

MANAGING EXPOSURE OF THE CATS TO PYRETHROID USING INTRALIPID THERAPY

MANAGEMENTUL EXPUNERII PISICILOR LA PIRETRINE FOLOSIND TERAPIA INTRALIPIDICĂ

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ABSTRACT | REZUMAT

The aim of this study was to establish the effect and results of lipid emulsions treatment in cats pyrethroid poisoning. The cause of intoxication was the application of canine permethrin spot-on product (Advantix) or Cyper-Vet and Superkiller by the owners to cats. Other source of contamination and poisoning was sprayed Superkiller in the garden against ticks (containing 1 gr/Lt imidacloprid and 500 g/Lt of permethrin in a 1 ml pipette).

The most common clinical signs observed were: hypersalivation (100%); mydriasis (98%); muscle tremor (95%); hypothermia (90%); seizures (80%) etc.

Principal clinical signs recommends the use of anticonvulsant drugs to treat seizures or neurological symptoms after initial stabilization and dermal decontamination.

Treatment protocols aim to control the clinical signs, seizure control and review the available evidence regarding the effect of ILE. Treatment was given symptomatically for all 18 cases and in two of them a fat emulsion was given. We evaluated the effect of association of ILE (intralipid emulsions) and treatment for clinical signs in permethrin intoxication. No adverse reaction such as thrombophlebitis, overload circulation or others was noticed during and after administration of ILE.

Keywords: pyrethroid, cats, therapy, lipid emulsion

Scopul prezentului studiu a fost de a stabili efectele și rezultatele terapiei cu emulsie lipidică în intoxicația cu piretrine la pisică. Cauzele intoxicațiilor au fost: aplicarea produselor cu piretrine, destinate câinilor, de tip spot-on (Advantix) sau Cyper-Vet și Superkiller de către proprietari, la pisici. O altă sursă de contaminare și intoxicare a fost utilizarea produsului Superkiller în grădină împotriva țânțarilor (produsul conține 1g/l imidacloprid și 500 g/l permetrin pentru pipeta de 1 ml). Cele mai frecvente simptome observate au fost: hypersalivația (100%); midriaza (98%); tremor muscular (95%); hipotermia (90%); convulsii (80%) etc. Principalele semne clinice recomandă utilizarea medicației anticonvulsivante pentru tratarea convulsiilor și altor semne neurologice, după stabilizare și decontaminare.

Scopul protocolului terapeutic a fost de a controla semnele clinice, convulsiile și de a stabili efectele evidente ale terapiei lipidice i.v. Tratamentul a fost simptomatic pentru toate cele 18 cazuri, iar pentru două dintre ele s-a administrat și emulsie lipidică. Am evaluat efectul asocierii tratamentului cu emulsie lipidică (ILE) (pentru 2 cazuri) și tratamentul simptomatic în intoxicația cu piretrine. Nu au fost observate efecte adverse ca tromboflebita, manifestări circulatorii patologice sau alte semne după aplicarea emulsiei lipidice.

Cuvinte cheie: piretroid, pisici, terapie, emulsie lipidică

Intoxications with pyrethroid in cats may lead to life-threatening emergencies. While stabilising the patient, therapy should focus on a rapid and effective elimination of the toxin. General measures for decontamination (gastro-intestinal, dermal, ocular) aim to effectively decrease the absorption of the poisonous substance. In the majority of cases, the poisoned animal entering the veterinary practice represents an

emergency which requires immediate therapeutical intervention without knowing the toxin which causes the clinical symptoms. Therefore, being familiar with the principle management options for acute intoxications is indispensable for initiating life-saving steps before valuable time passes. These procedures include patient stabilization, interruption of the exposure to the poisoning agent and acceleration of elimination of the toxin (9).

