Pediatric Exposures to Veterinary Pharmaceuticals

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abstract

OBJECTIVE: To describe the epidemiology of veterinary pharmaceutical-related exposures to children based on calls to a regional poison control center.

METHODS: A retrospective analysis of pediatric (≤19 years of age) exposures to pharmaceutical products intended for animal use, managed by a regional poison control center from 1999 through 2013, was conducted. Case narratives were reviewed and coded for exposure-related circumstances and intended species. Descriptive statistics were generated.

RESULTS: From 1999 through 2013, the Central Ohio Poison Center received 1431 calls that related to a veterinary pharmaceutical exposure for children ≤19 years of age. Most of the pediatric calls (87.6%) involved children ≤5 years of age. Exploratory behavior was the most common exposure-related circumstance (61.4%) and ingestion accounted for the exposure route in 93% of cases. Substances commonly associated with exposures included: veterinary drugs without human equivalent (17.3%), antimicrobial agents (14.8%), and antiparasitics (14.6%). Based on substance and quantity, the majority of exposures (96.9%) were not expected to result in long-term or lasting health effects and were managed at home (94.1%). A total of 80 cases (5.6%) were referred to a health care facility, and 2 cases resulted in a moderate health effect.

CONCLUSIONS: Children ≤5 years of age are most at risk for veterinary pharmaceutical-related exposures. Although most exposures do not result in a serious medical outcome, efforts to increase public awareness, appropriate product dispensing procedures, and attention to home storage practices may reduce the risk of veterinary pharmaceutical exposures to young children.

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DOI: 10.1542/peds.2016-1496

Accepted for publication Dec 1, 2016

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WHAT'S KNOWN ON THIS SUBJECT: With 74.1 million US households owning at least 1 pet and one-half of households with a child ≤19 years of age, unintentional pediatric exposure to pet medication may occur. No previous studies have examined these exposures.

WHAT THIS STUDY ADDS: This study calls attention to the potential risk of pediatric poisonings from veterinary pharmaceutical products and highlights some opportunities for public health officials, pediatricians, pharmacists, and veterinarians to improve education to parents and other childcare providers.

To cite: Tomasi S, Roberts KJ, Stull J, et al. Pediatric Exposures to Veterinary Pharmaceuticals. *Pediatrics.* 2017; 139(3):e20161496

Unintentional poisoning is one of the leading causes of injury and death among children ≤19 years of age.[1–4] Each year in the United States, preventable poisonings in children result in >60 000 emergency department visits and approximately one million calls to poison centers.[5–7] Almost one-half (48%) of the annual calls to poison centers involve children ≤5 years of age.[7,8] Young children are more likely to be exposed due to developmental changes, such as improved mobility, that allow them to explore and interact with their environment.[8–11] Additionally, parents and caretakers may underestimate the child's ability and developmental stage, thus leaving toxic substances within reach of the child.[8]

One of the most common sources for poisonings among children is unintentional exposure to general pharmaceutical products.[8,9] According to the Association of American Poison Control Centers, children <6 years of age account for more than half of all unintentional pharmaceutical exposures.[7,12–23] Previous research has described common risk factors, such as improper storage of medication in handbags, on the counter, or in containers that allow easy access to children.[9,11] Prevention strategies for reducing exposures include use of child-resistant containers, behavior modification through education, and regulations, such as requiring the use of child-resistant containers for topical products.[11]

Although previous veterinary pharmaceutical studies have focused on occupational hazards among veterinary health professionals, none have examined pediatric exposure.[24–28] With nearly 63% of all US households, or 74.1 million, owning at least 1 pet and one-half of households with a child ≤19 years of age, the risk for exposure to pet medication is high.[29] It is common for pets to be prescribed regular veterinary pharmaceutical products as preventives for internal and external parasites or to treat a chronic health condition, such as hypothyroidism or osteoarthritis.[24,30–33] Additionally, acute health conditions for pets may require introducing new medications to a household for a short period of time. Some products used in veterinary practice are specifically developed for veterinary use, whereas others are human pharmaceutical products that have been prescribed for a veterinary patient.[34,35] More recently, antineoplastic drugs, such as mitotane, cyclophosphamide, chlorambucil, and procarbazine as well as other highly toxic substances, have been prescribed more frequently to veterinary patients to treat a wider range of conditions.[36]

