J Antimicrob Chemother 2011; **66**: 920–927
doi:10.1093/jac/dkq543 Advance Access publication 2 February 2011

Journal of Antimicrobial Chemotherapy

Use of antimicrobials in companion animal practice: a retrospective study in a veterinary teaching hospital in Italy

Martina Escher[1]*, Michele Vanni[2], Luigi Intorre[2], Alfredo Caprioli[1], Rosalba Tognetti[2] and Gaia Scavia[1]

[1]Dipartimento di Sanità Pubblica Veterinaria e Sicurezza Alimentare, Istituto Superiore di Sanità, Rome, Italy; [2]Department of Veterinary Clinics, University of Pisa, Pisa, Italy

*Corresponding author. Present address: Cire Antille Guyane, Institut de Veille Sanitaire, ARS de Martinique, Centre d'affaires AGORA, ZAC de l'Etang Z'Abricot - Pointe des Grives, BP 656, 97261 Fort-de-France Cedex. Tel: +00596 (0)5 96 39 42 42; Fax: +00596 (0)5 96 39 44 14; E-mail: martina.escher@gmail.com

Received 16 September 2010; returned 26 October 2010; revised 22 December 2010; accepted 23 December 2010

Objectives: To describe the use of antimicrobials in a veterinary teaching hospital for companion animals in Italy, with particular regard to the agreement with recommendations of prudent use

Methods: The study was conducted with a retrospective, cross-sectional design. The population under investigation included 18 905 cats and dogs that were referred to the hospital between 2000 and 2007. Two different samples of the clinical paper forms were randomly selected to estimate the prevalence of animals receiving an antimicrobial prescription and to describe the pattern of antimicrobials used in relation to the condition being treated. The proportion of antimicrobials prescribed accomplishing recommendations of prudent use was also estimated, as well as the level of agreement with specific, diagnosis-based guidelines for antimicrobial use.

Results: Broad-spectrum antimicrobials, including penicillins with β-lactamase inhibitors, first-generation cephalosporins and fluoroquinolones, were the most frequently prescribed compounds. Antimicrobials prescribed with the support of microbiological analyses and susceptibility testing were less than 5%. Among the recommendation of prudent use, the availability of information from laboratory testing had the poorest degree of agreement, while the other evaluated items were accomplished in most of the cases.

Conclusions: Our results highlight the need to improve the procedures of antimicrobial prescription in the study setting. This can be achieved by supporting the guidance for antimicrobial use at the local level, with the adoption of specific guidelines, and at the national level with a further implementation of the policies of prudent prescriptions.

Keywords: antimicrobial resistance, prudent use, animal health, veterinary medicine

Introduction

Over the last several decades antimicrobial resistance has been considered one of the most relevant issues in public health due to its dramatic increase worldwide in both pathogenic and commensal bacteria. The relatively scarce availability in recent years of new antimicrobial drugs has also contributed to increase the concern.[1] The adoption of common and harmonized actions between countries and between human and animal health has been claimed, since 1998, as the most effective approach in facing this global problem.[2] In particular, the adoption of policies of prudent use such as those recommended by the European Union (EU) in human medicine,[3] as well as regulatory actions, including limiting the use of certain antimicrobials in food animals, have been seen as effective tools to preserve the efficacy of antimicrobials.

The threat for human health posed by antimicrobial use in animals arises from the risk of transferring resistant bacteria or resistance genetic determinants to humans.[4] The role of companion animals as potential reservoirs of resistant and multiresistant pathogens for humans has recently received increasing attention.[4–7] Companion animals live in close contact with humans and share with them the environment and exposures to many sources of pathogens, thus making easy the exchange of resistant bacteria.[4–6] Moreover, the uses of antimicrobials in companion animals and human beings are essentially identical,[7] and antimicrobial preparations licensed for human use as well as compounds of primary importance in the treatment of human infection are also utilized in dogs and cats.[5]

The prudent use of antimicrobials has been defined as the process of reducing the development and spread of antimicrobial resistance through the optimal selection of drugs, dosage and duration of treatment.[8] In companion animals, general recommendations of prudent use issued by international scientific bodies have been only partially implemented in specific regulatory acts, while different guidelines for prudent use in dogs and cats are available. Most of these are aimed at addressing educational purposes,[9–13] while others are more practically applicable in field conditions, guiding veterinarians in the treatment of specific conditions in pets.[14–16] In Italy, no specific guidelines for prudent use in companion animals are available and professional guidance for the responsible use of antimicrobials relies on the best practices addressed by general recommendations of prudent use issued by the Ministry of Health.[17] Antimicrobials are prescription-only drugs,[18] and although the regulations in force in both veterinary and human medicine assign the responsibility of the use of antimicrobials to prescribing veterinarians or physicians, the general regulatory framework of prudent use is low and no coordinated national action plans have been implemented in recent years in veterinary or human medicine.

Herein we present the results of a retrospective survey on the use of antimicrobials in dogs and cats in a university teaching hospital. The aim of the survey was to describe the pattern of use of antimicrobials with regard to the clinical condition to treat and evaluate how recommendations of prudent use have been applied.

