Why are cats still dying from permethrin toxicity?

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Permethrin is a synthetic pyrethroid. Pyrethrins and pyrethroids are insecticides used to control and prevent flea and tick infestations in domestic animals. They are available as sprays, collars, powders and spot-on treatments from pet shops, online suppliers and veterinary clinics.

Several years ago, International Cat Care ran a campaign to raise awareness of permethrin toxicity in cats. Many major retailers altered protocols to include alerts when products containing permethrin were bought, while manufacturers added clearer warning signs on packaging and dispensers. However, the Veterinary Poisons Information Service (VPIS) still includes permethrin in the top five toxins it receives enquiries about and fatality rates continue to be reported between 10% and 40% (Sutton et al, 2007; Gray, 2000).

Exposure

Figure 1. A cat treated with a dog spot-on product containing permethrin, treated with a propofol infusion and intubated to maintain the airway and provide oxygen.

Most cats are exposed to permethrin after a dog flea product is applied to the cat, or the cat comes into contact with a recently treated dog.

Some flea powders marketed for cats do contain permethrin, but at a low concentration, so rarely appear to be a cause of toxicity. Susceptibility to intoxication seems variable and, for some cats,

one drop of canine spot-on treatment can cause severe illness.

Dog flea products containing permethrin are easy for owners to buy; some are sold in veterinary clinics. Despite progress in warning stickers and labelling, well-meaning owners continue to poison their cats, causing a great deal of distress. More can be done to educate owners about the risks to their cats.

Susceptibility to permethrin poisoning

Pyrethroids slow the opening and closing of sodium channels in nerve endings, causing hyperexcitability in cells. Cats, with their genetically inherited reduced hepatic glucuronidation (Court and Greenblatt, 1997), are less efficient than other mammals at metabolising the chemical, resulting in an accumulation of the active parent insecticide at the sodium channels.

Their high surface area to weight ratio, and the high concentration of permethrin in large dog spot-on products, means a higher dose per kilogramme and, therefore, clinical signs of neurotoxicity (Martin and Campbell, 2000).

Clinical signs

Clinical signs usually appear rapidly after exposure, but can take 24 to 72 hours to become apparent (Linnett, 2008).

Boland and Angles (2010) reported the following clinical findings in affected cats:

- tremors/muscle fasciculations (86%)
- twitches (41%)
- hyperaesthesia (41%)
- seizures (33%)
- pyrexia (29%)
- ptyalism (24%)
- ataxia (24%)
- mydriasis (19%)
- temporary blindness (12%)

The severity of clinical signs may vary significantly, from mild facial twitching to persistent, severe, generalised seizures. Complications of seizure activity may be observed, such as hyperthermia, dyspnoea (from aspiration pneumonia) and respiratory or cardiac arrest.

Diagnosis is usually based on clinical signs and history of exposure, as biochemistry and haematology from affected cats is usually unremarkable. Differential diagnoses include intracranial (neoplasia, trauma) and extracranial (hypocalcaemia, hypoglycaemia) causes of neurological

signs, as well as other toxicities, such as metaldehyde and organophosphates.

Treatment

Panel 1. Lipid infusion regimen

Various regimes have been used in permethrin toxicity and usually 1.5ml/kg of a 20 per cent lipid emulsion is given as a bolus dose IV. This is followed by an infusion 0.25ml/kg/min over 30 to 60 minutes. This can be repeated once or twice if signs recur. Intermittent boluses of 1.5ml/kg every 4 to 6 hours over 24 hours is also described (Fernandez et al, 2011). An alternative dosing regimen has been proposed (Bates, 2016), using a lower dose for longer. The loading dose is 2.25ml/kg, followed by 0.025ml/kg/min constant rate infusion for up to 6.5 hours (Fettiplace et al, 2015).

It is advisable to contact the VPIS for advice on treatment and reporting purposes.

Treatment focuses on three main areas – decontamination, control of tremors and seizures, and supportive care.

Decontamination

Although removal of the cause of the toxicity is desirable, decontamination may need to be delayed until severe clinical signs are controlled.

Given most cats are exposed after application of a spot-on product, decontamination is vital to prevent further absorption of permethrin. Washing the cat with warm water (not hot, as this can cause vasodilation and further absorption of permethrin) containing mild detergent (washing-up liquid or hand wash) is recommended, but avoid hypothermia as it can potentiate the effects of the toxin. Clipping fur may facilitate removal of spot-on product from the skin.

After decontamination, an Elizabethan collar should be applied to prevent grooming any remaining product and contact with other cats restricted.

Gastric decontamination is rarely indicated and adsorbents may not be effective.

