Anti-emetic treatment of car-sick pets

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ELLIE MARDELL discusses treatment options for the reluctant travelling cat or dog that suffers with nausea

CAR journeys are an unavoidable aspect of most cats' and dogs' lives - from holidays, trips to the beach or park, and inevitable visits to boarding kennels or their vet. The car journey may signify to our pets a daily pleasurable outing, or a feared trip into the unknown.

Many dogs appear to love travelling in cars and show little or no objection. Others are more reluctant - they may put up little resistance but anxiety and nausea are evidenced by shivering and salivation, with or without emesis.

As a species, cats are notoriously bad travellers, often demonstrably resenting inevitable confinement to a basket, but also, not uncommonly, vomiting. Nausea and vomiting are unpleasant for owner and pet alike, and significantly contribute to the stress involved for pets that are reluctant travellers.

Motion sickness

To select an appropriate treatment for travel sickness in veterinary species, an appreciation is required of the physiological pathways and receptors that lead to vomiting - particularly in the specific context of motion sickness and, very importantly, the differences between cats and dogs.

Vomiting is a complex reflex that is not completely understood. Numerous chemical and neural mediators appear to be involved, several of which offer possible target sites of action for drugs to

reduce motion sickness and nausea. The diagram below outlines a simplified representation of the neural and chemical mechanisms that are involved in vomiting, with particular emphasis on motion sickness.

• Practical methods to reduce motion sickness

Withholding food prior to travelling will not strictly prevent motion sickness. However, it will lead to less dramatic effects, and will probably reduce any potentiating stimuli from the periphery (ie activated gut stretch receptors). Where possible, routes involving straight roads result in less vomiting than winding country lanes. However, if medication is required, it will have to be available in an oral form to be useful to the owner, and even then must be given well in advance of the journey (one to two hours) to allow absorption to occur before vomiting otherwise would.

• Pharmacological prevention

It is important to remember that motion sickness is centrally, rather than peripherally, mediated and to choose preventive drugs accordingly.

Many anti-emetic drugs act upon more than one chemical receptor and several have peripheral as well as central actions, dependent on the distribution of target receptors. For example, metoclopramide is classically considered a peripherally acting pro-motility agent within the intestine. However, it is its centrally acting dopamine antagonism within the chemoreceptor trigger zone (CRTZ) that makes it effective against motion sickness in canine patients. It is a less effective centrally acting drug in cats, partly because dopamine is a relatively unimportant neurotransmitter in the cat’s CRTZ. In addition, the species to be treated affects the choice of drug. Humoral pathways and the CRTZ are prominent in mediating motion sickness in the dog, whereas neural pathways and the vomiting centre are much more important in the cat. As a result, antihistamines can be used to prevent travel sickness in the dog, but would be a less effective choice in cats.

Considerations in dogs

Metoclopramide was traditionally used as an anti-emetic in veterinary patients, including for car sickness in dogs. However, it is not a licensed product in cats and dogs.

Combinations of drug classes are frequently used to control severe vomiting in people, reflecting the complex interplay between numerous pathways involved in vomiting. Neurokinin-1 (NK-1, substance-P) receptor antagonists were developed for use in humans mainly as potent anti-emetics for use in chemotherapy-induced nausea and vomiting, following the recognition that substance P was important in inducing emesis by its action on receptors within the vomiting centre.

NK-1 receptors are also found in some other pathways involved in vomiting, including in the motor nucleus of the vagus nerve. Recently, an NK-1 antagonist, maropitant (Cerenia, Pfizer) has

become available for use in dogs, and is licensed for the control of vomiting in this species, including vomiting induced by travel. The drug appears to be very effective, and side effects are minimal, and it is probably currently the drug of choice for canine motion sickness. It must be given with a small amount of food, otherwise it can paradoxically cause nausea and vomiting (presumably via peripheral input due to gastrointestinal irritation). It is also worth noting that the data sheet specifically notes that nausea and salivation can still occur in travel sick patients, despite medication with this drug.