Methods

Description of the hospital

The University of Pisa (central Italy) hosts one of the 14 schools of Veterinary Medicine present in Italy (5 in the north, 3 in the centre and 6 in the south, including the islands of Sicily and Sardinia), as well as a 3 year postgraduate school in small animal pathology and clinics. The mean annual number of students who graduate in the school in Pisa is 76, representing 6% of all new graduated veterinarians in Italy.[19]

The school is organized into three departments and includes a veterinary teaching hospital for companion animals. Activities carried out in the hospital include all diagnostic, clinical and preventive practices, including veterinary primary healthcare activities. Twelve practitioners usually participate in the clinical activities, which also involve the students, who compulsorily perform a training period of 6 months in the hospital before their graduation. The catchment area of the hospital includes mainly central Italy, and the hospital serves as the reference point for other practitioners working nearby. During the study period, a mean of 2350 dogs and cats per year were newly admitted to the hospital.

Study design, population under study and sampling

The study was conducted with a retrospective, cross-sectional design. The population under study included 18 905 clinical forms of cats and dogs that were referred to the hospital between 2000 and 2007.

All the data used in the study were obtained by reviewing the individual standardized clinical paper charts. These were filled in at the time of the first admittance of the animal to the hospital and included follow-up information and the results of any other examinations performed in the hospital. Each clinical chart was progressively identified by a unique identification code (year–number); the complete list was available in an electronic archive. In our study, only the information relative to the examination performed at the first admittance to the hospital was considered.

Two different samples were randomly selected from the population using randomly generated numbers: one for the estimation of the proportion of animals with an antimicrobial prescription (prevalence of prescription) and the other to more precisely describe the pattern of antimicrobials used and to evaluate how they had been prescribed according to the prudent use recommendations.

An antimicrobial prescription was defined as a unique prescription of one or more antimicrobial medicinal products issued on the same day by the veterinarian to treat the condition specified by the diagnosis.

To estimate the prevalence of prescriptions, a sample not smaller than 897 clinical forms was calculated (expected prevalence, 30%; maximum allowable error, 3%; confidence level, 95%).

The pattern of use of antimicrobials and how they had been prescribed with respect to the prudent use recommendations were studied only for the antimicrobials for systemic administration, with the exclusion of those prescribed in relation to a surgical procedure. The latter, mainly prescribed for prophylactic purposes, were excluded from the analysis because they were considered poorly informative with respect to the criteria adopted in our study for the evaluation of prudent use. Evaluation of the appropriateness focused, particularly, on drugs prescribed to treat gastroenteritis, urinary tract infections (UTIs), respiratory tract infections (RTIs) and pyoderma. The sample size was, therefore, calculated starting from the minimum required number of clinical charts with the prescription of systemic antimicrobials for the treatment of gastroenteritis, UTIs, RTIs and pyoderma. Because these charts accounted for 4.6% of the total clinical paper charts, as estimated in the first sample, the number needed for this purpose was 276 (expected proportion of appropriate use, 50%; maximum allowable error, 5%; confidence level, 95%), leading to a total sample size of 5804 charts. This would have yielded an expected number of 871 clinical charts with a prescription of systemic antimicrobials for the treatment of any condition, based on the estimate obtained in the first sample (15%).

Antimicrobials were described according to the class, the route of administration and the condition treated. They were categorized based on the anatomical therapeutic chemical (ATC) classification system,[20] implemented in 1976 by the WHO, or the ATC classification system for veterinary medicinal products,[21] and were also ranked by importance in human medicine according to the FAO/WHO/OIE categorization of Critically Important Antimicrobials for Human Medicine.[22]

Compliance with prudent use recommendations was evaluated for each antimicrobial using the items included in the guidelines issued by the Federation of Veterinarians of Europe.[9] These were availability of a diagnosis; availability of microbiological and susceptibility testing; use of a product approved for the species; respect of the dosage regimen and duration of treatment; avoidance of the empirical combination of two or more antimicrobials; and limitation, as much as possible, of the use of broad-spectrum antimicrobials. In particular, for evaluation of the intake daily dose and the duration of treatment, the criteria were considered satisfied if the intake daily dose respected the labelled dose range recommended by the manufacturer (±20%) in the package leaflet and if the duration of treatment was longer than 5 days. The intake daily dose was computed in mg/kg by multiplying the quantity of active compound prescribed times the daily number of administrations, divided by the weight of the animal.

Since the use of antimicrobials should not be evaluated without taking into account the specific condition being treated, the pharmacological properties of the antimicrobials and the characteristics of the animals, the diagnosis-based guidelines for antimicrobial use in companion animals, published by Guardabassi *et al.*[15] in 2008, were used to evaluate the appropriateness of the compounds prescribed for the treatment of gastroenteritis, UTIs, RTIs and pyoderma. Antimicrobials were, therefore, categorized as first choice (could be used empirically, without the indication of a microbiological examination or susceptibility testing), second choice (could be used based on a microbiological examination) and last resort (could be used based on susceptibility testing and only if no other antimicrobials of the first or second choice could be used). The use of an antimicrobial was defined as appropriate whenever all the specific requirements for the class of choice were met and only if the antimicrobial was not prescribed in an empirical combination with other antimicrobials. The use of antimicrobials under any other conditions was considered inappropriate.

