

In recent years, there are two medications (dexmedetomidine and imepitoin) which have been licensed for the treatment of acute noise fears/phobias in dogs and may be useful in the treatment of other situational fears/phobias. When using evidence based medicine to guide treatment interventions, both agents have demonstrated anxiolytic effects in the treatment of noise phobia: dexmedetomidine is an  $\alpha_2$ -adrenergic agonist, available as an oromucosal gel [16-19]; imepitoin is a partial GABA<sub>A</sub> agonist available in tablet form [20].

When a behaviour problem is identified or suspected, it is important for veterinarians to offer the client the option of referral to a behaviour specialist (if such services are not offered in the veterinary practice), in order to correctly identify the problem and to begin effective treatment as soon as possible.

#### References:

1. Overall, K., *Manual of Clinical Behavioral Medicine for Dogs and Cats - E-Book*. 2013: Elsevier Health Sciences.
2. Crowell-Davis, S.L. and T. Murray, *Veterinary Psychopharmacology*. 2008: Wiley.
3. Bowen, J. and S. Heath, *Behaviour Problems in Small Animals: Practical Advice for the Veterinary Team*. 2005: Elsevier Saunders.
4. Horwitz, D.F., *Blackwell's Five-Minute Veterinary Consult Clinical Companion: Canine and Feline Behavior*. 2017: Wiley.
5. Lindell, E.M., *Diagnosis and Treatment of Destructive Behavior in Dogs*. *Veterinary Clinics: Small Animal Practice*, 1997. **27**(3): p. 533-547.
6. Bergeron, R., et al., *Physiology and behavior of dogs during air transport*. *Canadian journal of veterinary research = Revue canadienne de recherche veterinaire*, 2002. **66**(3): p. 211-216.
7. Monteiro, E.R., et al., *Comparative study on the sedative effects of morphine, methadone, butorphanol or tramadol, in combination with acepromazine, in dogs*. *Veterinary Anaesthesia and Analgesia*, 2009. **36**(1): p. 25-33.
8. Monteiro, E.R., et al., *Effects of methadone, alone or in combination with acepromazine or xylazine, on sedation and physiologic values in dogs*. *Veterinary Anaesthesia and Analgesia*, 2008. **35**(6): p. 519-527.

9. Kojima, K., et al., *Comparison of Sedative Effects of Medetomidine-Midazolam, Acepromazine-Butorphanol and Midazolam-Butorphanol in Dogs*. Journal of Veterinary Medicine Series A, 1999. **46**(3): p. 141-148.
10. Grint, N.J., B. Alderson, and A.H.A. Dugdale, *A comparison of acepromazine-buprenorphine and medetomidine-buprenorphine for preanesthetic medication of dogs*. Journal of the American Veterinary Medical Association, 2010. **237**(12): p. 1431-1437.
11. Hofmeister, E.H., M.J. Chandler, and M.R. Read, *Effects of acepromazine, hydromorphone, or an acepromazine-hydromorphone combination on the degree of sedation in clinically normal dogs*. Journal of the American Veterinary Medical Association, 2010. **237**(10): p. 1155-1159.
12. Hellyer, P.W., et al., *Preliminary evaluation of pain behaviors following neutering in dogs: effect of acepromazine dose*. Veterinary Anaesthesia and Analgesia, 2002. **29**(2): p. 97-112.
13. Dugdale, A., *Veterinary Anaesthesia: Principles to Practice*. 2011: Wiley.
14. Sherman, B.L. and D.S. Mills, *Canine anxieties and phobias: an update on separation anxiety and noise aversions*. Veterinary Clinics: Small Animal Practice, 2008. **38**(5): p. 1081-1106.
15. Landsberg, G.M., W.L. Hunthausen, and L.J. Ackerman, *Behavior Problems of the Dog and Cat3: Behavior Problems of the Dog and Cat*. 2012: Saunders.
16. Crowell-Davis, S.L., T.F. Murray, and L.M. de Souza Dantas, *Veterinary Psychopharmacology*. 2019: Wiley.
17. Korpivaara, M., et al., *Dexmedetomidine oromucosal gel for noise-associated acute anxiety and fear in dogs—a randomised, double-blind, placebo-controlled clinical study*. Veterinary Record, 2017: p. vetrec-2016-104045.
18. Dean, R., *Using dexmedetomidine to alleviate noise-induced fear and anxiety in dogs*. Veterinary Record, 2017. **181**(25): p. 688-689.
19. Sherman, B.L. *Keynote presentation: use of psychopharmacology to reduce anxiety and fear in dogs and cats: a practical approach*. in *Proceedings of the 11th International Veterinary Behaviour Meeting*. 2017. Samorin, Slovakia, Wallingford.
20. McPeake, K.J. and D.S. Mills, *The use of imepitoin (Pexion™) on fear and anxiety related problems in dogs – a case series*. BMC Veterinary Research, 2017. **13**(1): p. 173.