Veterinary pharmaceutical products are commonly administered by using techniques that aid in improving the likelihood of the animal receiving the proper dose such as mixing medication with food or compounding oral medication into a topical formula. While these delivery techniques are more convenient for the owner and the pet, previous studies have found they increase the likelihood of human exposure in occupational settings.[36] It can be assumed that these same techniques used in households with young children may also increase the risk of pediatric exposure.

The purpose of this study was to describe the epidemiology of veterinary pharmaceutical exposures among children ≤19 years of age by examining help calls to a single regional poison center in the Midwest.

METHODS

Data from the Central Ohio Poison Center (COPC) were retrospectively analyzed to determine the epidemiologic characteristics and trends of pediatric (≤19 years of age) exposure to veterinary pharmaceuticals from January 1, 1999 through December 31, 2013. The COPC, 1 of 55 poison centers that service the United States and its territories, provides free, confidential poison prevention, assessment, and treatment advice for central and southeastern Ohio residents.[37]

Case Selection Criteria

During the study period (1999–2013), a total of 563 523 calls were placed to the regional poison center. A key word search of calls placed to the COPC was performed by using specific veterinary and animal-related terminology (ie, veterinary, veterinarian, animal, pet, and pocket pet) and specific animal species (ie, dog, canine, pup, cat, kitten, reptile, snake, rabbit, rodent, etc). A total of 5298 potential cases were identified. Case narratives were individually reviewed by 1 author (ST) and confirmed by a second author (KJR) and coded for inclusion criteria, circumstance surrounding the exposure, and animal species, for which the pharmaceutical product was intended. Cases for exposure to pet food, rat poison, animal bite or scratch wounds, and animal ingestion of human medication were excluded. In addition, 15 cases were excluded due to intentional misuse, abuse, or suicide involving a veterinary pharmaceutical product. After reviewing the narratives, 2954 cases met the inclusion criteria for human exposure to a veterinary pharmaceutical product, defined as a product prescribed for use in animals. Cases involving patients ≥20 years of age were excluded (n = 1523). A total of 1431 cases, involving children ≤19 years of age, were retained and included in the analysis. For calls involving exposure to multiple substances, each substance was ranked by the Poison Center Specialist in order of its perceived contribution to the

reported clinical effects. We limited data analysis to the first substance ranked, which was judged to be the primary contributor.

Variables

Circumstances of exposure were coded into 4 categories: (1) mistaken identification (eg, inadvertent use of the veterinary product when intending to use a human medication), (2) exploratory behavior (eg, unintentionally obtained medication, for example, by climbing on the counter or searching through a bag and finding the pet's medication), (3) unintentional delivery (eg, accidental exposure of a veterinary pharmaceutical product while attempting to medicate an animal), and (4) other (including when exposure circumstance was not specified). Cases were coded for animal species for which the prescribed medications were intended (ie, canine, feline, amphibian/reptile, small mammal/pocket pets/ferrets, birds, fish, other, or not specified). Substance description categories were collapsed into 17 pharmaceutical classifications based on type of use, such as topical products or body system treated. For example, antivomiting and antidiarrheal medications were collapsed into the same category as gastrointestinal products. Age groups were existing categories coded by Poison Center Specialists (ie, nurses or pharmacists: ≤5 years, 6–12 years, and 13–19 years of age). Medical outcomes was classified by Poison Control Specialists as no or minor effect ("minimally bothersome, rapidly resolving effects that usually involve the skin or mucous membranes"), not followed (judged as nontoxic exposures [clinical effects not expected] or minimal clinical effects possible [no more than minor effect possible]), unrelated effect, unable to follow (judged as potentially toxic exposure), and moderate effect ("more pronounced or more systemic in nature, treatment usually required, but not life threatening").[7]

Using the National Poison Data Systems' established definitions, other variables included patient's sex, exposure site (eg, residence, other residence, workplace, other), management site (eg, managed on site [patient treated at home or at any other non–health care facility [HCF]), patient referred to a HCF, other/unknown), route of exposure, medical outcome, and level of health care received.

