Paper

Survey on antimicrobial prescribing patterns in small animal veterinary practice in Emilia Romagna, Italy

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This investigation provides for the first time a general view of the prescribing patterns of antimicrobials in small animal practice in Emilia Romagna, Italy. In the context of a project on antimicrobial resistance managed by the Regional Veterinary Service, veterinary clinicians were invited to voluntarily complete an online questionnaire. This was designed to gather information on antimicrobial prescribing practices and biosecurity measures and to understand the perception of the issue specific to this region of Italy. In total, 266 questionnaires correctly completed were collected. Although clinicians seemed to follow different approaches when using antimicrobials, the data analysis revealed a general awareness on resistance. Penicillins were the most commonly prescribed class, followed by (fluoro)quinolones and cephalosporins. Among those who use laboratory testing more or less frequently (microbiological analysis and susceptibility testing) to support their prescribing habits, only 7 per cent make a habit of always waiting for the results before starting the treatment. Seventy-eight per cent of the respondents declared the use of antimicrobials licensed for human beings. Biosecurity measures were carefully taken into account by the majority of the veterinarians. The results identified the antimicrobial classes that are commonly prescribed and highlighted that perioperative hygiene measures and the use of laboratory diagnosis are critical aspects that need to be emphasised in drawing up guidelines on the prudent use of these drugs in pets.

Antimicrobial agents are essential drugs for therapeutic treatments of bacterial infections in both human beings and animals (OIE 2007, Passantino 2007). An inevitable side effect of the use of these drugs is the selection, development and dissemination of resistant bacteria, especially if overused or not properly employed (Van Den Bogaard and Stobberingh 2000). Antimicrobial resistance (AMR) is an increasing problem in both human and animal healthcare, and affects disease morbidity and mortality, with significant financial implications (Radford and others 2011). Already in 2002 the European Community recommended the prudent use of antimicrobial agents in human medicine (2002/77/EC). Recently, WHO published a report clearly underlining that, due to the alarming levels of resistance reached by common bacteria, many of the available treatment options are becoming ineffective, which is pushing us into the so-called postantibiotic era (WHO 2014).

Institutions which deal in the human, animal and plant sectors have a shared responsibility in preventing and minimising AMR selection pressures on both human and non-human pathogens (OIE 2007). AMR is a complicated phenomenon, involving different bacterial species, reservoirs, as well as resistance and transfer mechanisms (Guardabassi 2004). There is therefore the need to analyse the relationship between human beings, animals and environment in a One Health approach (Madec 2015). Bacteria have developed multidrug resistance, which has been disseminated among different microbial populations. This is even more alarming considering that in recent years there has been a marked decrease in the introduction of new antibacterial agents (Pränting and others 2010) and that the diffusion of generic drugs has been associated with an increased consumption of antibiotics (Finch 2010). In addition, Toutain and Bousquet-Melou (2013) have raised some concerns about the fact that the often recommended use of older, rather than more recent, molecules might not guarantee a more prudent use.

Although for a long time the food chain has been blamed for being responsible of the transmission of resistant zoonotic bacteria (Cohen and Tauxe 1986, Barber and others 2003), the scientific community has observed that this approach has led to an underestimation of non-foodborne sources. For these reasons, coordination among the different scientific sectors should be ensured, and the magnitude of the relationship between the occurrence of antimicrobial-resistant pathogens in human beings, animals and environment should be further clarified

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(Kummerer 2003). A large number of published studies propose a causal link between antimicrobial use in animals and resistant bacterial strains in human beings (Marshall and Levy 2011, Wegener 2012). Several case studies documented the presence of AMR in small animal veterinary medicine (Warren and others 2001, Faires and others 2009) and the potential role of pets as AMR reservoirs for human beings (Costa and others 2004, Guardabassi 2004, Morgan 2008, Nienhoff and others 2009). The number of companion animals has constantly increased in recent years, and pets live in closer physical contact with their owners than they did in the past. Pets and human beings share common bacterial flora and are often treated with the same drugs, including compounds of primary importance (eg, penicillins and fluoroquinolones). This justifies the concern about contribution of pets to the development of AMR in human beings (Lloyd and others 2007, Passantino 2007, Prescott 2008, Weese 2008, Radford and others 2011). In 2013, the European Medicines Agency stated that there is limited knowledge about the transfer of AMR between companion animals and their owners, which may be underestimated (EMA 2015).