Muscle tremor control

If the cat has tremors without seizures, the aim of treatment is to reduce clinical signs, but not anaesthetise the patient.

Benzodiazepines may not be sufficient in severe cases, although may be of use in mildly affected cats. Care is needed, as paradoxical exacerbation of signs have been reported with their use. Methocarbamol is a centrally acting muscle relaxant useful for control of severe tremors; however, its availability is limited in the UK, and even then only available in oral form.

Recommendations for management are (adapted from Boland and Angles, 2010):

- Methocarbamol: dose at 55mg/kg to 200mg/kg IV; can be repeated up to three times a day, but total daily dose should not exceed 330mg/kg. If injectable methocarbamol is not available, tablets may be used – crushed and given via nasogastric intubation or per rectum (same dose).
- Benzodiazepines: diazepam (0.25mg/kg IV as required) or midazolam (0.3mg/kg IV/IM as required, or 0.002mg/kg to 0.005mg/kg per minute IV as continuous rate infusion [CRI]).
- Propofol: 0.05mg/kg to 0.3mg/kg per minute IV as CRI.

Control of seizures

Figure 2. Use posters in the waiting room to warn clients.

Benzodiazepines may be adequate to control seizures in some cases, but, as mentioned, treated cats should be monitored closely.

If this treatment fails to control the seizures then a propofol CRI may be required and loading doses of phenobarbital have been used in some cases, although this drug has a 20-minute delay to onset of action.

Propofol has the potential to cause oxidative injury in cats, so infusion duration is ideally limited to 12 hours (Grave and Boag, 2010).

- Benzodiazepines: doses as aforementioned.
- Propofol: anaesthesia using a bolus (4mg/kg to 6mg/kg IV) followed by a constant rate infusion (0.05mg/kg/min to 0.3 mg/kg/min).
- Phenobarbital: can be given as a bolus (2mg/kg to 4mg/kg IV) and repeated every two hours to a maximum of 20mg/kg/day. A CRI could be considered.

Supportive treatment

Supportive care involves attention to hydration with IV fluid therapy, maintenance of normal body temperature, ocular lubrication and bladder management (catheterisation may be required).

Intubation may be indicated in deeply sedated or anaesthetised patients when concern exists regarding airway patency (**Figure 1**), oxygen supplementation and regular turning. Hypersalivation may require regular suction.

Affected cats should be kept in a quiet, darkened environment and handled gently, as they may be hyperaesthetic and worsen with noise and stimulation.

IV lipid infusion

Panel 2. Are your clients well informed?

Most cats are treated with permethrin by owners trying to do their best by preventing or treating fleas.

Think of ways your practice can raise owner awareness of this toxicity and encourage them to buy flea and tick products from your clinic. Ideas include:

- Awareness campaigns: client newsletters, posters in waiting rooms (**Figure 2**; download at http://bit.ly/2b3DVhw) and practice emails.
- Nurse consults: flea control is often discussed in these consults, so is an ideal time to educate clients.
- Kitten consults: an opportunity to raise awareness of potential toxins, not just permethrin.
- If, as a clinic, you still sell any products containing permethrin, ensure they only leave the clinic with a leaflet reminding clients not to apply to cats.
- Only sell/recommend spot-on products with labels and warnings on dispensers and packaging.

A treatment showing promise for managing permethrin toxicity in cats is IV lipid emulsion infusion, using products designed for parenteral nutrition (Haworth and Smart, 2012; Kuo and Odunayo, 2013; DeGroot, 2014). The exact mechanism of action is uncertain, but it is thought the lipid infusion helps draw the drug away from the tissues, lessening toxic effects.

Peacock et al (2015) showed cats suffering permethrin toxicity treated with a lipid infusion improved earlier than cats not receiving the infusion. While no standard regimen exists for lipid infusion in managing permethrin toxicity, see **Panel 1** for details.

Conclusion

Unfortunately, cats are still being poisoned with permethrin, and treatment is challenging and, for the client, expensive.

Prevention is desirable and ensuring your clients are well-informed when choosing flea and tick products is essential. Think about how your clinic can “spread the word” about this preventable toxicity (**Panel 2**) and ensure you report all cases to the VPIS and the VMD.

Free access to reference papers

To facilitate dissemination of information, Sage Publications, publisher of the *Journal of Feline Medicine and Surgery, and the International Society of Feline Medicine* have made three papers on permethrin toxicity in cats freely available. They are Malik et al (2010), Boland and Angles (2010) and Sutton et al (2007).

- Use of some drugs mentioned in this article would be under the UK cascade.

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Further Reading

- VPIS: https://vpisglobal.com