In most vertebrates, especially those who have enough enzymes for rapid decomposition, pyrethrins

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are considered safe but are extremely toxic to cats, their lacking the enzyme - glucuronidase participating in hepatic metabolism. Pyrethroids of II generation may also have skin and eye irritant effects. The main effects of pyrethroids are on sodium and chloride channels. Type II pyrethroids also decrease chloride currents through voltage-dependent chloride channels and this action probably contributes the most to the features of poisoning with type II pyrethroids.

At relatively high concentrations, pyrethroids can also act on GABA-gated chloride channels, which may be responsible for the seizures in type II poisoning.

Cats may be exposed from cutaneous application of topical products, oral ingestion, and direct contact with topically treated dogs.

Many pet products contain permethrins, including over the counter spot-ons, flea sprays, flea collars, and flea shampoos (5).

Treatment with lipid emulsion for enhanced elimination of lipophilic substances has become an important therapeutic option. In affected patients, it can rapidly improve clinical signs while side effects and complications are rarely encountered with this form of therapy (6).

In human medicine (clinical toxicology) intravenous lipid emulsions (ILE) has become a common practice (eg: local anesthetics overdose).

"The mechanism behind this 'antidotal' effect has not yet been fully elucidated. Case reports indicate ILE may be useful in the resuscitation from toxicity induced by a variety of other lipophilic cardiotoxic drugs like various tricyclic antidepressants (TCA), lipophilic β -blockers and calcium channel blockers. Several veterinary case reports and case series have demonstrated that ILE are primarily used in the management of long-lasting neurotoxicity like permethrin toxicosis in cats and ivermectin toxicosis in dogs" (4).

According to the literature "intravenous lipid emulsion (ILE) is an emerging treatment for certain lipophilic drugs" (O'Brien et al., 2010; Fernandez et al., 2011; Gwaltney Brant and Meadows, 2012; Kaplan and Whelan, 2012; Kidwell et al., 2014).

Because permethrins are very lipophilic molecules lipid emulsions was used a potential treatment. So in veterinary clinics some cases about the use of ILE in permethrin intoxication in cats were reported (3). Dosage of intravenous boluses or continuous infusion of lipids have not been assessed in animals for treatment of this type of toxicity. In rats, the LD50 for rapid high volume lipid infusion was estimated to be 67 ml/kg (7).

MATERIALS AND METHODS

The number of cases studied was a total of 18. For all settling presumptive diagnosis of poisoning by insecticides containing pyrethroids.

For setting the diagnosis of suspected poisoned cats all of them were clinically assessed, following the most common clinical signs found in such a poisoning, insisting on observation of the digestive and nervous symptoms. Contaminations (for n=17 and n=18 cases) it was after the owner applied a topical permethrin flea product Superkiller (containing 1 g/Lt imidacloprid and 500 g/Lt of permethrin in a 1 ml pipette) in the garden (against ticks).

The therapeutic procedure involves symptomatic therapy for 16 cases. Symptomatic therapy was made taking into account the therapeutic approach regarding pyrethrin toxicosis, such as the control of convulsions often accomplished by either diazepam or midazolam. In case of convulsions continue after administration of benzodiazepines, propofol or alfaxalone is recommended methocarbamol because this drug is most commonly used to control muscle fasciculation.

Other management was made by skin decontamination, ensuring a patent airway, IV crystalloids and temperature monitoring.

Also, for two of the 18 cases treatment with lipid emulsion (ILE) was co-administered with general medication (n=17; n=18).

We used intralipid emulsion (20 %; i.v. fat emulsion) (Table 1) and symptomatic therapy in two cases.

RESULTS AND DISCUSSION

Most frequently cats are intoxicated by owners by applying canine spot on products. Cats are more likely than dogs to develop pyrethroid toxicosis. This is due to the feline liver being inefficient at glucuronide conjugation. Glucuronide conjugation is needed to metabolize permethrin. The low concentration products approved for cats contain 0.05-0.1% of permethrin and do not seem to cause the signs that the concentrated (45-65% permethrin) canine spot-on do (3).

In Romania the most used products that cats can become contaminated with this toxic are spot-on antiparasitic pipettes for dogs (commonly used the commercial product Advantix - spot-on pipettes for dogs).