Data management and statistical analysis

Data entry and data management were carried out using EpiInfo 3.3.2 (CDC, Atlanta, GA, USA). The dataset was validated by checking the values for consistency, plausibility and coherence. Incorrect values were classified as 'missing'.

Categorical variables were described using counts and percentages with the relative 95% confidence interval (95% CI). Differences in proportions were assessed for statistical significance by the χ^2 or Fisher's exact test, when needed. The existence of trends in the use of the antimicrobial classes over the study period was tested by the Cochrane–Armitage test for linear trend against the null hypothesis that no association between proportions of antimicrobials used and years exists. P values <0.05 were considered statistical significant. All the statistical analyses were performed using SAS 9.1 (SAS Institute Inc., Cary, NC, USA).

Results

Prevalence of antimicrobial prescriptions

The prevalence of antimicrobial prescriptions, as estimated from the 854 sampled clinical paper charts eventually collected (688 concerning dogs and 166 cats), was 30.6% (95% CI 27.5%–33.8%). A significantly higher prevalence of prescriptions was found in cats (44.0%, 95% CI 36.3%–51.9%) compared with dogs (27.3%, 95% CI 24.0%–30.8%). Two hundred and ninety-three antimicrobials were recorded from the 261 animals with a prescription. Thirty-one prescriptions (11.9%) included only topical drugs, 222 prescriptions (85.1%) included only drugs to be administered systemically and 8 prescriptions (3.1%) included both. Animals receiving an antimicrobial prescription in relation to a surgical procedure were 122 (46.7% of all the prescriptions). These accounted for the 86.2% of total surgical cases recorded in the sample. The most frequently prescribed drugs in surgical patients were amoxicillin/clavulanate (n=89) and the association benzylpenicillin/streptomycin (n=15).

Pattern of prescriptions of systemic antimicrobials not related to surgical procedures

One thousand and two clinical paper charts (747 concerning dogs and 255 cats) with a prescription of at least a systemic antimicrobial not in relation to a surgical procedure were retrieved from the 5804 clinical forms sampled to study the pattern of use of antimicrobials. The total number of antimicrobials included in the prescriptions was 1071. For 68 animals, a prescription of two or more antimicrobials in an empirical combination was found.

Thirty-nine different antimicrobials, belonging to 12 pharmacological subgroups, were recorded. Three of these subgroups, in particular, included the majority of the prescribed antimicrobials: penicillins (n=327); cephalosporins (n=258); and quinolones (n=219). Among the penicillins, penicillins with β-lactamase inhibitors (n=287) prevailed over extended-spectrum penicillins (n=39). Among cephalosporins, the first-generation compounds (n=219) were prescribed most frequently, while fluoroquinolones (n=218) accounted for almost all the quinolones subgroup.

No significant time trends in the usage of the antimicrobial pharmacological subgroups were observed over the study period (Table 1), except for the rarely prescribed intestinal anti-infectives group.

Similarly, no significant differences in the use of the pharmacological subgroups were observed between the two animal species, with the exception of the first-generation cephalosporins, scarcely employed in cats and frequently used in dogs, and the spiramycin/metronidazole combination, more frequently employed in cats (Figure 1).

As far as the clinical conditions were concerned, most antimicrobials were prescribed to treat infections affecting the skin (23.2%) and the gastrointestinal tract (19.0%), followed by genitourinary (14.0%) and respiratory (13.6%) tract diseases. The distribution of antimicrobial compounds used for the treatment of conditions affecting the different systems is reported in Table 2.

Penicillins were prescribed in similar proportions (over the 20% of cases) for the treatment of all the conditions, but did not seem to represent the elective compounds for the treatment of any of them. Conversely, the treatment of skin and genitourinary tract infections was performed using elective compounds; first-generation cephalosporins for the treatment of skin infections and fluoroquinolones for the genitourinary infections. The treatment of gastrointestinal tract infections involved 14 pharmaceutical classes, with the three most frequently used antimicrobials (penicillins with β-lactamase inhibitors, spiramycin/metronidazole and fluoroquinolones) not exceeding, overall, the 59% of all compounds used to treat these conditions. It is remarkable that a non-negligible proportion of the antimicrobials used for the treatment of RTIs (9.7%) were third-generation cephalosporins, an antimicrobial group considered of highly critical importance in human medicine. In this respect, of the 1060 antimicrobials that could be classified according to the FAO/WHO/OIE classification,[22] 689 and 340 were critically important and highly important antimicrobials, respectively. Among the critically important group, 38.3% included compounds of the highest priority, namely fluoroquinolones (n=218), third-generation cephalosporins (n=36) and macrolides (n=9). The use of critically important antimicrobials predominated in all the conditions, except in those affecting the skin and the eye (Figure 2).

Information on the route of administration, available for 802 antimicrobials, showed that the use of products for oral administration (n=690) prevailed over those for parenteral administration (n=112), and accounted for 90% of the total antimicrobials prescribed in dogs and 73% of the total antimicrobials prescribed in cats ($P<0.001$).