During the last few years, authorities have been encouraging the adoption of a uniformed strategy to counteract AMR on different levels and a global action plan was adopted in May 2015 after the Sixty-Eighth World Health Assembly. The World Health Assembly also urged all Member States to develop and have in place by 2017 national action plans on AMR that are aligned with the objectives of the global action plan (WHO 2016). Some European countries (ie, Denmark, France, the Netherlands) already have specific action plans concerning this important issue. Moreover, in many countries most practices are computerised nowadays (eg, the UK, Denmark), providing precise information also on drug prescriptions. In Italy, the lack of computerised prescriptions for veterinary medical products is one of the main problems in understanding which are the most commonly used antimicrobials in each species (and the relative amounts). In this context, the Regional Veterinary Service of Emilia Romagna (ER), Italy, developed a specific four-year project (2014–2017) to evaluate the use of antimicrobials in veterinary medicine in order to help draw up guidelines for a prudent and rational use of these drugs. This paper focuses on the use of antimicrobials in pets and presents the data collected through a specifically created questionnaire for the project and addressed to small animal practitioners in ER.

Materials and methods

Study population and design

A questionnaire-based survey was conducted in 2015 in order to gather data on antimicrobial prescribing practices and biosecurity measures among small animal veterinarians working in the ER region. At the time of this survey, 3304 professionals were registered in the ER Regional Veterinary Federation (FREROVet); it is estimated that approximately 75 per cent of them practice on pets (FNOVI 2015). An email containing a cover letter describing the regional project and a link to an online platform questionnaire (using MiglioraPa system, promoted by the Italian Department of Public Administration) was sent by FREROVet to all its members. The questionnaire could be completed anonymously and on voluntary basis for a two-month period (16 February 2015–16 April 2015); after the first month, a reminder was published on FREROVet's website and another email was sent to all members.

Data collection and processing

The questionnaire was developed by epidemiologists, microbiologists, pharmacologists, small animal veterinarians and researchers with experience in working with pets, and then digitised with LimeSurvey, an open source survey tool. It consisted of 30 questions, divided into three different sections. It was mandatory to answer all the questions in each section before proceeding to the following one. The survey included open and closed (single-choice or multiple-choice) questions. In most cases, closed questions forced the responders to select the closest value to the frequency with which an event occurred (never: 0 per cent; sometimes: 30 per cent; often: 70 per cent; always: 100 per cent). From this, two subgroups (infrequently: 0 and 30 per cent; frequently: 70 and 100 per cent) were created. In the first section, the data collected concerned personal details of the clinician (years of experience, Continuous Professional Development courses—Continuing Professional Development (CPD), including specific courses on AMR), characteristics of the facility in which he/she was working at that time (ie, outpatient clinic, clinic, hospital) with particular focus on certain areas (ie, operating theatre, ward, laboratory and isolation room) and animal species most frequently treated. The questions in the second section helped build an understanding of prescribing patterns with regard to the use of laboratory tests to support the diagnosis and the choice of antimicrobials. Other questions focused on the classes that are used empirically and in specific clinical scenarios (ie, urinary tract infections, respiratory, cutaneous and gastroenteric diseases) and the approach in case of failed clinical recovery. In order to understand whether veterinarians follow good prescribing practices, they were also asked if they weigh the animal before prescribing antimicrobials, which sources of information they use to support their choice (including 'off-label' use), as well as the frequency of administration and the duration of therapy. Veterinarians were also queried if they consider specific guidelines a useful tool and how they would like them to be organised. The last section investigated the techniques used to assure biosecurity (ie, products and protocols used to disinfect personnel and environment). Data were analysed with the statistical software (SPSS, released 2009. PASW Statistics for Windows, V.18.0) and the χ^2 test was employed to evaluate the association between: years of experience/CPD; years of experience/good prescribing practices; empirical use/classes of antimicrobials.