Statistical Analysis and Ethical Considerations

Data were analyzed by using IBM SPSS Statistics version 22 (IBM Corporation, Armonk, NY) software, and descriptive statistics were generated. This study was reviewed and deemed exempt by the Institutional Review Board at Nationwide Children's Hospital (IRB13-00878).

RESULTS

General Characteristics

From January 1, 1999 through December 31, 2013, the COPC received 1431 pediatric (≤19 years of age) calls regarding human exposure to veterinary pharmaceutical products, averaging 95 pediatric exposure calls annually. The lowest number of pediatric veterinary pharmaceutical exposures (n = 56) occurred in 1999 and the highest number of exposures (n = 112) occurred in 2006. Exposed children ranged from 1 month to 19 years of age, with a mean age of 3.2 years (SD, 3.7). Exposure was the highest among children ≤5 years of age, accounting for 87.6% of calls for pediatric exposure to veterinary pharmaceutical products (Table 1). Boys accounted for 51.2% of all cases. The majority of exposures (88.0%) were related to veterinary pharmaceutical products intended for canine use. The most common route of exposure was ingestion (93.0%) followed by ocular (2.3%) and dermal (1.1%). The majority of exposures (96.4%) occurred at home, and 94.1% of all calls were managed on site without referral to an HCF.

Exposure Circumstance

The most common reason for exposure was exploratory behavior (61.4%) followed by unintentional delivery of medication (23.3%) (7.6% of calls did not have sufficient detail to determine the circumstances). Children ≤5 years of age accounted for the majority of exposures resulting from exploratory behavior and unintentional delivery (94.1% and 88.9%, respectively) (Fig 1). Mistaken identification, although less common, occurred among children in all age groups, but especially among children 13 to 19 years old (Fig 1). More than half (56.4%) of cases among children 13 to 19 years were classified as mistaken identification.

Substance Categories and Level of Care

The major substance categories associated with COPC calls included miscellaneous veterinary pharmaceutical products without human equivalent (17.3%), antimicrobial agents (14.8%), antiparasitics (14.6%), and analgesics (11.1%) (Table 2). Over the study period, there were 80 exposure calls (5.6%) that were en route or referred to a HCF, and the majority of these patients (88.8%) were ≤5 years of age and treated/evaluated and released (60.0%). Of the cases en route or referred to a HCF, the most common veterinary pharmaceutical substances associated with the exposure included analgesics (17.5%), antiparasitics (12.5%), miscellaneous veterinary pharmaceuticals (12.5%), and anticonvulsants (10.0%).

In most cases, patients had no or minimally bothersome symptoms

TABLE 1 Characteristics of Calls to the Central Ohio Poison Center for Exposure to Veterinary Pharmaceutical Products Among Children ≤19 Years, 1999 to 2013

