

The factors associated with the use of important human antimicrobials in Japanese small animal veterinary clinics

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World Organisation
for Animal Health
Founded as OIE



Background

Ministry of Agriculture, Forestry and Fisheries, National Veterinary Assay Laboratory

Monitoring animal-derived resistant bacteria in healthy and diseased small animals

Creating guidelines and useful tools

愛玩動物における
抗菌薬の
慎重使用の手引き
—2020—



農林水産省政策・安全担当水産安全管理課
「愛玩動物における抗菌薬の慎重使用に関するワーキンググループ」編
農林水産省

Japan Veterinary Medical Association (JVMA)

Survey on actual usage of antimicrobials for small animal veterinary clinics (veterinary, humans, and imported drugs) in 2018

- **60 %** of the medicines used are for human use (**4.3% are important antibiotics**)

Objectives

- To understand the reasons for using important human antibiotics in Japanese small animal clinics

Materials and methods

Questionnaire survey

The JVMA requested local veterinary associations to send

1. Mail the questionnaire to small animal medical facilities
2. Tokyo Veterinary Medical Association: Online survey

Survey period : November 29 , 2021 to January 10 , 2022 (February 18)

3. Hokkaido Veterinary Medical Association: Direct collection

Totalling

- Drug classification: Kyoto Encyclopedia of Gene and Genomes (KEGG) Medicus Drug Search
- Important antibacterial drugs : Food Safety Commission's list of extremely important antibacterial drugs
- Ordinal variables (three or four options) are weighted

Materials and methods

Questionnaire 1: Survey on human and imported antimicrobial use

- Antibiotic brand name, manufacturer, and dose per case for each animal species
- Number of cases used per year (categories 10 to 19, 20 to 49, 50 or more)
- Reasons for use by animal species, rationale for use, and precautions (options)

Materials and methods

Questionnaire 2: Knowledge and awareness regarding antibiotic use

- Clinic attributes: prefecture, years since opening, private or corporate management, animal species, number of employees
- Knowledge of antimicrobial drugs and drug resistance: second-line drugs, Japanese guidelines, action plans, prudent use, companion animal drug resistance monitoring, survey of human antimicrobial drug sales volume at veterinary clinics
- Attitudes towards antimicrobial resistance
- Antibiotic use: Target diseases, antibiotic choice decisions, and concerns about antibiotic resistance complicating treatment for humans and animals
- Use of approved veterinary drugs
- Antimicrobial resistance measures
- Status of drug susceptibility testing
- Improvements for veterinary drugs

Method – Statistical analysis –

Factors associated with use of important human antibiotics

- Factors related to medical facility attributes, knowledge, and awareness
- Generalized linear model (GLM) with binomial errors

Factors associated with the proportion of important antibiotics used

- Factors related to medical facility attributes, knowledge, and awareness
- There were facilities that do not use important human antibiotics, and the vector generalized additive model with zero-excess binomial error (statistical software R , package VGAM)

Factors associated with the annual use frequency of important antibiotics

- Reasons for and awareness of antibiotic use
- GLM with Poisson errors
- To adjust for the effect of the size of the medical facility, offset term "log number of employees" was added

Result: response rate

- Usage survey 71.2 %
- Knowledge and attitude survey 72.3 %

TABLE 2 Survey responses and response rates by region.

Region	Number of allocated facilities	Usage survey		Awareness survey	
		Number of responses	Response rate (%)	Number of responses	Response rate (%)
Hokkaido and Tohoku	25	14	56.0	16	64.0
Kanto	103	60	58.3	64	62.1
Chubu	41	36	87.8	36	87.8
Kinki	48	37	77.1	37	77.1
Chugoku	13	9	69.2	8	61.5
Shikoku	6	6	100.0	5	83.3
Kyushu-Okinawa	24	23	95.8	22	91.7
Total	260	185	71.2	188	72.3

Results: usage

- Percentage of veterinary facilities using important human antibiotics
 - 57.1%
- Proportion of important antibacterial drugs among the number of cases of antibacterial drugs used for humans
 - 21.7%
- Among the survey subjects
 - Human drugs: 98.2%
 - Imported drugs: 1.8%
- Prescription of human antibiotics
 - Oral: 69.8%
 - Intravenous: 9.1%
 - Eye drops: 8.2%
 - Subcutaneous: 4.2%

TABLE 3 Ranking of antibiotic classes among antimicrobials for human use according to the number of animal treatment cases per year.