Results

A total of 386 questionnaires were returned, but only 266 were complete in all sections and could be included in the analysis. The majority of the veterinarians taking part in the survey were working in small outpatient clinics (78 per cent), while only 22 per cent worked in bigger institutes (clinics or hospitals). Among the facilities, 88 per cent had a dedicated area for surgery, 59 per cent were equipped with a clinical laboratory, 53 per cent had a ward room and only 21 per cent had an isolation area. Twenty per cent of the institutes, namely the clinics and the hospitals, included all the above-mentioned areas. Almost all the animals (95 per cent) visited by the veterinarians were cats and dogs; the remaining 5 per cent included other small mammals and reptiles.

Seventy-five per cent of the clinicians had more than eight years of professional experience (general range 1–42 years). No correlations were observed between experience (less than or greater than 8 years) and CPD followed every year, the habit of weighing animals before prescribing antimicrobials, actions adopted after ineffective therapy and frequency of 'off-label' prescriptions. On the other hand, an association was found between years of professional experience and how the treatment protocol is chosen. In particular, those who had been practising for <8 years declared that they mainly follow therapy manuals and reference guidelines (χ^2=9.138; P=0.003), while those who had >8 years of experience seem to primarily observe the indications given in the leaflet (χ^2=5.129; P=0.024). CPD seems to be a common practice among the clinicians (78 per cent attend one to five courses per year, while 18 per cent more than five courses per year) and in 38 per cent of cases AMR is the theme of the course. However, 61 per cent of the respondents reported that pharmaceutical companies are one of the main sources of information on this issue, while 25 per cent keep their knowledge updated through consultation of internet blogs and websites.

The main goal of the second section of the questionnaire was to understand the prescribing patterns of antimicrobials, with particular attention to how they are selected and employed.

Microbiological analysis and antimicrobial susceptibility testing (such as culture and sensitivity testing, or minimal inhibitory concentration test) are used by 91 per cent of the veterinarians, with variable frequency (69 per cent 'sometimes', 20 per cent 'frequently' and 2 per cent 'always'). Seven per cent of the clinicians who make use of such laboratory support declared to 'always' wait for the results before prescribing an antibiotic, 56 per cent wait 'only in non-urgent cases' and 17 per cent 'only in the event of a recurrence'. While awaiting the laboratory results, more than half of the veterinarians (58 per cent) tend not to adopt empirical treatment, while the remaining 34 per cent and 8 per cent adopt it 'often' and 'always', respectively. Moreover, given 13 different classes of antimicrobials, veterinarians were asked to select their first choices when empirical treatment is required: penicillins combined with inhibitors of β-lactamases were the most prescribed (198 votes), followed by (fluoro)quinolones (150) and first-generation to second-generation cephalosporins (94). Carbapenems, glycopeptides and monobactams were not prescribed (Fig 1). No statistical correlation was observed between adoption of empirical therapy and specific antimicrobial classes.

Based on the collected data, it seems that veterinarians in the ER region do not frequently prescribe combinations of different antimicrobials (78 per cent 'sometimes', 17 per cent 'often' and 5 per cent 'never'). In order to understand what is mainly used to treat infections involving specific organ systems, veterinarians were asked to indicate the class of antimicrobials or the active compound of preference. The results showed that for urinary tract infections they prescribe mainly (fluoro)quinolones, for cutaneous diseases cephalosporins, while for respiratory and gastrointestinal diseases penicillins (Table 1). In the present study, 78 per cent of the clinicians declared to routinely use antimicrobials in elective surgery and in the perioperative.

The majority of the participants in the survey (74 per cent) reported to 'always' weigh the animals before prescribing antibiotics, 19 per cent 'frequently', 6 per cent 'sometimes' and only 1 per cent 'never', demonstrating that few underestimate this aspect. Moreover, the choice of the antibiotic is based on therapy handbooks for 53 per cent of veterinarians, while 25 per cent follow indications given by the leaflet and 22 per cent their own professional experience. When asked to identify the non-scientific factors that influence the selection of the antimicrobial therapy (ie, ease of administration, costs, duration of treatment), the 'ease of administration' was found to be the most relevant element, although 18 per cent of the veterinarians declared to take into consideration the three components together.