Table 1. Frequency distribution of systemic antimicrobials prescribed in the period 2000–07 to treat dogs and cats not in relation to a surgical procedure, by pharmacological class (ATC classification) and year (*n*=1063); antimicrobial prescriptions impossible to classify were not included (*n*=8)

	Antimicrobials prescribed by year, *n* (%)								
Class of antimicrobials	2000	2001	2002	2003	2004	2005	2006	2007	*P* value[a]
Penicillins/β-lactamase inhibitors	13 (18.8)	35 (26.1)	40 (25.5)	44 (29.1)	37 (26.6)	55 (33.1)	33 (24.6)	30 (26.5)	0.45
Fluoroquinolones	15 (21.7)	30 (22.4)	40 (25.5)	26 (17.2)	25 (18).0	36 (21.7)	28 (20.9)	18 (15.9)	0.32
First-generation cephalosporins	16 (23.2)	24 (17.9)	30 (19.1)	34 (22.5)	34 (24.5)	28 (16.9)	29 (21.6)	22 (19.5)	0.94
Tetracyclines	5 (7.2)	6 (4.5)	16 (10.2)	10 (6.6)	11 (7.9)	15 (9.0)	9 (6.7)	12 (10.6)	0.36
Spiramycin/metronidazole	4 (5.8)	11 (8.2)	13 (8.3)	8 (5.3)	9 (6.5)	13 (7.8)	7 (5.2)	11 (9.7)	0.86
Extended-spectrum penicillins	3 (4.3)	5 (3.7)	6 (3.8)	6 (4.0)	4 (2.9)	8 (4.8)	7 (5.2)		0.48
Third-generation cephalosporins	3 (4.3)	5 (3.7)	5 (3.2)	3 (2.0)	5 (3.6)	2 (1.2)	4 (3.0)	9 (8.0)	0.46
Nitroimidazole derivatives	1 (1.4)	2 (1.5)	4 (2.5)	5 (3.3)	3 (2.2)		5 (3.7)	4 (3.5)	0.48
Sulphonamides	2 (2.9)	3 (2.2)	1 (0.6)	7 (4.6)	1 (0.7)	1 (0.6)	3 (2.2)	2 (1.8)	0.52
Lincosamides	1 (1.4)	3 (2.2)	1 (0.6)	2 (1.3)	1 (0.7)	3 (1.8)	2 (1.5)		0.47
Benzylpenicillin/streptomycin	2 (2.9)	2 (1.5)			3 (2.2)	3 (1.8)	3 (2.2)		0.95
Macrolides		2 (1.5)		3 (2.0)	3 (2.2)	1 (0.6)		3 (2.7)	0.48
Intestinal anti-infectives	3 (4.3)	4 (3.0)	1 (0.6)	1 (0.7)				1 (0.9)	<0.01
Aminoglycosides		1 (0.7)			2 (1.4)		4 (3.0)	1 (0.9)	0.07
Miscellaneous[b]	1 (1.4)	1 (0.7)		2 (1.3)	1 (0.7)	1 (0.6)			0.25

[a]Cochrane–Armitage test for linear trend.
[b]Includes second-generation cephalosporins, systemic antimicrobials for the treatment of tuberculosis (rifamycin), quinolones other than fluoroquinolones (flumequine), amphotericin B and β-lactamase-sensitive penicillins.

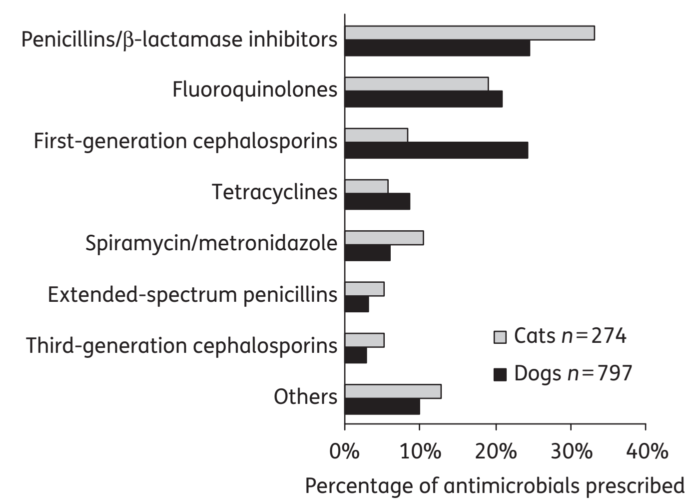

Figure 1. Frequency distribution (%) of systemic antimicrobials prescribed in dogs and cats in the period 2000–07, not in relation to a surgical procedure, by animal species and pharmacological class (ATC) classification.

Compliance with prudent use principles

The compliance of the prescriptions with the prudent use recommendations was evaluated for each antimicrobial and the results are reported in Table 3.

Information on the diagnosis was available for almost all the antimicrobials, while a high proportion of compounds were prescribed without the support of microbiological analyses or susceptibility tests. Off-label use, with regard to the species, was reported for a relevant proportion of antimicrobials (23.8%). Almost all of them were products labelled for human use (*n*=234), including first- and second-generation cephalosporins (*n*=117), third-generation cephalosporins (*n*=32) and nitroimidazole derivatives (*n*=24).

The daily intake dose could be calculated for only 311 of the 1071 antimicrobials (29.0%) due to a lack of information on the weight of the animal (*n*=428), strength of the drug (*n*=461), number of daily administrations (*n*=471) and dosage (*n*=450). Antimicrobials prescribed in accordance with the dosage indicated by the manufacturer (±20%) were 166 (53.4%).

Information about the duration of the treatment, available for only 398 antimicrobials, showed that the minimum length of 5 days of treatment was respected in most cases (*n*=386). Broad-spectrum antimicrobials were 996, while those with a restricted or intermediate spectrum of activity accounted for 69 and 1, respectively.

Use of antimicrobials in UTIs, gastroenteritis, pyoderma and RTIs

A total of 269 antimicrobials were prescribed for the treatment of UTIs, gastroenteritis, pyoderma and RTIs. Of these, 76 (28.2%) were classified as first choice, 33 (12.2%) as second choice and 39 (14.5%) as last resort (Table 4). In 121 cases (45.0%) the prescribed antimicrobial was not listed in any of the classes of choice provided by the guidelines for the given species and for the specific condition to treat. Only one and three of the second-choice and last-resort antimicrobials, respectively, were supported by laboratory investigations.

Table 2. Frequency distribution of systemic antimicrobials prescribed in the period 2000–07 to treat dogs and cats not in relation to a surgical procedure, by pharmacological class (ATC classification) and system involved by the condition treated ($n=1007$); antimicrobials that could not be classified and those lacking information on diagnosis were not included ($n=64$)

	Antimicrobials prescribed by condition treated (anatomical system mainly involved), *n* (%)								
Class of antimicrobials	skin ($n=248$)	digestive system ($n=203$)	genitourinary system ($n=150$)	respiratory system ($n=145$)	musculo-skeletal system ($n=52$)	eye ($n=39$)	ear ($n=28$)	other[a] ($n=142$)	all the conditions ($n=1007$)
Penicillins/β-lactamase inhibitors	56 (22.6)	52 (25.6)	33 (22.0)	48 (33.1)	19 (36.5)	9 (23.1)	8 (28.6)	48 (33.8)	273 (27.1)
First-generation cephalosporins	137 (55.2)	7 (3.4)	7 (4.7)	24 (16.6)	10 (19.2)	6 (15.4)	3 (10.7)	17 (12.0)	211 (21.0)
Fluoroquinolones	28 (11.3)	22 (10.8)	94 (62.7)	26 (17.9)	8 (15.4)	1 (2.6)	11 (39.3)	18 (12.7)	208 (20.7)
Tetracyclines	1 (0.4)	12 (5.9)	4 (2.7)	3 (2.1)	5 (9.6)	16 (41.0)	0	32 (22.5)	73 (7.2)
Spiramycin/metronidazole	6 (2.4)	46 (22.7)	1 (0.7)	3 (2.1)	2 (3.8)	2 (5.1)	4 (14.3)	7 (4.9)	71 (7.1)
Extended-spectrum penicillins	6 (2.4)	9 (4.4)	3 (2.0)	10 (6.9)	1 (1.9)	1 (2.6)	1 (3.6)	4 (2.8)	35 (3.5)
Third-generation cephalosporins	5 (2.0)	5 (2.5)	2 (1.3)	14 (9.7)	3 (5.8)	1 (2.6)		3 (2.1)	33 (3.3)
Nitroimidazole derivatives	1 (0.4)	15 (7.4)	1 (0.7)	2 (1.4)				5 (3.5)	24 (2.4)
Sulphonamides		11 (5.4)	3 (2.0)	3 (2.1)			1 (3.6)	1 (0.7)	19 (1.9)
Lincosamides	3 (1.2)	1 (0.5)	1 (0.7)		2 (3.8)	2 (5.1)		4 (2.8)	13 (1.3)
Macrolides	1 (0.4)	6 (3.0)		5 (3.4)					12 (1.2)
Benzylpenicillin/streptomycin	2 (0.8)	3 (1.5)		1 (0.7)	2 (3.8)	1 (2.6)		2 (1.4)	11 (1.1)
Intestinal anti-infectives	1 (0.4)	9 (4.4)							10 (1.0)
Aminoglycosides		5 (2.5)	1 (0.7)	1 (0.7)				1 (0.7)	8 (0.8)
Miscellaneous[b]	1 (0.4)			5 (3.4)					6 (0.6)

[a]Includes infections of the lymphatic system, CNS and cardiovascular system, systemic infections, mastitis and tick-borne bacterial infections.
[b]Includes second-generation cephalosporins, systemic antimicrobials for the treatment of tuberculosis (rifamycin), quinolones other than fluoroquinolones (flumequine), amphotericin B and β-lactamase-sensitive penicillins.

The overall number of antimicrobials prescribed in agreement with the guidelines, with respect to both the condition to treat and the antimicrobial used, were 80 (27.0%). Pyoderma was the group with the largest proportion of antimicrobials accomplishing the indications of the guidelines (74.6%), followed by UTIs (36.1%), RTIs (10.5%) and gastroenteritis (4.3%).