Antibiotic class name	Rank	Number of cases of use	Percentage
Penicillins	1	7,432	21.93%
Tetracyclines	2	6,754	19.93%
First-generation cephalosporins	3	4,602	13.58%
14- and 15-membered ring macrolides	4	3,092	9.12%
Aminoglycosides	5	2,020	5.96%
Fluoroquinolones	6	1,978	5.84%
Third-generation cephalosporins	7	1,834	5.41%
Amphenicols	8	1,126	3.32%
Lincosamides	9	1,110	3.27%
Fosfomycin	10	1,026	3.03%
Sulfamethoxazole-trimethoprim	11	850	2.51%
Penems	12	476	1.40%
Second-generation cephalosporins	13	396	1.17%
Carbapenems	14	348	1.03%
Sulfamethoxazole	15	246	0.73%
New quinolones	16	196	0.58%
erythromycin	17	132	0.39%
Steroids	18	82	0.24%
Amphotericin B	19	78	0.23%
4th generation cephalosporins	20	48	0.14%
16-membered ring macrolides	21	28	0.08%
Antituberculosis drugs	22	28	0.08%
Glycopeptides	23	14	0.04%
Total		33, 896	1 00%

*Important antibiotics for human use are indicated in bold.

Result: knowledge/awareness

Item	Percentage
Use of prudent use guidelines	
Frequently used	2.2% (4/184)
Sometimes	26.1% (48/184)
I know but I don't use it at all	32.1% (59/184)
Monitoring of drug-resistant bacteria from companion animals	
Know about it	41.6% (77/185)
The results are used in clinical practice	30.1% (52/173)
Have experienced antibiotics not working	83.2% (153/182)
Drugs that are not approved as veterinary medicines in Japan	
Should not be used	1.6% (3/183)
Should not be used unless there is no other option	21.9% (40/183)
May be used if deemed necessary by a veterinarian	66.7% (122/184)
Points to keep in mind when using antibiotics	
Efficacy	87.6% (162/185)
Suppression of drug-resistant bacteria	58.4% (108/185)
Safety	57.3% (106/185)
Price	35.1% (65/185)

Results: antimicrobial resistance measures

Item	Percentage
Holding a seminar on antibacterial drugs	44.5% (81/182)
Holding seminars on prudent use	6.4% (11/182)
Infection prevention measures	34.1% (63/185)
Selection of antibacterial agents based on antimicrobial susceptibility tests	3.2% (6/185)
Periodic bacterial testing	88.6% (164/185)
Susceptibility testing of isolated bacteria	
Always	38.5% (70/182)
Occasionally	45.1% (84/182)
Explanations to pet owners when prescribing antibiotics	
Explain the importance of AMR and how to use it as indicated	42.2% (78/185)
Not explains the importance of AMR, but the importance of using it appropriately	41.1% (76/185)

TABLE 4 Results of univariable analysis of factors associated with the use of important human antimicrobials ($p < 0.2$).

Item	Odds ratio	95% confidence interval	p -value
Empirical antibiotic use	1.58	0.82–3.02	0.171
Drugs that are not approved as veterinary medicines in Japan should not be used, or should not be used except in unavoidable circumstances	0.57	0.28–1.18	0.132
I am aware of the monitoring survey of bacteria in companion animals conducted by the Ministry of Agriculture, Forestry and Fisheries	0.53	0.28–1.00	0.049

TABLE 5 Results of multivariable analysis of factors associated with the use of important human antimicrobials.

Item	Odds ratio	95% confidence interval	p -value
Drugs that are not approved as veterinary medicines in Japan should not be used, or should not be used except in unavoidable circumstances	0.60	0.29–1.25	0.171
I am aware of the monitoring survey of bacteria in companion animals conducted by the Ministry of Agriculture, Forestry and Fisheries	0.60	0.31–1.13	0.113

TABLE 6 Results of univariable analysis of factors associated with the proportion of important antimicrobials among human antibacterial drugs used ($p < 0.2$).