The phenothiazines, acepromazine, chlorpromazine and prochloperazine, are antagonists of alpha-2 adrenergic receptors, found within both the CRTZ and the vomiting centre. Acepromazine is licensed for veterinary use, and its list of indications as an oral preparation includes anti-travel sickness. It can be used safely in many dogs, but can cause hypotension, and will not always be suitable for older patients or those with questionable cardiovascular stability. Its sedative effects may also be unpredictable and undesirable.

Stimulation of central histamine (specifically, H-1) receptors located within the vestibular apparatus and in the CRTZ contribute to motion sickness - particularly in the dog. Numerous centrally acting antihistamine drugs are available, and are reportedly effective in controlling travel sickness in the dog, as they are in people, via antagonism at these H1 receptors. Suitable agents include diphenhydramine (Nytol), cyclizine (Valoid) and meclizine (Sealegs). Antihistamines appear to be safe in veterinary species, although they can cause drowsiness. However, efficacy and dose rates are not well established and are largely anecdotal, as none are licensed.

Considerations in cats

Very few anti-nausea and antisickness medications are licensed for use in the cat, and the following discussions refer largely to drugs that must be used “off label”. Skullcap and valerian tablets (Dorwest Herbs) are licensed for use in both cats and dogs and are indicated for prevention of anxiety and travel sickness. Acepromazine (ACP) tends to be an unreliable sedative in the cat when given orally on its own and, perhaps, would not be an instinctive choice for an anti-emetic.

No other anti-emetics are licensed for use in the cat. However, the ACP-related drugs chlopromazine and prochloperazine offer very effective central anti-emetic actions against motion sickness in the cat, due to their action upon adrenergic receptors in the vomiting centre, which becomes evident at higher doses (lower doses only seem to act upon the CRTZ). However, hypotension and sedation are potential side effects, which can be marked, and this may limit the use of these drugs in some patients.

Clinical experience with metoclopramide is quite extensive. However, extra-pyramidal side effects can occur, whereas its central anti-emetic effects are very limited in the cat, and the resultant effect on motion sickness is unpredictable to poor. Anecdotally, maropitant appears effective in cats (at a lower dose than is given to dogs), perhaps unsurprisingly, given its mechanism and location of

action. However, maropitant is not licensed in the cat, and experience with it is, so far, limited - such that other drugs may currently be a better choice.

Other drugs that can be used in car-sick feline patients include mirtazepine, a seratonin antagonist that appears to also have an anxiolytic effect (similar to that of amytriptyline). However, its duration of action is very long (administration is only necessary every three days), which is unnecessary for most journeys, and it is a potent appetite stimulator, which may be an irritating side effect if the desired action is only anti-sickness.

Cyproheptadine (Periactin) is an antihistamine with additional serotonin antagonistic effects. It is employed mainly as an appetite stimulant, but it is possible that its anti-seratonin effects would be useful against motion sickness. Some authorities recommend other centrally acting antihistamines for travel sickness in the cat, as in dogs, although efficacy would not be predicted given their site of action (CRTZ).

The cat’s vestibular nuclei has been shown to contain GABA-A receptors, and benzodiazepines appear to have a suppressant activity here, and are sometimes recommended for use in feline motion sickness. Caution is required with oral diazepam, which has been associated with hepatic necrosis in some individuals. Alprazolam is a safer alternative, and has the added benefit of an anxiolytic effect.

Other methods of reducing travel sickness

• Higher centre input

The benefits of early exposure and acclimatisation/desensitisation to travelling should not be overlooked. Puppies tend to suffer with car sickness more frequently or more severely than adult dogs (as is the same in their human counterparts), suggesting that a number of canines “grow out of” motion sickness and become accustomed to the feeling of travel such that it no longer stimulates vomiting. Early experiences have a profound effect on the development of the adult mind.

Not all pets that suffer car sickness are also anxious, but we know that such higher centre input can be directed into the vomiting centre within the brain and contribute to vomiting. The effect of anxiety and fear can have profound effects on both dogs and cats, increasing the likelihood of vomiting.