Discussion

This is the first study conducted in Italy aimed at investigating the use of antimicrobials in companion animals under field conditions and with particular regard to prudent use recommendations. The availability of similar studies in the literature is limited because either the public health relevance of the antimicrobial resistance in companion animals is often neglected or proper information enabling a detailed description of the use of antimicrobials in practice conditions is often missing.

Our study was performed in a university clinical setting, not only because of the easy availability of clinical information, but also because we considered it important to evaluate the prescription behaviours of those practitioners who are contributing to the prescription behaviours of future practitioners. On the other hand, focusing on such a specific setting implies important constraints in terms of the representativeness of the study, limiting the possibility of providing a broader picture of antimicrobial prescription practices in companion animals and in Italy. Whether our results reflect the behaviours of companion animal practitioners in prescribing antimicrobials, at the local or national level, cannot be assessed due to the lack of availability of other information sources, such as quantitative and qualitative data on antimicrobials consumption.

However, our findings are in agreement with the results of a nationwide telephone sampling survey performed in Italy in 2006, with the aim to describe, on a self-reported basis, the behaviours of small animal practitioners in prescribing antimicrobials.[23] In particular, both studies highlighted the frequent attitude of veterinarians in using antimicrobials belonging to the last-generation classes as first-line antimicrobials, in contrast with the indications of all the available guidelines. From a

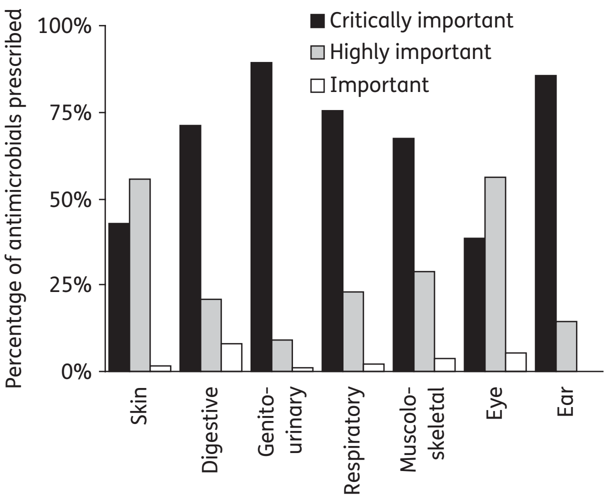

Figure 2. Frequency distribution of the antimicrobials prescribed according to the FAO/WHO/OIE categorization of Critically Important Antimicrobials for Human Medicine,[22] according to the condition treated (anatomical system mainly involved) (*n*=887).

Table 3. Frequency distribution of the antimicrobials prescribed in the period 2000–07 to treat dogs and cats by compliance to general recommendations of antimicrobial prudent use (*n*=1071)

Prudent use recommendation	Antimicrobials evaluable, *n*	Antimicrobials in accordance, *n* (%)
Availability of:		
diagnosis	1071	1014 (94.7)
microbiological examination	1071	51 (4.8)
antimicrobial susceptibility testing	1071	22 (2.1)
Agreement with:		
use of a product approved for the animal species	1049	799 (76.2)
respect of the dose range	311	166 (53.4)
respect of the minimum duration of treatment	394	386 (98.0)
not in an empirical combination	1071	934 (87.2)

public health perspective, this is a critical behaviour, potentially enabling the emergence and transmission to humans of bacterial clones resistant to the antimicrobials that are considered of greatest importance in human medicine.

In our study, critically important antimicrobials were the most frequently prescribed drugs. It is necessary to highlight, however, that this class includes antimicrobials very commonly used in companion animal practice, such as penicillins or first-generation cephalosporins, which are frequently indicated by prescription guidelines for companion animals as first-line antimicrobials.[8,15,16] Penicillins and first-generation cephalosporins were prescribed in proportions similar to those reported in other countries.[8,24–26] Conversely, the use of fluoroquinolones was much more common than in any other study available in the literature, accounting for 20.4% of total prescriptions. In two different studies carried out in Finland,[24,25] fluoroquinolones represented 3% and 5% of the antimicrobials prescribed in dogs and cats, respectively. These antimicrobials represented 4.8% of the compounds used in both these species in a veterinary hospital in Canada,[8] and 1.6% and 3.2% of the antimicrobials administered to dogs and cats, respectively, in a recent survey carried out in Switzerland.[26] Concerns about the extensive use of fluoroquinolones and other critically important drugs, such as third-generation cephalosporins, in companion animals were also raised by Heuer *et al.*,[27] who underlined the lack of proper policies for antimicrobial use in companion animals compared with food-producing animals.

In the present study, the frequent use of last-resort and/or broad-spectrum antimicrobials was associated with a very low rate of laboratory testing support. As an example, prescriptions of fluoroquinolones were guided by susceptibility testing in only 3.7% of cases, a proportion not significantly higher compared with the other antimicrobial groups. Similarly, the recommendation to prescribe last-resort antimicrobials based on susceptibility testing was followed in a very low proportion of cases with pyoderma, UTIs, gastroenteritis and RTIs. Similar results had already been reported in Italy by Sala *et al.*,[23] who found that the attitude of practitioners in not performing susceptibility testing was associated with a high use of last-resort antimicrobials. It is unclear whether the availability of such molecules, whose efficacy is expected *a priori* to be the highest, discourages practitioners from performing laboratory testing, or rather, the lack of information on the susceptibility to antimicrobials drives practitioners to consider the use of such compounds the best therapeutic option.