Characteristics	No. of Exposure Calls (n = 1431)	Percent
Age, y		
≤5	1254	87.6
6–12	94	6.6
13–19	83	5.8
Sex		
Boy	732	51.2
Girl	699	48.8
Exposure site		
Residence	1379	96.4
Other residence	39	2.7
Workplace	6	0.4
Other (ie, school or public area)	7	0.5
Circumstance		
Exploratory behavior	879	61.4
Unintentional delivery	333	23.3
Mistaken identification	110	7.7
Other/not specified	109	7.6
Route of exposure		
Ingestion	1331	93.0
Ocular	33	2.3
Dermal	16	1.1
Parenteral	10	0.7
Otic	5	0.3
Inhalation	1	0.1
Multiple routes	33	2.3
Other/not specified	2	0.1
Medical outcome		
No or minor effect	702	49.1
Not followed[a]	685	47.9
Unrelated effect	24	1.7
Unable to follow[b]	3	0.2
Moderate effect	2	0.1
Confirmed as no exposure	15	1.0
Management site		
Managed on site (non-HCF)	1347	94.1
Patient referred to HCF	80	5.6
Other/unknown	4	0.3
Level of health care received		
Managed on site	1347	94.1
Treated and released	71	5.0
Patient refused referral/did not arrive at HCF	5	0.3
Patient lost to follow-up	2	0.1
Admitted to a non-critical care unit	1	0.1
Admitted to a critical care unit	1	0.1
Unknown	4	0.3

[a] Not followed, judged as nontoxic exposures (clinical effects not expected) or minimal clinical effects possible (no more than minor effect possible).

[b] Unable to follow, judged as a potentially toxic exposure.

(49.1%) or did not require additional follow-up because the exposure was determined to be nontoxic or only minimal clinical effects were expected (47.9%). Of the cases with no or minor effects (n = 702), 99 (14.1%) had a minor effect. Two cases were recorded as having a moderate medical outcome. The first moderate outcome case involved a 3-year-old child who ingested the pharmaceutical product ivermectin, which is routinely used as an oral preventive for canine heartworm disease and requires a veterinary prescription. The second moderate outcome case involved a 9-month-old child who ingested 100 mg of doxepin, a dibenzoxazepine tricyclic compound generally prescribed for canines with psychogenic dermatoses related to stress or anxiety.[38]

DISCUSSION

During the 15-year study period, there were 1431 calls to the COPC regarding pediatric exposure to a veterinary pharmaceutical product, with an average of 95 calls per year. The majority of cases involved children ≤5 years of age, occurred at home as a result of the child's exploratory behavior, and resulted in no or minor health effects. Most cases were managed at home, and thus required significant health resources from the poison center, such as follow-up calls and time involved researching product safety efficacy.

Similar to previously published toxicology studies that investigated pediatric exposure to human pharmaceuticals, the children in our study experienced few adverse outcomes.[2,4,8,9,39,40] Children are most commonly exposed to pharmaceutical toxic substances as a result of their exploration of their environment without the intention of causing self-inflicted harm; therefore, they are not typically exposed to dose ranges that could lead to moderate or major health effects. However, some prescriptions, both human and veterinary, could be highly dangerous even at low dosages, especially for small children.

Although pediatric exposure to veterinary pharmaceuticals may exhibit many of the same characteristics of pediatric exposure to human pharmaceuticals and other toxic substances, this study highlights some unique aspects associated with veterinary pharmaceutical product exposures. Knowledge of these unique circumstances could help health professionals expand preventive educational materials on toxic substances as well as more effectively organize