However just being in contact with insecticides containing pyrethrin, can be dangerous. Insecticides as Superkiller or Cyper-vet, even Decis can cause toxicosis in felines.

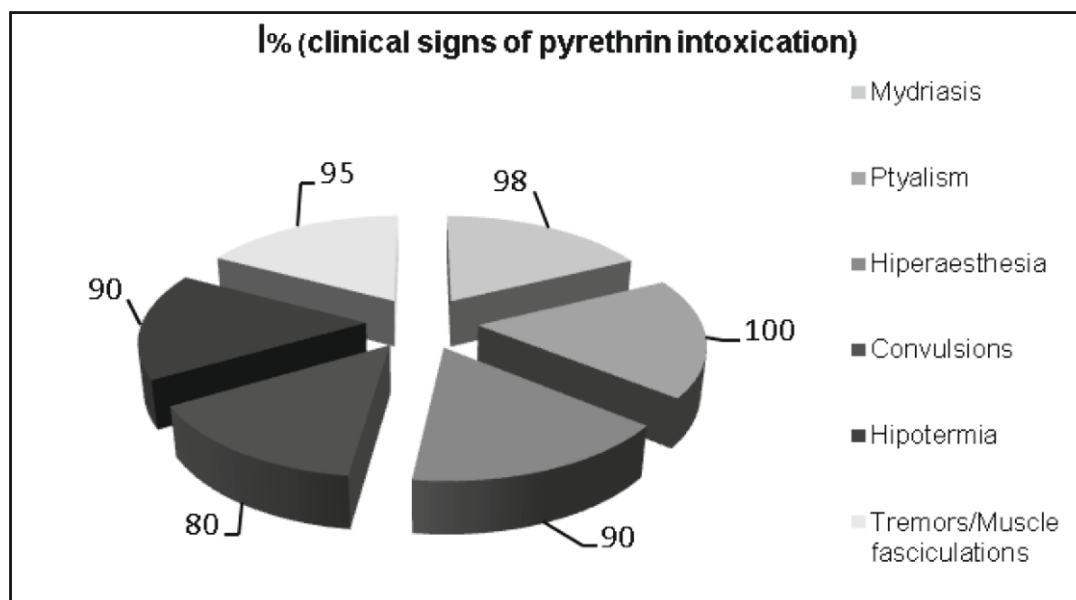


Fig. 1. The main clinical signs present pyrethrins and pyrethroids poisoning in 18 cats
(original paper – Amfim A. et al., *Lucrări Științifice Medicină Veterinară*, vol. XLIX, 2016, Timișoara)

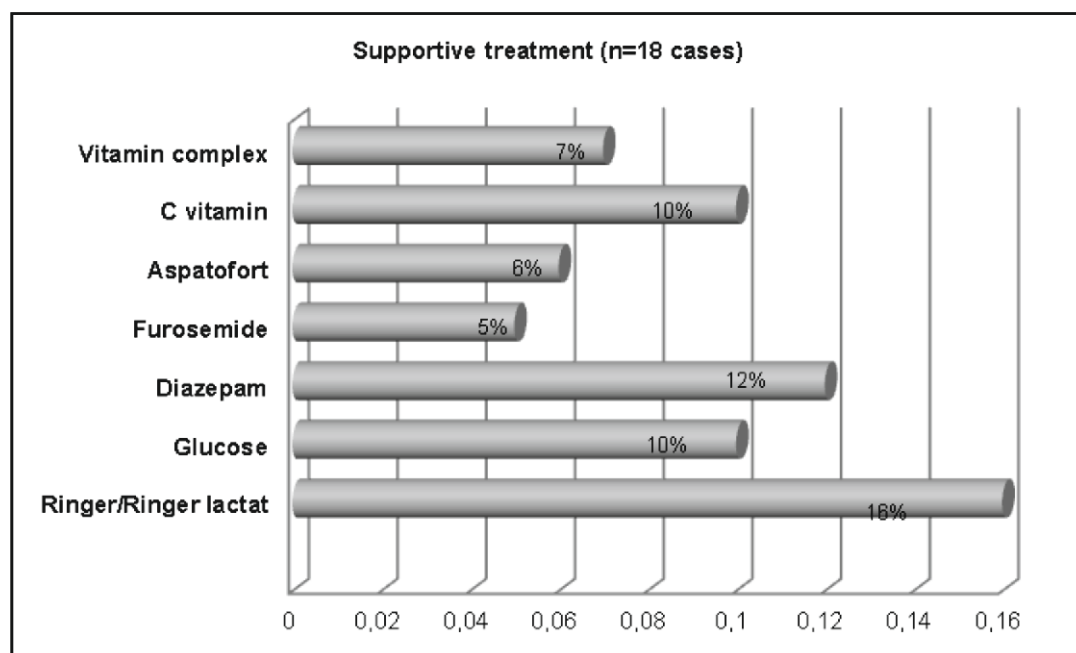


Fig. 2. The most commonly drugs used to treat symptomatically

In our study, following the epidemiological inquiry carried out over the year, it has been estimated that most cases (77%) were registered after using the commercial **Advantix**, containing permethrin 2,000 mg imidacloprid 400 mg for a dog over 25 kg, while the lowest frequency after using **Cyper-vet** (6%) at a concentration of 10 g per 100 ml product and **Superkiller** product was also used for deworming dogs.

Case 1 (n=17):

A 4-month-old, 1,300 kg, female domestic Euro-

pean cat was presented twitching and muscle tremors after the owner applied a topical permethrin flea product **Superkiller** (containing 1 gr/Lt imidacloprid and 500 g/Lt of permethrin in a 1 ml pipette) in the garden (against ticks). At presentation the cat (after 4 hours from contamination) was tachypnoic (45 beats per minute), heart rhythm was 250 beats per minute, oral membranes were pink and rectal temperature was 38.5°C (Table 2). The cat was depressed and had convulsions, hypersalivations, intensive pruritus.

Table 1

Intralipid 20% (drug description)

No.	Name	Weight	Composition	Weight
1.	Intralipid 20 %	100 ml	Soybean oil	20 g (20 %)
			Egg yolk phospholipids	1.2 g
			Glycerin	2.25 g/ 2.2 g
			Sodium Hydroxide	q.s. pH 8 (pH 6-9)
			Distilled aqua	q.s. ad 500/1000 ml

Table 2

Vital signs of the two cats treated with ILE

No. cases	HR (Bmp)	RR (Bmp)	MC	RT (°C)
Case 1 (n=17)	250	45	Pink	38.5
Case 2 (n=18)	180	55	Pink	37.0

Table 3

Hemathological and biochemical parameters after ILE therapy

Parameters	Cases 17	Cases 18	References Values
Hematology			
Leucocytes (G/I)	9	10.5	6-11
Eritrocites (T/I)	8.12	8.58	5-10
Hb(g/I)	120	102	80-170
Ht(I/I)	0.23	0.18	0.29-0.47
MCV (fl)	38.2	40.2	40-55
HBE (MCH)(pg)	12.2	13.8	13-17
MCHC(g/dl)	32	31.5	25-31
Trombocyte (G/I)	85	189	180-430
Biochemical			
Alkaline phosphatase	17	13	0-63
AST (U/I)	25	28	0 – 59
ALT (U/I)	31	27	0 – 91
GGT (U/I)	0	0	0 – 7
Glutamate dehydrogenase	3.5	1.2	0 – 11.2
LDH (U/I)	115	117	0 – 278
Bilirubin (micromol/I)	2.51	4.32	0 – 8.55
Cholesterol (mmol/I)	3.21	4.11	1.81 – 3.88
Tryglicerides (mmol/I)	0.20	0.41	0.57 – 1.14
Creatinine	107.5	209.5	0 – 168
Urea (mmol/I)	5.14	11.52	5 – 11.4

Case 2 (n=18):

A 6-month-old, 2 Kg, female domestic European cat with muscle fasciculation, tremors and hypersalivation, was presented in our clinic after the owner applied permethrin flea –Superkiller. The cat has muscle fasciculation, tremors, hypersalivation, hyperthermy. Heart rhythm, rectal temperature other vital signs are presented for both cases below (Table 2).