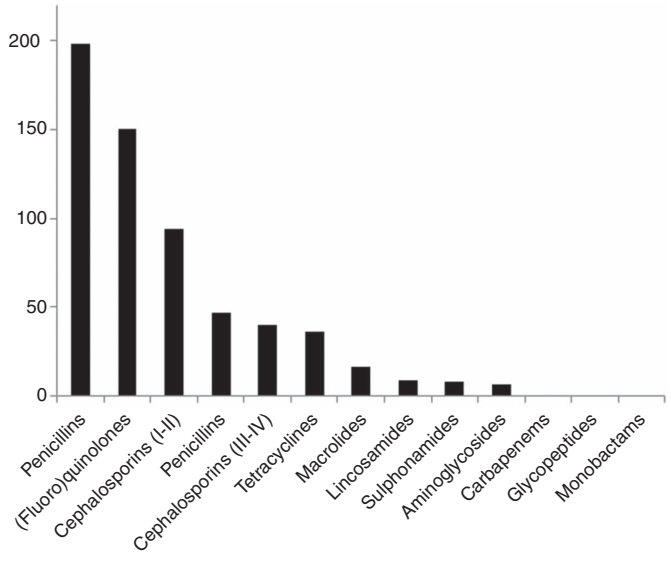

FIG 1: The most used classes of antimicrobials for empirical therapy in pets (multiple-choice question). Bars express total votes

TABLE 1: Antimicrobial drugs prescribed to treat infections involving different organ systems

Antimicrobial class	Total	Urinary tract infections	Cutaneous infections	Respiratory infections	Gastrointestinal infections
Penicillins	427	67	105	123	132
(Fluoro) quinolones	269	166	8	38	57
Cephalosporins	198	22	129	28	19
Tetracyclines	71	1	1	65	4
Macrolides	18	2	3	2	11
Nitroimidazoles	18	–	–	–	18
Lincosamides	8	–	3	1	4
Aminoglycosides	4	2	1	–	1
Sulphonamides	4	1	–	2	1
Cyclosporins	2	–	1	–	1
Not declared		5	15	7	18

Data are expressed as number of respondents indicating each class

In case of failed clinical recovery, 81 per cent of the participants reformulate the diagnosis performing a specific exam, while the others usually change the type of antimicrobial or continue the administration for seven more days, without any microbiological investigation. Among the interviewed veterinarians, 66 per cent 'sometimes' use 'off-label' antimicrobials, 12 per cent 'frequently' and 22 per cent 'never'.

The aim of the third section of the questionnaire was to investigate the preventive measures adopted by veterinarians to contain AMR in their facilities. Handwashing between each visit resulted in a common practice for almost all the respondents (97 per cent), who in 76 per cent of the cases use antimicrobial soaps. While cleaning the veterinary table after each patient seems a well-established routine, the daily disinfection of the isolation area and the waiting room is performed by 69 per cent and 54 per cent of the clinicians, respectively. Quaternary ammonium salts (59 per cent), followed by hypochlorite solution (25 per cent), were the most employed agents for this purpose.

Discussion

The number of veterinarians taking part in the present survey represents approximately 10 per cent of practitioners in small animal medicine in the ER region. Such a population is comparable to that of a study conducted in the UK, based on 14 per cent of small animal veterinarians (Hughes and others 2012).

The inclination to perform microbiological testing (91 per cent) suggested by the outcomes of the questionnaire is rather encouraging, especially taking into account that a study conducted in a veterinary teaching hospital in Pisa (Tuscany, Italy) between 2000 and 2007 reported that not even 5 per cent of the antimicrobials prescribed for pets were supported by such tests (Escher and others 2011). In other research conducted in Italy in 2005, laboratory diagnosis was performed before treatment 'always' or 'often' only in 12 per cent of the cases of gastroenteritis, and in 41 per cent and 50 per cent of pyoderma and urinary tract infections cases, respectively (Sala and others 2006). It is well known that the empirical use of antimicrobials should be avoided, and that the causal infectious agent and its susceptibility to the active substance should be ascertained before starting the therapy. However, when the animal is seriously ill or there is an outbreak of a bacterial infection with high mortality or rapid spread, therapy may be initiated on the basis of clinical diagnosis (Guardabassi and Kruse 2008).