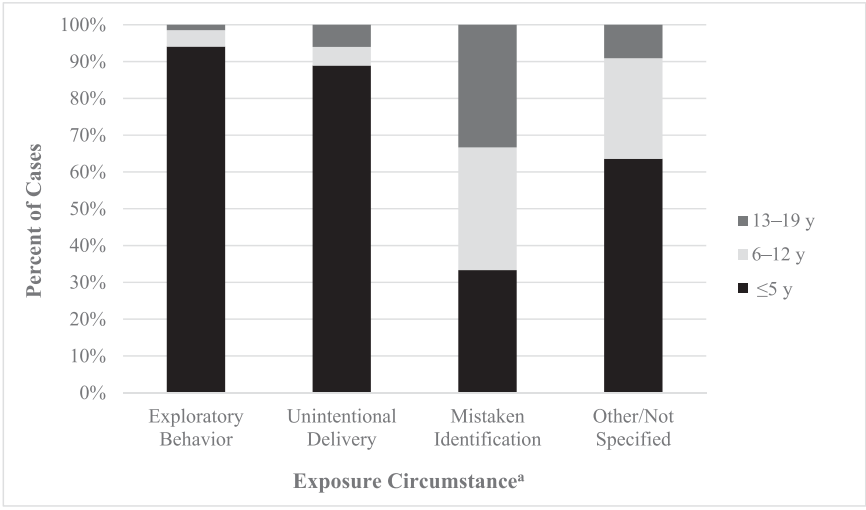

FIGURE 1
Percentage of each age group exposed to veterinary pharmaceutical products by exposure circumstance. [a] n = 1333 due to exclusion of 98 cases where circumstances were not specified.

TABLE 2 Substance Categories Recorded During Calls to the Central Ohio Poison Center for Exposure to Veterinary Pharmaceutical Products Among Children ≤ 19 Years, 1999 to 2013

Substance Category	No. of Exposure Calls With Substance Category Coded (n = 1402)	Percent
Veterinary drugs without human equivalent[a]	242	17.3
Antimicrobials	207	14.8
Antiparasitics	205	14.6
Analgesics	155	11.1
Hormones/hormone antagonists	123	8.8
Anticonvulsants	71	5.1
Dietary/herbal/homeopathic supplements	67	4.8
Topical medications for ears, eyes, and skin	65	4.6
Corticosteroids	64	4.6
Antihistamines	53	3.8
Antivomiting/antidiarrheal drugs	36	2.6
Cardiovascular/respiratory/urinary/renal	32	2.3
Other[b]	82	5.8

[a] Includes pharmaceutical products, such as flea and heartworm medication, or other pharmaceutical products that are label-approved for veterinary use but have no label-approved human equivalents.
[b] Includes vaccines, medicated shampoos, chemotherapeutic, and nonpharmaceutical products.

and manage future cases. For example, exploratory behavior is still an important circumstance that increases the risk of pediatric exposure, and therefore, veterinary pharmaceuticals should be stored with the same recommendations as human pharmaceuticals.[41] However, unintentional delivery of medication is a common circumstance of veterinary pharmaceutical exposures that is not commonly associated with other pediatric exposures. Approximately one-fourth of the children in this study were exposed to a veterinary pharmaceutical during the process of attempting to administer the medication to animals. Common scenarios stated in the case narratives involved the pet spitting out the medication and the child retrieving it from the floor. Other narratives described that pet owners would mix the veterinary medications in food to encourage ingestion by the animal. Although this is a common practice recommended by veterinary health professionals for easier administration of veterinary medication to animals, it may also increase the risk of pediatric exposure because children can access the medication, especially if the animal does not ingest the food immediately. Providing guidance for mixing medication with food could include keeping it out of the child's reach until ready to administer it to the pet and instructing owners to make sure that the pet finishes all the food before allowing the child to have contact with the pet or the food. For topical medications, health professionals could suggest the child not be present when administering medications to avoid accidental exposure. One alternative option could be to deliver pet medications after the child has gone to bed. Parents should also be instructed to give topical products time to dry before permitting the child to interact with the pet.

Mistaken identification was an important circumstance leading to exposure to veterinary pharmaceutical products, particularly in the 13- to 19-year-old age group. Older children may be responsible for administering their own medications as well as assisting with the family pet's medications. These products can resemble human pharmaceutical products or be stored in similar child-resistant containers, leading to a simple confusion between products. Therefore, storing veterinary medications in a separate location from human medications may reduce the number of unintentional exposures due to mistaken identification. Users should also keep all products, including human and veterinary pharmaceutical products, in their original, child-resistant containers with the label attached.