The minimum toxic dose is still unknown, but it would be expected to be lower. Cats should be considered more sensitive to permethrin compared with dogs, rats, or human; permethrin products formulated for dogs can contain up to 65% of permethrin, those formulated for cats less than 0.2%. Regarding the clinical aspects, we could determine the main clinical signs recorded in all the 18 cases, which coincided with literature indicating this type of toxicosis. In present study, clinical aspects was those in Fig. 1.

In the last decade an increasing amount of evidence supports the use of ILE to reverse or attenuate the clinical manifestations of many lipophilic toxins (8). At present, the maximum daily dosage of intravenous lipids in veterinary patients is still unknown. Previous authors suggested to check for gross lipemia via, before administering additional doses (7).

In our study, we used for both of cases: ILE and supportive treatment (Fig. 2).

Treatment ILE and symptomatic therapy for both cats was applied following the next protocol:

- » the cats was washed with a mild detergent;
- » Ringer lactate solution infusion was started with the maintenance dose (6 ml/kg/h) for maintaining hydration and promote diuresis; infusion rate was then adjusted hourly on the base of evaluation of perfusions parameters (heart rate, pressure, quality of pulse);
- » due to the severity of tremors was given diazepam 0.05 ml (n=17); 0,1 ml (n=18), at to 3-5 minutes (0.25 - 0.5 mg/kg IV);
- » after administration, cats was quieter and tremors were reduced;
- » ILE (Intralipid 20% IV Fat Emulsion) bolus was administered using venous access at 2 ml/kg in 3 minutes, followed by a constant rate infusion at 4 ml/kg/h for one hour, with a total dosage – 10 ml/Kg (published literature for **20% Intralipid** - Fresenius Kabi dosage and administration is between 10-15 ml/kg during 30-120 minutes or **20% ClinOleic** - Baxter Healthcare, with a initial dosage = 2 ml/kg followed by 16 ml/kg administration in 4 hour (10);
- » On day 2, the both cats (n=17; n=18) was successfully discharged and no additional doses of anti-

convulsant or ILE drug were used;

» None of the cats showed any phlebitis, infection or cutaneous hyperaemia at the site of infusion;

» The average duration for symptomatic treatment for the 18 cases was between 2-3 days; for the treatment of one case it lasted for 4 days; for two cases (n=17; n=18) duration for ILE therapy was 1 day;

» In both cases (n=17; n=18) we tried to reduce at minimum the use of anticonvulsant drugs because and preferred to use ILE as a part of the decontamination protocol. According to the literature, in feline pyrethroid intoxication, hematology and biochemistry parameters are usually without abnormal finding (1). Hyperglycemia status is stress-related responses and neutrophilia also reported an increase in hematocrit and blood urea nitrogen (2).

In our cases, after treatment with ILE both cats showed low values of hematocrit (Table 3). This could be related to the fact that they received intravenous fluids. The rest of values were within normal range. We observed a moderate hypercholesterolemia for one case (n=18; 4.11 mmol/l).

CONCLUSIONS

Treatment was given symptomatically for 16 cases, and in two of them a fat emulsion was given. ILE seemed to be well tolerated and no adverse effects were noticed. In our study, by applying therapy for two cases, we reduce the time of hospitalization (at 3-4 days – cases n=1 to n=16) at 1 day for case n=17 and case n=18, and the cost of recovery was reduce.

Following the imposition of symptoms therapy and assessing each individual case we was able to determine the median duration of the symptomatic treatment for the 18 cases was between 2-3 days.

Although we think the use of ILE like single treatment, is not recommended without any further seizure control and adjuvant therapy .

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