The combination of different antimicrobials is suggested in certain cases to achieve a synergistic or additive effect, to allow lower doses of either compounds (thus reducing the toxicity), and to prevent the emergence of resistance (Walsh 2000, Rahal 2006). However, this strategy has not been implemented due to cost concerns and to the potential enhanced toxicity deriving from the use of more than one agent, especially when, instead of using an authorised combination product, the practitioner decides autonomously the compounds to combine and their

relative doses (Laximarayan and others 2006). In addition, the mixture of antimicrobials with different mechanisms of action can even be antagonistic or inefficacious (Jawetz and others 1952). The low tendency to prescribe antimicrobial combinations expressed by the veterinarians practising in the ER region is in contrast with a UK survey where the simultaneous prescription of two different classes was common (Hughes and others 2012). However, the specific associations in the ER survey were unfortunately not investigated.

Penicillins, (fluoro)quinolones and first-generation to second-generation cephalosporins resulted in the mostly prescribed antimicrobials in pets, as evidenced also in other studies (Hölsö and others 2005, Escher and others 2011, Mateus and others 2011, Wayne and others 2011). It has been suggested that the use of some antimicrobial classes, such as cephalosporins (third to fourth generation) and (fluoro)quinolones, should be banned in animals in order to preserve their effectiveness in human medicine (WHO 2011). However, some of these drugs are often considered a good first choice for specific treatments, such as (fluoro)quinolones in the case of pyelonephritis and other urinary tract infections (Weese 2008). The antimicrobial classes generally chosen for each organ system are similar to what has been previously described in Italy (Escher and others 2011), the UK (Hughes and others 2012) and across Europe (De Briyne and others 2014).

Routine prophylactic use of antimicrobials is generally unnecessary, also in relation to common surgical procedures, since appropriated aseptic techniques and hygiene measures may be sufficient in most cases (Guardabassi and Kruse 2008). Such preventive measures should be pointed out when drafting guidelines, especially in consideration of the excessive preventive use of antimicrobials emerging from the present survey. According to practitioners responding to the questionnaire, guidelines are a useful tool that should be of help to understand the priorities in choosing the most appropriate drug. According to the authors' results, the importance of laboratory diagnosis, to correctly identify the bacterial agent and assess its susceptibility to antimicrobials, seems to be a further aspect that should be stressed in the guidelines. A database could also be set up to gather information on the detected resistances, helping to monitor the problem at a local/national scale.

The use of antimicrobials licensed for human beings in animals ('off-label') should be exceptional, under the professional responsibility of the veterinarian, and limited to cases where no other suitable products are available (Dlgs 193/06). This 'off-label' practice seems quite common among the veterinarians who responded to this questionnaire, especially considering that a previous paper (Escher and others 2011) reported its adoption in 23.8 per cent of the cases, which is lower than the authors' data. However, it must be observed that the choice of a human antimicrobial product in Italy might be often due to its lower cost compared with the equivalent veterinary product.

Companion animals represent potential sources for the spread of AMR. For this reason, veterinary clinics are risky environments and biosecurity measures are vital. The importance of thoroughly cleaning and disinfecting the entire veterinary facility, including animal cages and waiting room areas, on a regular basis is another point on which guidelines should insist.

In conclusion, the lack of information on veterinarians prescribing patterns of antimicrobials in Italy led the ER region to conduct a survey on this topic, as previously done in other countries. This type of approach could represent a useful tool in those countries where veterinary prescriptions are not monitored. Although campaigns for raising awareness on AMR seem to bear fruit, the results of the present investigation highlighted a number of differences and weaknesses in the use of antimicrobials. Moreover, considering that it is likely that the veterinarians answering the questionnaire were among the most conscious of the AMR issue, the collected data might provide a view that is too optimistic on certain aspects. However, while waiting for stronger actions at a national level, the collected information will be of help for the ER Veterinary Service in drawing up guidelines on the right and prudent use of these drugs in pets, paying particular attention to the critical aspects that emerged.

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