Item	Odds ratio	95% confidence interval	<i>p</i> -value
Know the specific ingredients of first- and second-line drugs	0.88	0.82–0.94	<0.001
First- and second-line drug knowledge scores	0.91	0.86–0.96	0.001
Select antibiotics based on route of administration	1.15	1.07–1.23	<0.001
Antibiotics are selected based on the results of antimicrobial sensitivity tests	0.94	0.88–1.01	0.070
Use from first-line drugs	0.61	0.55–0.68	<0.001
Use of effective antibiotics	0.85	0.79–0.91	<0.001
Use from broad-spectrum antibiotics	1.05	0.98–1.12	0.187
Drugs that are not approved as veterinary medicines in Japan should not be used	0.60	0.43–0.83	0.003
Using cephalexin-containing preparations for use in animals	0.87	0.81–0.93	<0.001
Using amoxicillin-containing preparations for use in animals	0.93	0.87–0.10	0.038
Considering the cost when using antibiotics	1.12	1.05–1.20	0.001
No in-house training is provided	1.12	1.04–1.20	0.001
No microbiological testing is performed when administering antibiotics	1.46	1.25–1.72	<0.001
No antimicrobial sensitivity testing of isolated bacteria	1.46	1.29–1.67	<0.001
Gram staining not performed in-house	1.05	0.98–1.12	0.174
There is no concern that AMR bacteria selected through the use of antimicrobials in animals in routine veterinary practice could lead to treatment difficulties in human medicine	1.57	1.37–1.80	<0.001
Address off-label use of approved veterinary drugs	0.80	0.72–0.89	<0.001
Explain to owners the importance of administering antibiotics properly	0.87	0.81–0.93	<0.001
Know about the prudent use of antibiotics	0.90	0.84–0.97	0.003

TABLE 7 Final multivariable model for factors associated with the proportion of important antimicrobials among human antibacterial drugs used.

Item	Odds ratio	95% confidence interval	<i>p</i> -value
Know the specific ingredients of first- and second-line drugs	0.83	0.77–0.89	<0.001
Select antibiotics based on route of administration	1.34	1.24–1.44	<0.001
Antibiotics are selected based on the results of antimicrobial sensitivity tests.	0.90	0.83–0.97	0.008
Use from first-line drugs	0.57	0.51–0.64	<0.001
Use of effective antibiotics	0.74	0.68–0.79	<0.001
Drugs that are not approved as veterinary medicines in Japan should not be used	0.43	0.29–0.63	<0.001
Using cephalexin-containing preparations for use in animals	0.89	0.81–0.97	0.012
Using amoxicillin-containing preparations for use in animals	0.88	0.80–0.96	0.006
Considering the cost when using antibiotics	1.31	1.21–1.41	<0.001
Gram staining not performed in-house	1.25	1.16–1.36	<0.001
There is no concern that AMR bacteria selected through the use of antimicrobials in animals in routine veterinary practice could lead to treatment difficulties in human medicine	1.34	1.15–1.57	<0.001
Address off-label use of approved veterinary drugs	0.68	0.59–0.78	<0.001
Explain to owners the importance of administering antibiotics properly	0.87	0.81–0.94	<0.001

TABLE 8 Results of univariable analysis of factors associated with the annual frequency of use of each important human antimicrobial drug.

Item	Estimated value	Standard error	<i>p</i> -value
Reasons for use			
There are no other veterinary medicines sold in Japan that contain the same ingredients	−0.50	0.028	<0.001
Cheap price	0.55	0.033	<0.001
easy to use	0.12	0.044	<0.001
Points to keep in mind when using			
Use only when other antibiotics are ineffective and necessary	−0.61	0.039	<0.001
When efficacy is expected, it is used preferentially as a first-choice drug	0.51	0.028	<0.001
No special awareness, used as needed	0.13	0.045	<0.001

Summary

- 21.7% of human antibiotics used in companion animal clinics are important antibiotics
 - The One Health Report found that sick dogs and cats were more likely to be resistant to erythromycin, ciprofloxacin, and cefotaxime than healthy dogs and cats.
 - In 2018, 12.6% of antibiotics used in veterinary clinics in Japan were human important antibiotics (significantly higher than 5-6% in UK in 2016-2017)
 - In 2018 survey based on powder weight, important antibacterial drugs account for 7.0% of all human antibacterial drugs. The present study (21.7%) was much higher.
- 57.1% of veterinary facilities use important antibacterial drugs for humans.
- Prudent use
 - In the UK , use of important human antibiotics has fallen sharply since 2014 as prudent use became widely accepted
 - In Japan, the sales of important drugs declined from 2016 to 2021, but use of penicillin is increasing
- