SciVerse ScienceDirect xxx (xxxx) xxx-xxx

Contents lists available at ScienceDirect

SciVerse ScienceDirect

journal homepage: www.elsevier.com

Suspected environmental poisoning by drugs, household products and pesticides in domestic animals

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ARTICLE INFO

Keywords:
Domestic animals
Drugs
Household products
Pesticides
Poisoning

ABSTRACT

Animal poisoning by chemicals (pesticides and household products) and drugs is a frequent occurrence and special attention should be paid to this phenomenon to improve prevention and treatment strategies and because of the fundamental role that animals may play as bioindicators. From January 2017 to March 2019 the Poison Control Centre of Milan (CAV) in collaboration with the University of Milan, collected and analyzed epidemiological data on animal poisoning. During this period, the CAV received a total of 442 enquiries on domestic animal poisoning episodes and, among these, 80.3 % were related to chemicals and drugs. Pesticides and drugs were the two major causes of poisoning (34.1 % and 33.5 %, respectively), followed by household products (29.3 %) and other causative agents (3.1 %, n = 11). In conclusion, these findings can provide useful information for the identification and monitoring of known and emerging toxicants, with positive repercussions on human, animal and environmental health.

1. Introduction

Animal poisoning is a frequent occurrence (Berny et al., 2010a; Bertero et al., 2020a; Caloni et al., 2018; McFarland et al., 2017) and is an issue that is receiving special attention nowadays, thanks also to the spreading of a new public sensibility and awareness. Epidemiological data concerning toxicant exposure in animals are crucial, either to help veterinarians in the diagnosis and treatment of poisoning cases or to implement preventive measures, but also for the role that animals can plays as bioindicators for human and environmental health.

A centralized veterinary poison centre does not exist in Italy (Caloni et al., 2012) and the collection of data relies on the efforts of universities, research institutes, government institutions and poison centers. The human Poison Control Centre in Milan (CAV), established in 1967, consists of a dedicated team of specialists that offer telephone consultations to the public and to healthcare professionals on toxicant exposures, 24 h a day, 7 days a week. Due to the absence of a veterinary-specific poison centre, the CAV also provides consultations on episodes of suspected animal poisoning. Moreover, thanks to an ongoing collaboration with the University of Milan, epidemiological data are extrapolated from the toxicology consultations classified, inserted in a databank and analyzed.

In this paper, epidemiological data on animal poisoning enquiries concerning drugs, household products and pesticides received by the CAV between January 2017–March 2019 will be presented and analyzed. The purpose is to provide comprehensive information on toxicant exposure in terms of incidence, species involved, causative agents, route of exposure, clinical sign and outcome, also analyzing causative agent trends and the emergence of new tendencies/compounds.

2. Material and methods

Since 1990 the Poison Control Centre of Milan (CAV) records, analyzes and archives data related to animal poisoning episodes occurring in Italy. On request, the CAV gives telephone consultations providing information and suggestions for the management of animal poisoning to veterinarians but also to animal owners.

The typical procedure for the collection of data during the toxicology consultation includes information on the animal species, potential poisoning agents, route of exposure and clinical signs. Veterinary toxicologists at the University of Milan collaborate with the CAV to handle the enquiries. Moreover, continuous update on cases from follow-up calls are included, in order to maintain the database as up-to-date, complete and accurate as possible. The data on this paper have been collected from January 2017 to March 2019 and the toxic compounds have been classified according to the following categories: pesticides (insecticides, rodenticides, molluscicides, herbicides and fungicides), drugs (human and veterinary medicinal products, tobacco/nicotine and drugs of abuse), household products and other compounds.

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https://doi.org/10.1016/j.etap.2020.103471
Received 29 May 2020; Received in revised form 12 August 2020; Accepted 13 August 2020
Available online xxx
1382-6689/ © 2020.

2.1. Statistical analysis

Descriptive statistic was performed using IBM SPSS Statistics for Mac, Version 26.0 (Armonk, NY: IBM Corp.) and graphs were created using Prism for Mac, Version 8.4.1 (GraphPad Software Inc., La Jolla, CA, USA).

3. Results

From January 2017 to March 2019, the CAV received a total of 442 toxicology consultations related to animal poisoning episodes. Among these, 80.3 % (n = 355) were related to chemicals (household products and pesticides) and drugs. As for the latter, 70.4 % of the toxicology consultations (n = 250) were from veterinarians, 28.7 % (n = 102) from animal owners and for 0.8 % of the enquiries (n = 3) the caller was unknown. The majority of the calls were from Lombardy (36.3 %, n = 129), followed by Emilia Romagna (12.4 %, n = 44), Veneto (11.5 %, n = 41) and Sicily (6.8 %, n = 24) (Fig. 1). The dog was the species most frequently involved (83.7 %, n = 297), followed by the cat (14.6 %, n = 52). Two calls regarded rabbits (0.6 %) and single enquiries were received concerning a pony, a ferret and an African hedgehog (0.3 % each) (Fig. 2). The majority of the exposures occurred indoor (78.9 %, n = 280), 17.2 % (n = 61) outdoor, whereas for 3.9 % of the episodes (n = 14) the site of exposure was unknown. The route of the exposure was ingestion in most of the cases (87.9 %), but also dermal (3.62 %) and mucosal (3.40 %) exposures were also observed. Toxicant exposures were generally accidental (93 %, n = 330), but in some cases they were due to owner errors/misuses (2.8 %, n = 10), one (0.3 %) episode was due to an intentional poisoning and for 14 cases (3.9 %) the circumstances that led to the intoxication were unknown. In the majority of the cases, symptoms of the intoxication appeared within 24 h after the exposure (62.5 %, n = 222). The outcome was positive for 187 animals (52.7 %), fatal for 15 animals (4.2 %) and unknown in 153 cases (43.1 %).

3.1. Classes of toxic compounds

The data analysis showed that, among the considered toxicants (chemicals and drugs) (Fig. 3), pesticides and drugs were the two major causes of poisoning (34.1 %, n = 121 and 33.5 %, n = 119, respectively), followed by household products (29.3 %, n = 104) and other causative agents (3.1 %, n = 11).