At the initial puppy or kitten clinic and, ideally, even prior to a pet’s first visit to the vet, owners should be educated on how to make travelling a stress-free, rewarding experience for dogs, and how to introduce cats to a carry basket and subsequent car travel in a non-threatening manner. Puppies can be introduced into a stationary vehicle first until they are confident in this environment, and short car journeys to somewhere pleasant, associated with reward, can be gradually

lengthened in time.

Cats that are gradually introduced to carriers as kittens generally learn to tolerate the procedure of being loaded into their basket. Helpful methods in early exposure include leaving the basket out as if it is part of the furniture, so that the cat can investigate in its own time, and feeding treats in and around the basket.

Once the kitten is secure and confident in the basket, short dummy run car journeys can be commenced. For rescue cats, or those whose early training has been overlooked, good results can still be achieved by leaving the basket out in advance of when it is required, spraying some synthetic pheromone spray inside and placing some bedding inside that smells familiar.

• **Sedation**

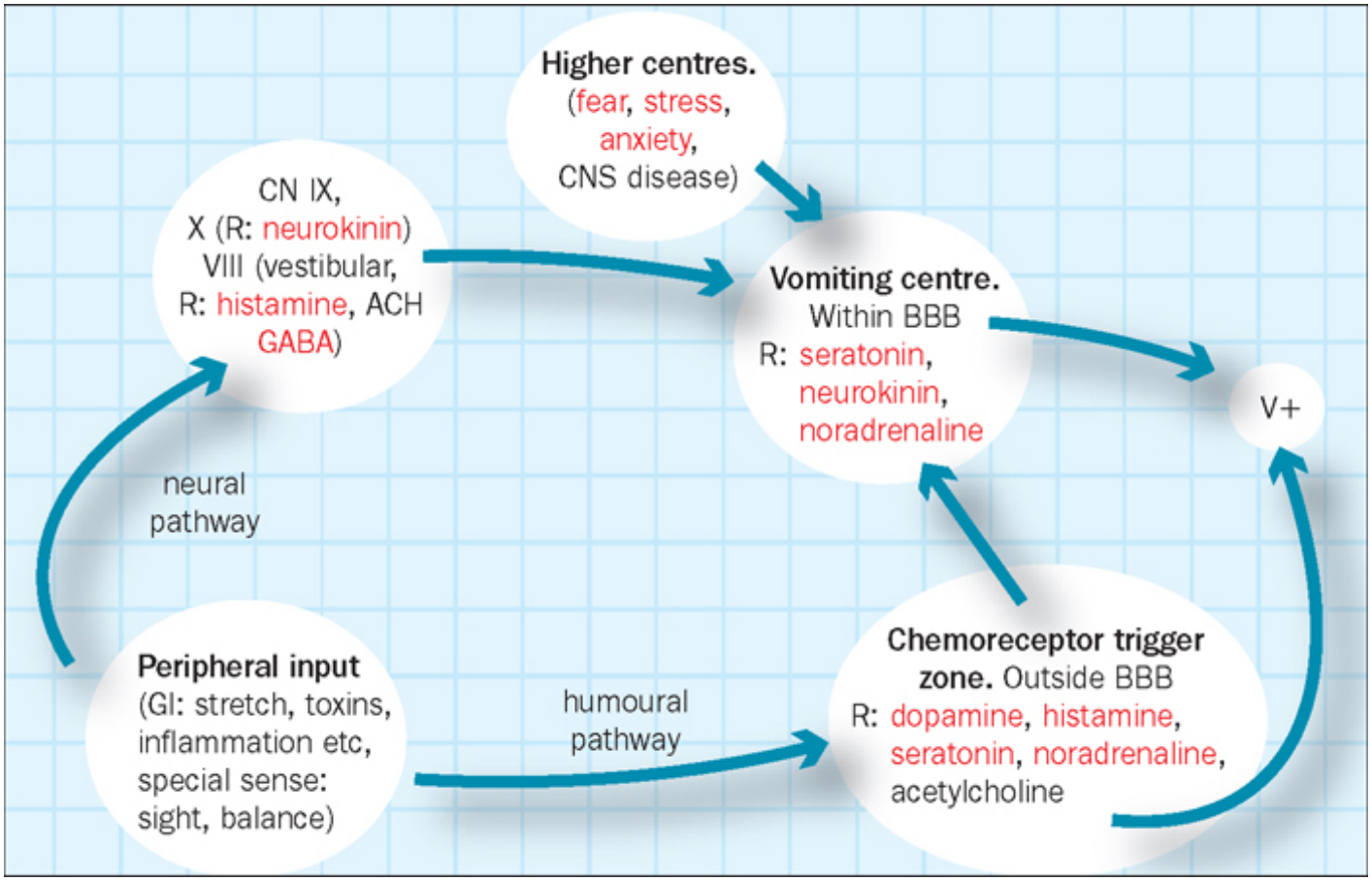
Sedation may well bring with it undesirable effects on blood pressure and thermoregulation, and may be detrimental where there is any pre-existing disease, particularly cardio-respiratory. It should, therefore, probably be considered only as a last resort, for pets that become extremely distressed on travelling.