Table 4. Frequency distribution of systemic antimicrobials prescribed in the period 2000–07 to treat gastroenteritis, UTIs, pyoderma and RTIs in dogs and cats by class of choice according to the diagnosis-based guidelines for antimicrobial use in companion animals issued by Guardabassi *et al.*[15]

Class of choice	Gastroenteritis (*n*=69), *n* (%)	UTIs (*n*=61), *n* (%)	Pyoderma (*n*=63), *n* (%)	RTIs (*n*=76), *n* (%)	Total (*n*=269), *n* (%)
First choice	2 (2.9)	19 (31.1)	47 (74.6)	8 (10.5)	76 (28.3)
Second choice	3 (4.3)	8 (13.1)	7 (11.1)	15 (19.7)	33 (12.3)
Last resort		31 (50.8)	8 (12.7)		39 (14.5)
Not listed in any class of choice	64 (92.8)	3 (4.9)	1 (1.6)	53 (69.7)	121 (45.0)

Despite the frequent lack of information on antimicrobial susceptibility testing, in this study, most of the cases of pyoderma were treated with properly chosen antimicrobials, mainly due to the frequent use of drugs that fit the guideline requirements. Conversely, appropriate antimicrobials represented only a small proportion of those administered in gastroenteritis and RTIs, primarily due to the inappropriate use of antimicrobials in self-limiting infections that rarely require antimicrobial treatment.[14] In such cases, the lack of a proper diagnostic approach could have led to excess use of antimicrobials, which represents a critical issue not only from a public health point of view, but also for animal welfare.

The frequent use of antimicrobials licensed for human use represents another critical point of the prescription behaviours observed in our study, since off-label use of human medicinal products in animals is one of the most clearly regulated issues of prudent use. In Italy, as in the EU, the use of antimicrobials in companion animals is strictly limited to those products properly authorized to treat specific conditions in the target species, while the off-label use of products licensed for other animal species or for the treatment of other conditions in the same species, or for human use, is only allowed whenever no authorized products or alternative antimicrobials for veterinary use are available, by way of exception and under the direct personal responsibility of the prescribing veterinarian.[18,28,29] Unfortunately no information on the reasons why human antimicrobials were so frequently prescribed was available in our study. However, it cannot be excluded that, for the same antimicrobial compound, the lower cost of products for human use compared with those for veterinary use may have played a role.

In conclusion, the need to strengthen the professional guidance of prudent prescription is clearly pointed out by the results of our study. At the local level, the development of hospital guidelines for the stewardship of antimicrobials has been reported to be effective,[8] especially in supporting the choice of antimicrobials for empirical use. In any case, the adoption of a full diagnostic approach, including laboratory testing, represents a crucial step that will help in preventing excess use or facilitate the use of specific guidelines for prudent prescription. Further support for prudent use, even at the local level, would arise from the implementation of stronger policies governing antimicrobial use at the national level, considering the current poor regulatory framework in force in Italy and the lack of specific strategies supporting the prudent use of antimicrobials in both companion animals and human medicine.

Acknowledgements

Preliminary results of the study were presented at the Fifth Med-Vet-Net Annual Scientific Meeting, El Escorial, Madrid, Spain, 2009 (Abstract GEN20) and at the European Scientific Conference on Applied Infectious Disease Epidemiology, Stockholm, Sweden, 2009 (Abstract 20090259).

We would like to acknowledge Giovanna Ciaravino for her practical help in collecting the information. We would also like to acknowledge Luca Busani for providing valuable expertise during the course of the project.

Funding

The data presented in this work were generated as part of the routine work performed at the Istituto Superiore di Sanità, Rome, and the Department of Veterinary Clinics of the University of Pisa, Italy.

Transparency declarations

None to declare.

References

1 Frimodt-Møller N. Microbial threat—the Copenhagen Recommendations Initiative of the EU. *J Vet Med B Infect Dis Vet Public Health* 2004; **51**: 400–2.

2 *The Copenhagen Recommendations: Report from the Invitational EU Conference on the Microbial Threat, Copenhagen, Denmark, 1998*. http://soapimg.icecube.snowfall.se/strama/Kopenhamnsmotet_1998.pdf (24 May 2010, date last accessed).

3 Second report from the Commission to the Council on the Basis of Member States' Reports on the Implementation of the Council Recommendation (2002/77/EC) on the Prudent Use of Antimicrobial Agents in Human Medicine. http://ec.europa.eu/health/antimicrobial_resistance/docs/amr_report2_en.pdf (15 December 2010, date last accessed).

4 Lloyd DH. Reservoirs of antimicrobial resistance in pet animals. *Clin Infect Dis* 2007; **45** Suppl 2: 148–52.

5 Guardabassi L, Schwarz S, Lloyd DH. Pet animals as reservoirs of antimicrobial-resistant bacteria. *J Antimicrob Chemother* 2004; **54**: 321–32.

6 Weese JS. Antimicrobial resistance in companion animals. *Anim Health Res Rev* 2008; **9**: 169–76.

7 Prescott JF. Antimicrobial use in food and companion animals. *Anim Health Res Rev* 2008; **9**: 127–33.

8 Weese SJ. Investigation of antimicrobial use and the impact of antimicrobial use guidelines in a small animal veterinary teaching hospital: 1995–2004. *JAVMA* 2006; **228**: 553–8.

9 Federation of Veterinarians of Europe. *Antibiotic Resistance & Prudent Use of Antibiotics in Veterinary Medicine*. http://www.fve.org/news/publications/pdf/antibioen.pdf (24 May 2010, date last accessed).

10 Canadian Veterinary Medical Association. *Guidelines on the Prudent Use of Antimicrobial Drugs in Animals*. http://canadianveterinarians.net/Documents/Resources/Files/85_Resources_Prudent-Use-of-Antimicrobial-Drugs-in-Animals.pdf (24 May 2010, date last accessed).

11 American Veterinary Medical Association. *Judicious Therapeutic Use of Antimicrobials*. http://www.avma.org/issues/policy/jtua.asp#1 (24 May 2010, date last accessed).

12 American Veterinary Medical Association. *American Association of Feline Practitioners/American Animal Hospital Association Basic Guidelines of Judicious Therapeutic Use of Antimicrobials*. http://www.avma.org/issues/policy/jtua_aafp_aaha.asp (24 May 2010, date last accessed).

13 Morely S, Apley MD, Besser TE *et al*. Antimicrobial drug use in veterinary medicine. *J Vet Intern Med* 2005; **19**: 617–29.

14 Prescott JF, Hanna WJB, Reid-Smith R *et al*. Antimicrobial drug use and resistance in dogs. *Can Vet J* 2002; **43**: 107–16.

15 Guardabassi L, Geoffrey A, Linda A *et al*. Guidelines for antimicrobial use in dogs and cats. In: Guardabassi L, Jensen LB, Kruse H, eds. *Guide to Antimicrobial Use in Animals*. Oxford: Wiley-Blackwell, 2008; 183–205.

16 *Recommendations for the Use of Antimicrobial Agents in the Treatment of the Most Significant Infectious Diseases in Animals, Helsinki, 2003*. http://wwwb.mmm.fi/julkaisut/tyoryhmamuistiot/2003/tr2003_9a.pdf (24 May 2010, date last accessed).

17 Italian Ministry of Health. *Uso Responsabile Degli Antibiotici*. http://www.salute.gov.it/farmaciVeterinari/paginaInternaMenuFarmaciVeterinari.jsp?id=1450&lingua=italiano&menu=antibiotici (15 December 2010, date last accessed).

18 Decreto Legislativo 6 Aprile 2006, n. 193. "Attuazione della direttiva 2004/28/CE recante codice comunitario dei medicinali veterinary". http://www.camera.it/parlam/leggi/deleghe/testi/06193dl.htm (15 December 2010, date last accessed).

19 La professione medico veterinaria: condizioni e prospettive nei primi 10 anni di attività. Rapporto Nomisma 2010. http://www.fnovi.it/index.php?pagina=pubblicazioni (21 December 2010, date last accessed).

20 *ATC/DDD Index 2010*. http://www.whocc.no/atc_ddd_index/ (24 May 2010, date last accessed).

21 *ATCvet Index 2010*. http://www.whocc.no/atcvet/atcvet_index/ (24 May 2010, date last accessed).

22 *Joint FAO/WHO/OIE Expert Meeting on Critically Important Antimicrobials*. 2007 ftp://ftp.fao.org/docrep/fao/010/i0204e/i0204e00.pdf (24 May 2010, date last accessed).

23 Sala M, Malandrucco L, Binkin N *et al*. Attitudine all'uso prudente degli antibiotici e percezione del rischio antibiotico-resistenza: un'indagine campionaria tra i veterinari clinici dei piccoli animali. *Not Ist Super Sanità* 2006; **19**: i–ii.

24 Rantala M, Hölsö K, Lillas A *et al*. Survey of condition-based prescribing of antimicrobial drugs for dogs at a veterinary teaching hospital. *Vet Rec* 2004; **155**: 259–62.

25 Thomson K, Rantala MHJ, Viita-Aho TK *et al*. Condition-based use of antimicrobials in cats in Finland: results of two surveys. *J Feline Med Surg* 2009; **11**: 462–6.

26 Regula G, Torriani K, Gassner B *et al*. Prescription patterns of antimicrobials in veterinary practices in Switzerland. *J Antimicrob Chemother* 2009; **63**: 805–11.

27 Heuer OE, Jensen VF, Hammerum AM. Antimicrobial drug consumption in companion animals. *Emerg Infect Dis* 2005; **11**: 344–5.

28 *Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Veterinary Medicinal Products*. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:311:0001:0066:EN:PDF (15 December 2010, date last accessed).

29 *Directive 2004/28/EC of the European Parliament and of the Council of 31 March 2004, Amending Directive 2001/82/EC on the Community Code Relating to Veterinary Medicinal Products*. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:136:0058:0084:EN:PDF (15 December 2010, date last accessed).