3.1.1. Pesticides

A total of 121 enquiries (34.1 %) were related to pesticides. Among these, the greater number of calls involved insecticides (44.6 %, n = 54), followed by rodenticides (28.9 %, n = 35), fungicides (9.1 %, n = 11), herbicides (7.4 %, n = 9) and molluscicides (6.6 %, n = 8), whereas in 4 cases (3.3 %) the involved pesticide was not further characterized (Fig. 4).

3.1.1.1. Insecticides The enquiries on insecticides have been classified as reported in Fig. 5. Pyrethrins/pyrethroids were the most common cause of intoxication (42.6 %, n = 23), with cypermethrin-tetramethrin combinations being the most frequently involved, followed by neonicotinoids (acetamiprid and imidacloprid, 25.9 %, n = 14), organoarsenic compounds (dimethylarsinate; 14.8 %, n = 8), carbamates (5.6 %, n = 3), isothiazolinones (1.9 %, n = 1), phenylpyrazoles (1.9 %, n = 1) and pyrroles (1.9 %, n = 1), while in 3 cases the insecticide involved was unknown (5.6 %).

Specifically, concerning the dog, 16.5 % of all the enquiries on this species were due to insecticides (49 out of 297), and pyrethrins/pyrethroids were the most involved class (40.8 %, n = 20), followed by neonicotinoids (24.5 %, n = 12), organoarsenic compounds (dimethylarsinate; 16.3 %, n = 8) and carbamates (6.1 %, n = 3). In cats, 5.8 % (3 out of 52) of the calls were related to insecticides, with 2 calls involving neonicotinoids (acetamiprid and imidacloprid) and 1 call pyrethroids (deltamethrin). Both in dogs and cats the major route of exposure was accidental ingestion.

Chlorfenapyr, a novel pyrrole insecticide (Ngufor et al., 2016), was reported as the causative agent in one case of intoxication concerning a dog. A poisoning episode of a ferret involved the mucosal exposure to pyrethroids, and the same class was involved in the intoxication of a pony through the gastrointestinal route.

3.1.1.2. Rodenticides Rodenticides accounted for 9.9 % (n = 35) of all the calls received by CAV concerning chemicals and drugs, and 28.9 % of the enquiries on pesticides (Fig. 6). The dog was the only species involved (accidental indoor exposures). Anticoagulant rodenticides accounted for 31.4 % of the enquiries (n = 11) and non-anticoagulant compounds were responsible for 5.7 % (n = 2) of the calls, while in 22 cases the involved molecule was unknown (62.9 %). Bromadiolone and difenacoum were the most frequently involved compounds (14.3 %, n = 5 and 8.6 %, n = 3, respectively), but brodifacoum, coumatetralyl, difethialone, thallium and α-chloralose were also reported (2.9 %, n = 1, each).

3.1.1.3. Molluscicides All the enquiries received by CAV on molluscicide intoxications were related to the accidental ingestion of metaldehyde by dogs (6.6 % of the call concerning pesticides and 2.3 % of the total calls on chemicals and drugs).

3.1.1.4. Herbicides Herbicides accounted for 7.4 % of the enquiries involving pesticides (Fig. 4) and for 2.5 % of the calls concerning chemicals and drugs. Dogs and cats were the species most frequently involved (44.4 %, n = 4, each). Glyphosate was the major culprit (66.7 %, n = 6) in dogs (3 cases out of 4) as well as in cats (2 cases out of 4). In the dog species, synthetic auxins (fluroxypyr and triclopyr) were also reported (1 case). In cats, other involved compounds were dicamba and metribuzin (1 case each).

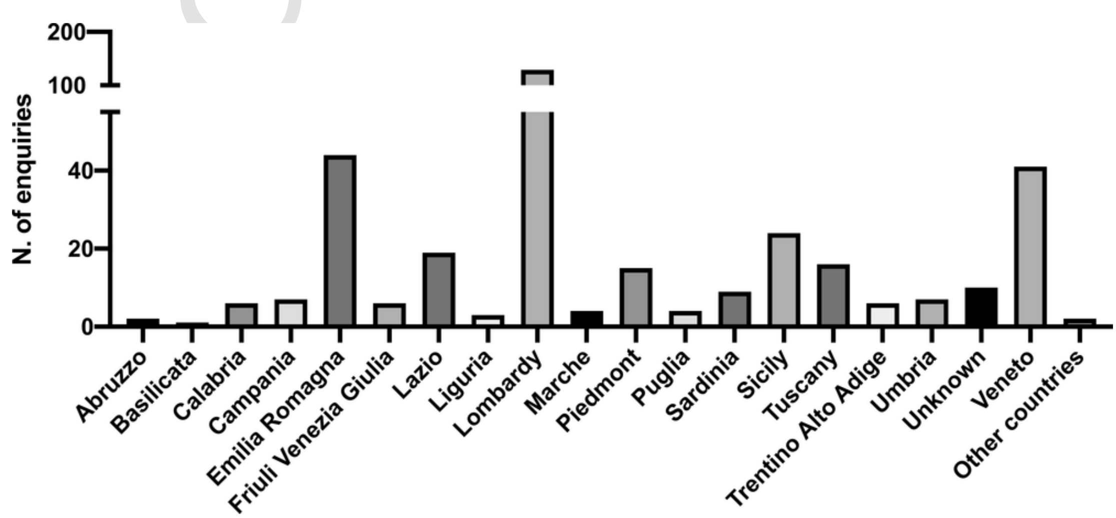

Fig. 1. Geographical distribution in Italy of the enquiries received by the Poison Control Centre of Milan (CAV) during the period January 2017 - March 2019 on animal exposures to

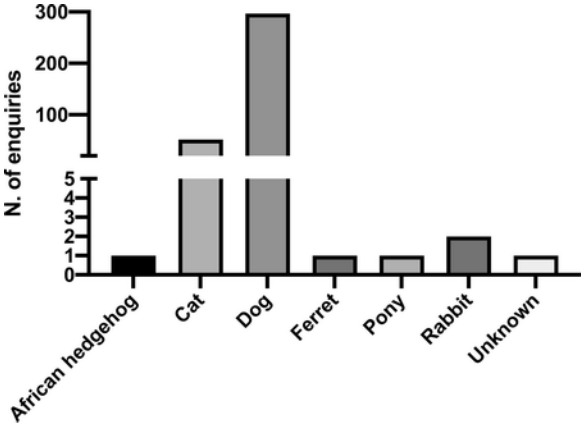

Fig. 2. Species involved in suspected poisoning by drugs, household products and pesticides, according to the calls received by the Poison Control Centre of Milan (CAV) during the period January 2017–March 2019.

Glyphosate was also involved in one enquiry concerning an African hedgehog which after the exposure to this herbicide showed dyspnea and oral edema.

3.1.1.5. Fungicides Fungicide exposure accounted for 9.1 % of the enquiries involving pesticides (Fig. 4) and for 3.1 % of the calls received by CAV on chemicals and drugs. The dog was the only species affected, with copper sulphate and dodine being the most frequently implicated compounds (27.3 %, n = 3, each), followed by ziram (18.2 %, n = 2) and dicopper chloride trihydroxide (9.1 %, n = 1). In 2 cases (18.2 %) the involved fungicide compound was not identified.

3.1.2. Drugs

In this category (Fig. 7) are included human (84 %, n = 100; Table 1) and veterinary (10.1 %, n = 12; Table 2) medicinal products, tobacco/nicotine (2.5 %, n = 3) and drugs of abuse (3.4 %, n = 4). As for dogs (86.6 % of the calls, n = 103), the majority of the enquiries involved the exposure to human drugs (85.4 %, n = 88), with CNS drugs (20.5 %, n = 18) and NSAIDs (12.5 %, n = 11) together with alpha and beta blockers (12.5 %, n = 11) being the most involved classes of compounds (Table 1). Veterinary drugs (mainly parasiticides and NSAIDs) were responsible for 7.8 % of the intoxications in dogs (n = 8) (Table 2) and drugs of abuse, specifically *Cannabis indica* (n = 1) and hashish (n = 3), were involved in 3.9 % of the cases, followed by the exposure to tobacco/nicotine (2.9 %, n = 3) (Fig. 7).

A significantly lower number of drug intoxications were reported in cats, which accounted for 13.4 % of the calls (n = 16). Human drugs were the major culprit (75 %, n = 12), particularly CNS drugs (33.3 %, n = 4), muscle relaxers (25 %, n = 3) and NSAIDs (16.7 %, n = 2) (Table 1), followed by veterinary drugs (25 %, n = 4)(Table 2). As for the latter, the most involved classes of compounds were parasiticides (75 %, n = 3), with 2 cases due to adverse reactions to pyrethroids. A sporadic case of acute intoxication with dyspnea was reported in a cat after the accidental ingestion of feline facial pheromones (Table 2).

3.1.3. Household products

In general, detergents (20.2 %, n = 21) accounted for the majority of the calls involving household products, followed by caustic agents (16.3 %, n = 17), fertilizers (15.4 %, n = 16), antifreezes (7.7 %, n = 8) and firelighters (6.7 %, n = 7).

The dog species accounted for the majority of the calls on household products (71.2 %, n = 74), followed by the cat (26.9 %, n = 28) and just 2 enquiries (1.9 %) were about rabbits (Fig. 8). As for dogs, the majority of the cases were due to the exposure to fertilizers and detergents (20.3 %, n = 15 and 18.9 %, n = 14, respectively), followed by caustic agents such as strong acids and bases, anti-limescales and bleaches (16.2 %, n = 12). Other frequent implicated classes of compounds were antifreezes (mainly ethylene glycol) and firelighters (8.1 %, n = 6 each). Concerning cats, many enquiries were about detergents (25 %, n = 7), caustic agents (anti-limescales, bleach and sodium hydroxide, 17.9 %, n = 5), essential oils (liquid potpourri for home fragrance, 14.3 %, n = 4) and antifreezes (7.1 %, n = 2). The 2 calls received on rabbits were about the ingestion of a firelighter and a washable mural paint.

3.1.4. Other causative agents

Other causative agents are reported in Table 3. Among those, a chemiluminescent glow-stick was responsible of an intoxication in a cat which ingested its liquid content. The ingestion of a firecracker by a dog was reported to cause vomiting and sensory alterations (the animal was lethargic/comatose). These 2 cases had positive outcomes whereas a fatal episode was reported in a dog after the ingestion of coal tar, due to aspiration pneumonia.

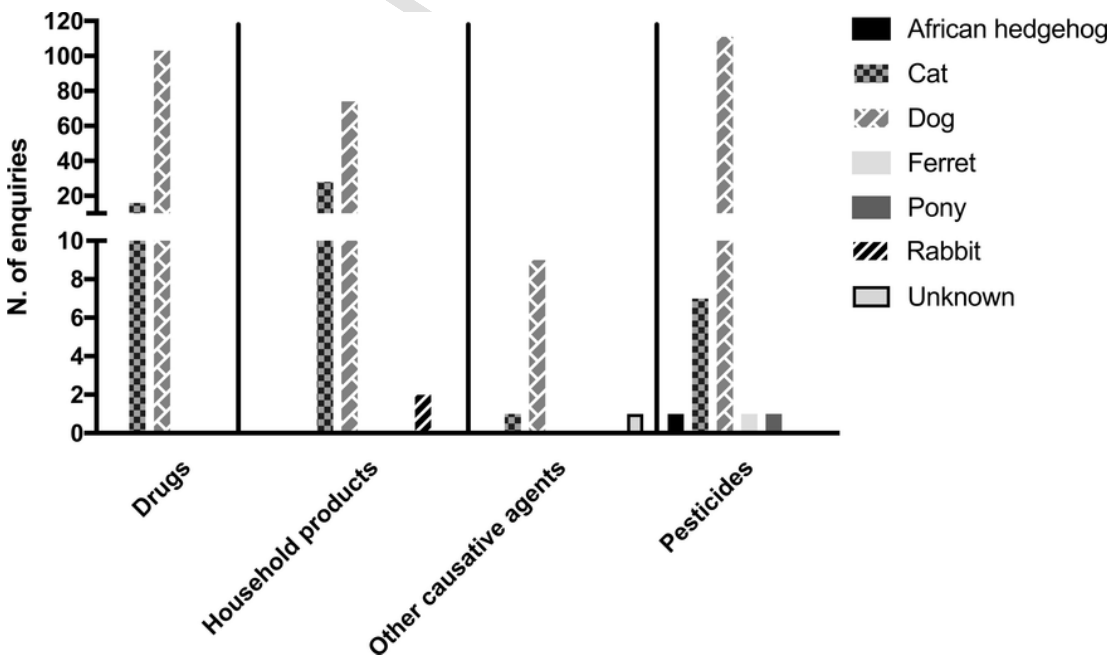

Fig. 3. Classes of toxicants (drugs, household products and pesticides) involved in suspected animal poisoning (calls). Poison Control Centre of Milan (CAV), data from January 2017 to March 2019.

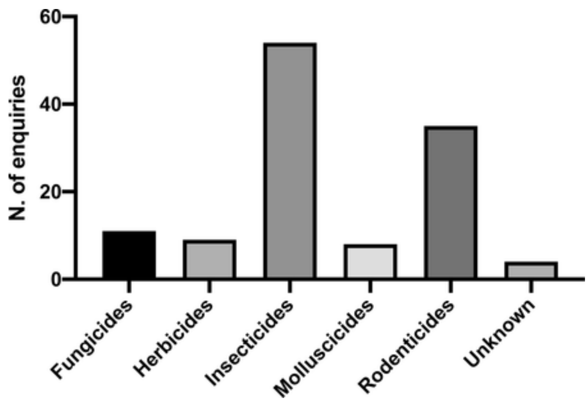

Fig. 4. Pesticide poisoning (calls) in animals. Poison Control Centre of Milan (CAV), data from January 2017 to March 2019.

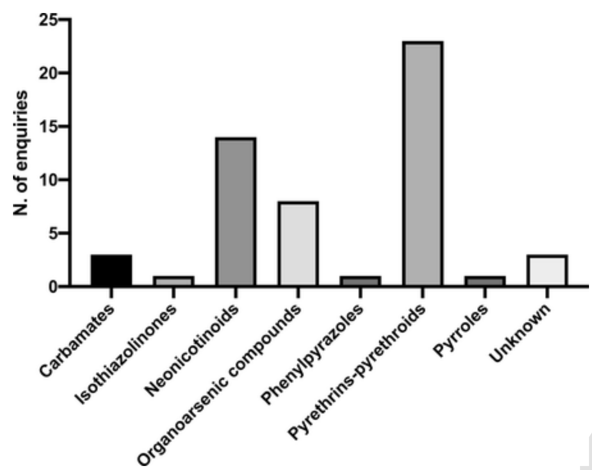

Fig. 5. Classes of insecticides involved in suspected animal poisoning (calls). Poison Control Centre of Milan (CAV), data from January 2017 to March 2019.

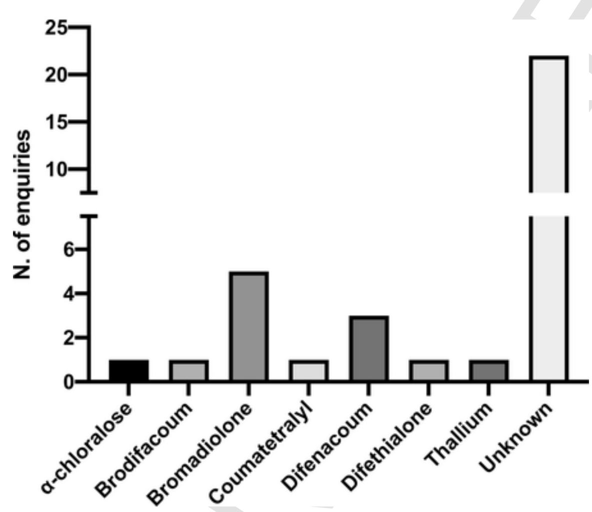

Fig. 6. Rodenticides involved in suspected animal poisoning (calls). Poison Control Centre of Milan (CAV), data from January 2017 to March 2019.

3.2. Clinical signs

The most frequent clinical signs due to toxicant exposure were gastrointestinal (mainly vomiting), neurological (especially convulsions, tremors and ataxia) and cardiological (arrhythmias, bradycardia and tachycardia) signs. Death occurred in 7.4 % of the cases with a known outcome. Household products (53.3 %, n = 8), pesticides (20 %, n = 3) and drugs (20 %, n = 3) were the most common causes of death.

4. Discussion

This work aims to provide an overview on animal exposure to toxicants (drugs, household products and pesticides).

In this context, animals may play a fundamental role as bioindicators for the determination and assessment of environmental toxicants (Bertero et al., 2020b; Bischoff et al., 2010; Braouezec et al., 2016; Henriquez-Hernandez et al., 2017; Serpe et al., 2018; Srebocan et al., 2019). Moreover, animals have shown to be very sensitive to the detrimental health effects of environmental pollutants, often more than humans, being also able to furnish key information on the rise of emerging toxicants (Gulson et al., 2009; Tsuchiya, 1992).

Results on toxicant exposure collected in this paper are quite similar to those previously reported in Italy and in other European countries (Barbier, 2005; Berny et al., 2010a; Bertero et al., 2020a, b; Caloni et al., 2018, 2012; Caloni et al., 2016; McFarland et al., 2017; Modrá and Svobodová, 2009; Schediwy et al., 2015; Vandenbroucke et al., 2010; Wang et al., 2007), but some peculiarities and new trends are emerging.

From national perspective, a great number of calls were from the Northern part of Italy (*i.e.* from Lombardy, Veneto and Emilia Romagna) but Southern and Central regions are also well represented since a remarkable number of enquiries had been received from these territories, enabling to outline a fair view of the phenomenon at a national level.

Most of the toxicology consultations were related to dogs and cats (Fig. 2), revealing a better predisposition for pet owners and veterinarians to use the CAV consultation service, maybe because these figures are more likely to know the existence of this opportunity. The majority of the enquiries related to dogs were due to the exposure to pesticides and drugs, followed by household products (Fig. 3), whereas for the feline species household products, followed by drugs and pesticides, have been identified as the major culprits. A similar situation has been reported in a previous work by CAV (Caloni et al., 2012), in which the data collected from 2000 to 2010 revealed that pesticides and drugs, followed by household products were the toxic classes most frequently involved in calls related to suspected animal poisonings. A similar trend has been observed in Europe, where pest control substances and drugs are common causative agents of poisoning in pets, followed by other toxicants such as household products (Barbier, 2005; Caloni et al., 2018; McFarland et al., 2017; Vandenbroucke et al., 2010).