Since the passing of the 1970 Poison Prevention Package Act (PPPA), US human pharmaceutical products are required to be dispensed in child-resistant packaging to reduce the chance of pediatric exposure and decrease the volume of exposure to the toxic substance.[5] The PPPA

regulates special child-resistant packaging for any drug for human use that is intended for oral administration and is required by federal law to be prescribed by a licensed practitioner.[4,5,34,40] Other than animal products that contain iron, the PPPA states no regulations over veterinary pharmaceutical products for oral administration.[5,34,42] However, most states, including Ohio, have state laws that regulate the dispensing of veterinary pharmaceutical products.[34] In Ohio, drugs that are required to be prescribed by a licensed health professional must be labeled and packaged in accordance with state and federal drug laws. Although the federal child-resistant packaging laws specifically refer to human oral pharmaceutical products, under Ohio's law, veterinarians who prescribe and dispense medications for their patients are required to obtain a Terminal Distributor of Dangerous Drugs license.[43] This license classifies veterinary pharmaceutical products as dangerous drugs, which then indicates oral veterinary products are to follow the same packaging, labeling, and record keeping regulations as human oral pharmaceutical products.[44] On a national level, the use of child-resistant packaging for all veterinary pharmaceutical products dispensed by veterinarians for at-home use is also recommended by the American Veterinary Medical Association's Council on Biological and Therapeutic Agents.[45]

There are limited data on veterinary compliance with child-resistant packaging regulations. Although veterinarians are encouraged to dispense pharmaceutical products in child-resistant containers, actual compliance is unknown. There are numerous examples of products that may not be routinely dispensed in child-resistant containers, including: single doses of flea, tick, and heartworm prevention, injectable formulations of buprenorphine for feline mucosal administration, topical creams and ear medications, and liquid intestinal deworming medications. These medications are generally loaded into an oral syringe with a slip-on cap and placed in a plastic, sealable bag or are dispensed as a single blister pack dose in a plastic bag, both with the label on the outside of the bag. This type of packaging could easily lead to separation of the pharmaceutical product from the prescription label as well as allow easy access for a young child.

This study has limitations. Data were from a single poison center, which receives calls and handles cases from a limited geographical region in a Midwestern state. Obtaining data from a single regional poison center limits the ability to generalize the results for other regions of the United States and determine the true impact of veterinary pharmaceutical products in pediatric poisonings. Another potential limitation was the inconsistency with recording substance classifications. For example, 1 case with a moderate outcome listed the substance category as a nonpharmaceutical product when the narrative statement recorded that the child had ingested ivermectin in the form of canine heartworm prevention. Other examples include the inconsistency seen with recording other veterinary antiparasitic products, such as piperazine. Some of the poison control specialists coded these substances as antiparasitics, whereas others recorded the same pharmaceutical product in the miscellaneous veterinary drug without human equivalent category, demonstrating that poison control specialists are sometimes unfamiliar with some veterinary pharmaceutical product categories and their uses. Developing an inclusive veterinary pharmaceutical product guide for poison control specialists could aid with consistent coding of veterinary pharmaceutical substances and expedite the search for specific cases in future epidemiology studies. Finally, this study only reviewed data that were voluntarily provided to the COPC. Other pediatric veterinary pharmaceutical exposures might have sought medical care at other health care facilities or private physician offices without reporting the data to the COPC. Alternatively, some cases may have decided not to seek any form of medical advice or treatment. Therefore, this study may underestimate the impact of pediatric exposure to veterinary pharmaceutical products. Despite these limitations, this study is the first to our knowledge to examine pediatric exposure to veterinary pharmaceutical products.

CONCLUSIONS

To our knowledge, this is the first study to describe the epidemiologic characteristics of veterinary pharmaceutical products among children ≤5 years of age. Although the majority of exposures resulted in no or a minor health effects, efforts to prevent these types of injuries are still needed. Despite current pharmaceutical prevention efforts and packing regulations, parents and caregivers may not recognize the potential risk for veterinary pharmaceutical product exposures in their home. Prevention and education efforts should focus on appropriate product dispensing, home storage practices, and proper medication delivery to help reduce the risk of veterinary pharmaceutical exposure to young children.

ABBREVIATIONS

COPC: Central Ohio Poison Center
HCF: health care facility
PPA: Poison Prevention Package Act

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest relevant to this article to disclose.

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