Some medications indicated for use in motion sickness - for example, anthistamines, phenothiazines and benzodiazepines - do cause mild sedation as a side effect, which may have an additional useful anxiolytic effect.

Any sedative effect is less welcome when the pet is, for example, travelling to a show, or to a veterinary practice where anaesthesia will be required, and this may influence the choice of drug. With antihistamines, the sedative effect tends to be quite mild, causing increased sleepiness. However, the phenothiazines tend to have more profound systemic effects and, added to this, their central anxiolytic effect can be unpredictable.

In summary, nausea and vomiting are common and unpleasant effects of travelling that, for some pets and owners, may have a significant impact on certain aspects of life. The complexity of the vomiting reflex offers numerous sites for pharmacological intervention, but this also means that the array of drugs on offer can be bewildering.

Ultimately, the choice of drug used is likely to be influenced by licensing laws, individual patient variations, personal experience and preference, and collective clinical information.



Outline of the neural and humoral pathways involved in vomiting. Receptors highlighted in red indicate possible targets for pharmacological intervention of vomiting and behavioural training to reduce motion sickness. Key: CN = cranial nerve, ACH = acetylcholine, BBB = blood brain barrier, GI = gastrointestinal, R = receptors, V+ = vomiting.

Feelings of nausea can ruin a car journey for dogs and owners.

Feline patients can be trained to accept travelling without fear.

Drug	Mechanism of action	Trade name	Comments
Acepromazine	A-2 adrenergic antagonist	ACP	Hypotension may occur
Skullcap and valerian	Herbal anxiolytic		
Prochlorperazine	A-2 adrenergic antagonist	Stemetil	Hypotension may occur
Alprazolam	GABA-A activity suppression	Xanax	Efficacy poorly established
Mirtazepine	5-HT-3 antagonist	Zispin	Polyphagia possible side effect

TABLE 1. Anti-emetic drugs used for cats with motion sickness (licensed medications shown in red)

Drug	Mechanism of action	Trade name	Comments
Maropitant	NK-1 receptor antagonist	Cerenia	Give with a little food
Acepromazine	A-2 adrenergic antagonist	ACP	Hypotension may occur
Skullcap and valerian	Herbal anxiolytic		
Diphenhydramine	H-1 receptor antagonist	Nytol	May cause drowsiness
Ciclizine	H-1 receptor antagonist	Valoid	May cause drowsiness
Meclizine	H-1 receptor antagonist	Sealegs	May cause drowsiness
Metoclopramide	Dopaminergic antagonist	Metoclopramide	

TABLE 2. Anti-emetic drugs used for dogs with motion sickness (licensed medications shown in red)