Concerning pesticides, insecticides (Fig. 4) were the most involved class of compounds. Among them (Fig. 5), pyrethrins/pyrethroids were the predominant agents of poisoning in dogs, followed by neonicotinoids, whereas just few cases involved carbamates. These data confirm the findings reported by Caloni et al. (Caloni et al., 2016), who described the exposure to pyrethrins/pyrethroids as the primary cause of insecticide poisoning in pets delineating a new tendency since previous trends have seen carbamates as one of the most frequent cause of insecticide poisoning. Indeed, in the dog species, anticholinesterase insecticides (carbamates and organophospates) were reported as the most commonly found insecticide compounds in a previous epidemiological study on animal poisoning by CAV (Caloni et al., 2012). Besides, in this scenario, neonicotinoids appear as emerging molecules in our study, with many cases recorded in dogs (Fig. 5). Moreover organochlorines, insecticides that are still responsible of pet intoxications (Barbier, 2005; Berny et al., 2010a; Bertero et al., 2020a; Caloni et al., 2012, 2016; Martínez-Haro et al., 2008), have not been found as a cause of animal poisoning in this study, whereas a case concerning the exposure to chlorfenapyr, a novel pyrrole insecticide (Ngufor et al., 2016), has been reported in a dog (Fig. 5). On the other hand, the toxicology consultations related to insecticide intoxications in the feline species were mainly due to neonicotinoid (acetamiprid and imidacloprid) intoxications and just one case involved pyrethroids (deltamethrin) (Fig. 5). Even if only 3 cases of insecticide poisoning have been recorded for this species in the present study, these data may be interesting, introducing possible new trends on causative agents since, besides the most frequently reported anticholinesterase and pyrethrin/pyrethroid intoxication episodes (Berny et

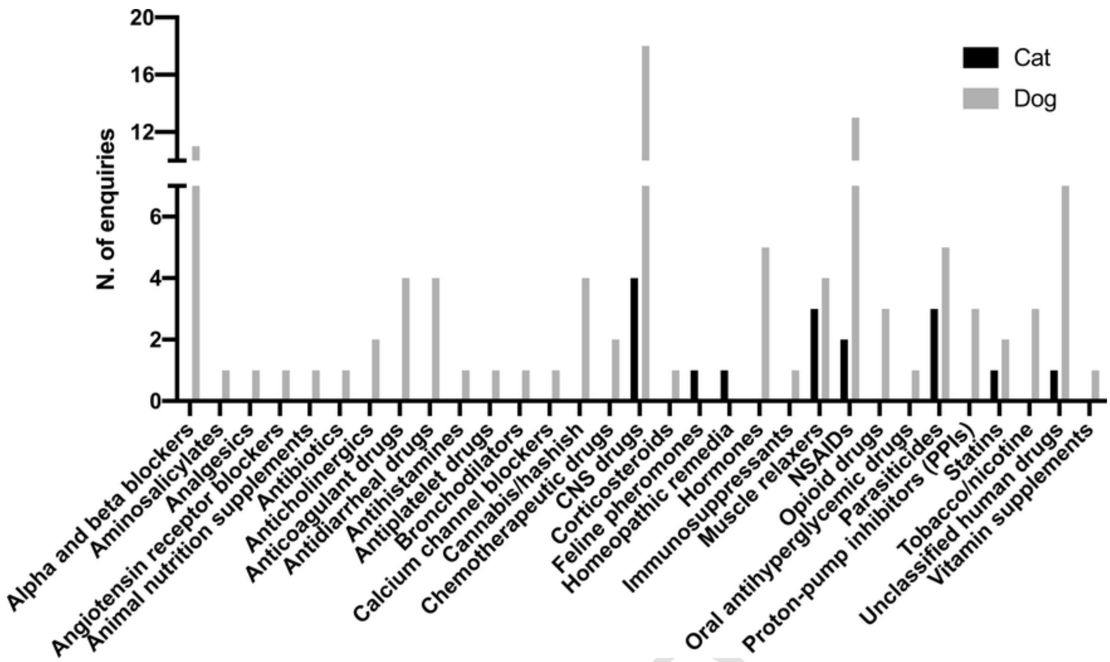

Fig. 7. Drugs (including human and veterinary medicinal products, tobacco/nicotine and drugs of abuse) involved in suspected animal poisoning (calls). Poison Control Centre of Milan (CAV), data from January 2017 to March 2019.

al., 2010a; Caloni et al., 2012, 2016; Giuliano Albo and Nebbia, 2004; Modrá and Svobodová, 2009; Schediwy et al., 2015), neonicotinoids seem to emerge among the main causes of insecticide poisoning (Caloni et al., 2016). The reasons of this rise may lay on the relatively low toxicity towards mammals, in the face of a high toxicity towards insects (Goulson, 2013), together with a great versatility (various formulations are available, for home gardening and for indoor use as baits).

As for rodenticides (Fig. 6), anticoagulant compounds and in particular second generation molecules such as bromadiolone and difenacoum remained a major cause of intoxication (Barbier, 2005; Berny et al., 2010a; Caloni et al., 2012, 2016; McFarland et al., 2017; Modrá and Svobodová, 2009; Schediwy et al., 2015). Non-anticoagulant rodenticides were found responsible of just 2 poisoning episodes, one due to the exposure to α-chloralose and the other to thallium, thus, despite the restrictions applied to the use of the latter as a rodenticide in many countries, this molecule is still responsible for poisoning cases. Interestingly, no rodenticide intoxications have been reported in cats: all the enquiries on these compounds involved dogs, species that is known to be more subject to rodenticide poisoning (Berny et al., 2010b; Caloni et al., 2016; Vandenbroucke et al., 2010). Metaldehyde was the only molluscicide compound related to animal intoxication and it was responsible of 6.6 % of the enquiries involving pesticides (Fig. 4), percentage that is in line with those detected in another recent study performed in Italy (Bertero et al., 2020a). In this regard it seems that metaldehyde intoxication, which sees in the domestic carnivores the target species (Bertero et al., 2020a), is undergoing a slight decrease in comparison with data from previous Italian studies (Caloni et al., 2012, 2016), even if it continues to be a major issue (Caloni et al., 2018; Modrá and Svobodová, 2009; Schediwy et al., 2015; Vandenbroucke et al., 2010; Wang et al., 2007), probably because of the palatability and wide availability that characterize this compound. As reported also by other authors (Barbier, 2005; Caloni et al., 2012, 2016; Vandenbroucke et al., 2010), glyphosate was the herbicide most frequently involved in animal poisoning episodes, mainly in cats and dogs, while other compounds (synthetic auxins, dicamba and metribuzin) were involved only sporadically. With regard to glyphosate, attention must be paid to the formulations available in the market since it seems that the toxicity of this molecule is influenced (and increased) by the surfactants/adjuvants (*i.e.* polyoxyethylene amine) added in the commercial products (Coalova et al., 2014; Cortinovis et al., 2015). In accordance with other data from European literature (Barbier, 2005; Berny et al., 2010a; Caloni et al., 2012, 2016), the fungicide implicated in the highest number of enquiries was copper sulphate, together with dodine. Additional involved compounds were ziram and dicopper chloride trihydroxide, which have also been reported in cases of fungicide intoxications by other authors (Barbier, 2005; Caloni et al., 2012, 2016).

Drugs (Fig. 7) generally account for a great number of intoxications in domestic animals, mainly because of owner improper/off-label use (*i.e.* administration without a prescription) or accidental ingestion (Barbier, 2005; Berny et al., 2010a; Caloni et al., 2014, 2012; McFarland et al., 2017; Modrá and Svobodová, 2009; Schediwy et al., 2015; Vandenbroucke et al., 2010). In the present work, the dog was the species most affected (86.6 % of the calls), with the majority of the enquiries concerning exposure to human drugs (Table 1) (86.6 %; mainly CNS drugs, NSAIDs and alpha/beta blockers) and just few toxicology consultations (7.8 %, n = 8) related to veterinary drugs (Table 2) (parasiticides and NSAIDs). These results are in line with those of a previous survey by CAV (Caloni et al., 2012), which reported CNS drugs and NSAIDs as the classes of human medicines most involved in dog intoxications. Similar results were obtained in another study by CAV (Caloni et al., 2014) and in other surveys performed by European authors (Barbier, 2005; Berny et al., 2010a; Caloni et al., 2018; Schediwy et al., 2015), probably because of to the widespread use of these drugs by people. As for the cats, this species accounted for a lower number of drug intoxications (13.4 %); human medicines (Table 1) were again the principal cause of poisoning (75 %; CNS drugs, muscle relaxers, NSAIDs), followed by veterinary drugs (Table 2) (25 %; mainly parasiticides). In addition, an interesting case was related to the oral exposure of a cat to feline facial pheromones, which led to an acute intoxication with respiratory symptoms that ended with a positive outcome but draws attention to the toxicological aspects connected to these relatively new products (pheromones). Previous data from CAV (Caloni et al., 2012) reported, for this species, several cases of misuse of veterinary parasiticides (mainly pyrethroids and in particular permethrin-based spot on) together with episodes of acetaminophen intoxications, and similar results have been reported by other authors (Berny et al., 2010a; Caloni et al., 2014; McFarland et al., 2017; Schediwy et al., 2015). Therefore, our data seem to differ from those of many European researches that found veterinary parasiticides as the major culprit of drug intoxications in cats (Berny et al., 2010a; Caloni et al., 2014; McFarland et al., 2017; Schediwy et al., 2015), while, considering all the enquiries on drugs, our data are in line with the general tendency reported in the European literature which sees

Table 1
Human medicinal product poisoning (calls) in animals. Poison Control Centre of Milan (CAV), January 2017–March 2019.

Drug	Class	Frequency	Species
Acetaminophen	Analgesics	1	Dog
Antibiotic ointment	Antibiotics	1	Dog
Apixaban	Anticoagulant drugs	3	Dogs
Apomorphine	Dopaminergic agents/CNS[a] drugs	1	Dog
Arsenic trioxide	Chemotherapeutic agents	1	Dog
Atenolol	Beta blockers	4	Dogs
Atorvastatin	Statins	1	Dog
Azathioprine	Immunosuppressants	1	Dog
Baclofen	Muscle relaxers	6	Cats, dogs
Bisoprolol	Beta blockers	1	Dog
Bromazepam	Benzodiazepines/CNS[a] drugs	1	Cat
Buprenorphine	Opioid drugs	1	Dog
Caffeine	CNS[a] stimulants	1	Dog
Calcium carbonate & cholecalciferol	Vitamin supplements	1	Dog
Candesartan cilexetil	Angiotensin receptor blockers	1	Dog
Carprofen	NSAIDs[b]	1	Cat
Diclofenac	NSAIDs[b]	2	Dogs
Doxazosin	Alpha blockers	1	Dog
Duloxetine	SSRI[c]/CNS[a] drugs	3	Cat, dogs
Escitalopram	SSRI[c]/CNS[a] drugs	1	Dog
Esomeprazole	PPI[d] drugs	1	Dog
Flurbiprofen	NSAIDs[b]	1	Dog
Homeopathic peony ointment	Homeopathic remedia	1	Cat
Hydroxyurea	Chemotherapeutic agents	1	Dog
Ibuprofen	NSAIDs[b]	5	Dogs
Ketoprofen	NSAIDs[b]	1	Dog
Lansoprazole	PPI[d] drugs	1	Dog
Lercanidipine	Calcium channel blockers	1	Dog
Levothyroxine	Hormones	5	Dogs
Loperamide	Antidiarrheal agents	4	Dogs
Loratadine	Antihistamines	1	Dog
Lovastatin	Statins	1	Dog
Mefenamic acid	NSAIDs[b]	1	Dog
Melevodopa & carbidopa	Dopaminergic agents/central nervous system drugs	1	Dog
Mesalazine	Aminosalicylates	1	Dog
Metformin & glibenclamide	Oral antihyperglycemic drugs	1	Dog
Metoprolol	Beta blockers	1	Dog
Nebivolol	Beta blockers	2	Dogs
Nimesulide	NSAIDs[b]	2	Cat, dog
Olanzapine	Atypical antipsychotics/central nervous system drugs	1	Dog
Omeprazole	PPI[d] drugs	1	Dog
Other	–	8	Cat, dogs
Perphenazine	Phenothiazine antipsychotics/ CNS[a] drugs	1	Dog
Phenobarbital	Barbiturates/CNS[a] drugs	2	Dogs
Prazepam	Benzodiazepines/CNS[a] drugs	1	Dog
Prednisolone	Corticosteroids	1	Dog
Pregabalin	Gabapentinoids/CNS[a] drugs	1	Cat
Risperidone	Atypical antipsychotics/CNS[a] drugs	3	Dogs
Rivaroxaban	Anticoagulant drugs	1	Dog
Salbutamol	Bronchodilators	1	Dog
Sertraline	SSRI[c]/CNS[a] drugs	1	Dog
Silodosin	Alpha blockers	1	Dog
Solifenacin	Anticholinergics	1	Dog
Statins	Statins	1	Cat
Tamsulosin	Alpha blockers	1	Dog
Tiapride	Dopaminergic receptor blocking agents/CNS[a] drugs	1	Cat
Ticlopidine	Antiplatelet drugs	1	Dog
Tizanidine	Muscle relaxers	1	Dog
Tramadol	Opioid drugs	2	Dogs
Trihexyphenidyl	Anticholinergics	1	Dog
Valproate	Anticonvulsants/CNS[a] drugs	2	Dogs
Venlafaxine	SNRI[e]/CNS[a] drugs	1	Dog
Tot	–	**100**	–

[a]Central Nervous System; [b]Nonsteroidal Anti-Inflammatory Drugs; [c]Selective Serotonin Reuptake Inhibitors; [d]Proton-Pump Inhibitors; [e]Serotonin–Norepinephrine Reuptake Inhibitors.

Table 2
Veterinary medicinal product poisoning (calls) in animals. Poison Control Centre of Milan (CAV), January 2017 - March 2019.

Drug	Class	Frequency	Species
Liver Support Supplement	Animal nutrition supplements	1	Dog
Deltamethrin	Parasiticides	1	Dog
Diazinon	Parasiticides	2	Dogs
Fipronil	Parasiticides	1	Dog
Firocoxib	COX-2 inhibitors/ NSAIDs[a]	1	Dog
Imidacloprid & flumethrin	Parasiticides	1	Dog
Imidacloprid & permethrin	Parasiticides	2	Cats
Meloxicam	NSAIDs[a]	1	Dog
Synthetic feline facial pheromones	Feline pheromones	1	Cat
Praziquantel	Parasiticides	1	Cat
Tot	–	**12**	–

[a]Nonsteroidal Anti-Inflammatory Drugs.

the parasiticides as the major class of veterinary drugs involved in animal poisoning (Berny et al., 2010a; Caloni et al., 2014, 2012; McFarland et al., 2017; Schediwy et al., 2015), and CNS drugs and NSAIDs as the human medicines most frequently implicated (Barbier, 2005; Berny et al., 2010a; Caloni et al., 2014, 2012; McFarland et al., 2017; Schediwy et al., 2015; Vandenbroucke et al., 2010). The dog was the only species exposed to drugs of abuse (Fig. 7), with percentages similar to those detected in a previous paper by CAV (Caloni et al., 2012). Household products accounted for a large number of enquiries (Fig. 3), being the domestic environment reach in potentially toxic chemicals, whose numerousness and assortment is continuously increasing due to the incessant placing on the market of new products. Detergents accounted for the majority of the enquiries involving household products, followed by caustic agents, fertilizers, antifreezes (mainly ethylene glycol) and firelighters (Fig. 8), results that are in accordance with those reported in a previous epidemiological study performed by CAV (Caloni et al., 2012) and in many researches carried out around Europe (Barbier, 2005; Berny et al., 2010b; Caloni et al., 2018; McFarland et al., 2017; Schediwy et al., 2015). Dogs accounted for the majority of the enquiries on household products, followed by cats, and just 2 enquiries were related to rabbits (Fig. 8). In dogs, fertilizers (20.3 %) and detergents (18.9 %) were the major culprits, but also caustic agents (16.2 %), antifreezes (8.1 %, mainly ethylene glycol) and firelighters (8.1 %) were among the most frequent causes. In cats, the greatest number of calls were about detergents (25 %), followed by caustic agents (17.9 %), essential oils (liquid potpourri, 14.3 %) and antifreezes (7.1 %). Interestingly, with regard to the feline species, essential oils emerged as a frequent cause of poisoning incidents. In literature a general tendency seems to depict detergents as often involved both in cat and dog intoxications (Caloni et al., 2018; Giuliano Albo and Nebbia, 2004; McFarland et al., 2017), as in our work, whereas fuel (petroleum distillate) intoxications seem to affect particularly cats (just one case recorded in our study, no cases in dogs) (Berny et al., 2010a; Caloni et al., 2018; Giuliano Albo and Nebbia, 2004), probably because of the grooming behavior of this species, which may lead to a high oral absorption. As for ethylene glycol, intoxications are frequently observed in the dog (5 cases in the present work) as well as in the feline species (2 cases concerning cats have been observed in our survey) (Amoroso et al., 2017; Berny et al., 2010a; Caloni et al., 2018; Potter et al., 2015). Moreover, it should be noted that household products were the major cause of fatal poisoning incidents in this study (53.3 %), and in particular ethylene glycol alone accounted for 26.7 % of the recorded fatal cases, which is

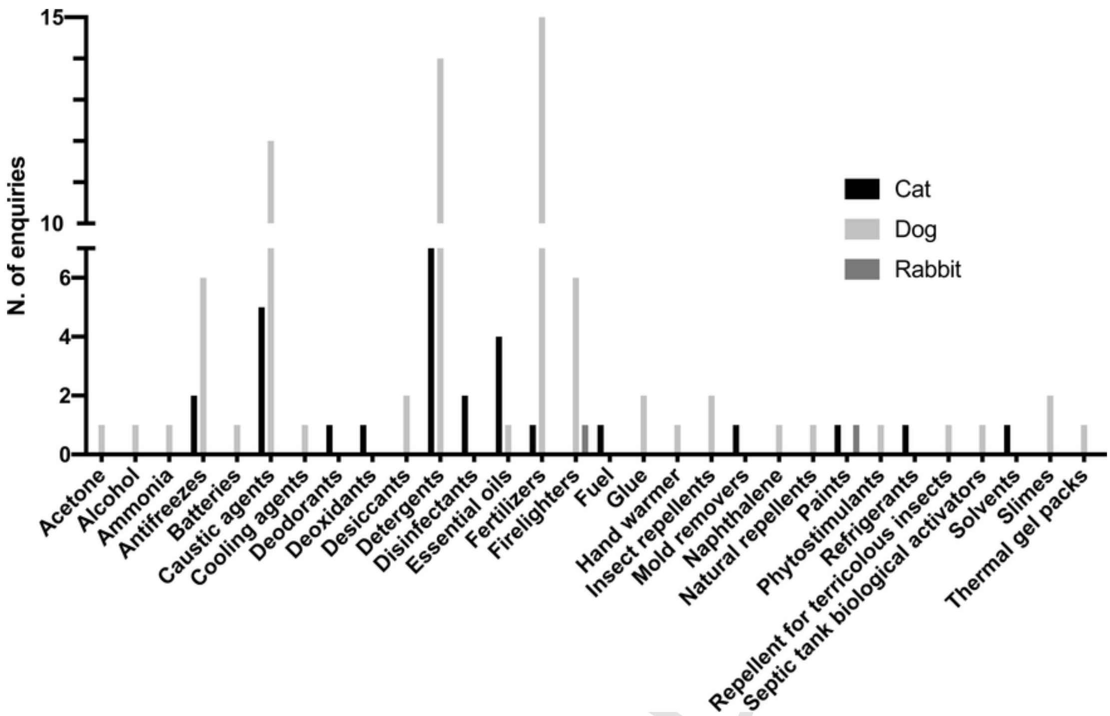

Fig. 8. Household products involved in suspected animal poisoning (calls). Poison Control Centre of Milan (CAV), data from January 2017 to March 2019.

Table 3
Poisoning (calls) in animals concerning other causative agents. Poison Control Centre of Milan (CAV), January 2017–March 2019.

Causative agent	Frequency	Species
Cadmium	1	Unknown
Calcium carbide	1	Dog
Carbon monoxide	1	Dog
Chemiluminescent glow-sticks	1	Cat
Firecrackers	1	Dog
Heliotrope	1	Dog
Photos	1	Dog
Poisoned bait (meatball)	1	Dog
Coal tar	2	Dogs
Zinc oxide	1	Dog
Tot	**11**	–

in line with the high mortality rate generally observed for this compound (Bates, 2016; Berny et al., 2010a; García-Ortuño et al., 2006; Popa et al., 2018; Schweighauser and Francey, 2016).

Other causative agents are indicated in Table 3, where an intentional poisoning with a positive outcome is also reported. Moreover one poisoning episode due to the ingestion by a cat of the liquid content of a chemiluminescent glow-stick (plastic rods used as decorative items that sparkle in the dark as a result of a chemical reaction) has been observed. Indeed these products are becoming a popular fashion accessory, particularly among young people, and cases of intoxication are sprouting up in pets (Schediwy et al., 2015) as well as in humans, particularly children (Cairns et al., 2018; Garnier et al., 2012). In our study the cat exposed developed, one hour after the ingestion, vomiting and reddening of the oral mucosa, symptoms that are similar to those (hypersalivation, retching/vomiting, hyperemia of the oral mucosa) described in other episodes in literature and that are due to the irritant effects exerted by the liquid content (Schediwy et al., 2015). However, even if the symptoms in case of an accidental acute exposure are reported to be not severe and the outcome favorable, attention should be paid to this emerging product, since the chemiluminescent dyes are usually composed of polycyclic aromatic hydrocarbons (PAH) and phthalates, substances that may pose cancerogenic, genotoxic and reprotoxic risks (Garnier et al., 2012). Other reported causes of intoxication are fireworks/ firecrackers. In our work, a dog developed vomit and a comatose state after the ingestion of firecrackers and in the literature episodes of animal poisoning caused by explosives (mainly due to components such as cyclonite, barium, and chlorate (Gahagan and Wismer, 2018)) are also described (Stanley et al., 2019), sometimes with a fatal outcome (Schediwy et al., 2015). Two enquiries were related to coal tar ingestion by dogs, in one case the animal developed gastrointestinal symptoms with a favorable outcome, whereas the other developed a fatal aspiration pneumonia. Cases of coal tar-related poisoning have been reported in farm as well as in domestic animals (Osweiler, 2013). Symptoms may change in relation to the particular composition of the coal tar but in general acute/chronic hepatic damage and eventually renal tubular damage (due to the presence of phenolic components) are observed (Osweiler, 2013).

5. Conclusion

Animals are greatly affected by environmental toxicants and may play a crucial role as bioindicators. Indeed, toxico-epidemiological studies on animal poisoning can be useful tools to identify, monitor and anticipate environmental, human and animal health hazards, through a one health approach.

The data collected in this work provide a complete and up-to-date overview on toxicant (drugs, household products and pesticides) exposure in animals. The observed trends in the major toxicant categories share similarities with those reported in previous Italian and European studies, but some peculiarities and new tendencies are emerging, stressing the need to perform a continuous surveillance to carry out a proper and comprehensive risk evaluation on environmental pollutants.

Conflict of interest

The authors declare no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Uncited references

Ruiz-Suárez et al. (2015)

CRediT authorship contribution statement

Alessia Bertero: Investigation, Data curation, Writing - original draft. **Marina Rivolta:** Investigation. **Franca Davanzo:** Methodology, Investigation. **Francesca Caloni:** Conceptualization, Investigation, Supervision, Writing - review & editing.

Acknowledgements

The authors are very grateful to Francesca Assisi, Maurizio Bissoli, Rossana Borghini, Valeria Dimasi, Marcello Ferruzzi, Paola Angela Moro, Antonella Pirina, Ilaria Rebutti, Angelo Roberto Travaglia, Fabrizio Maria Sesana, Giovanni Milanesi, Joannhe Georgatos and Paolo Severgnini.

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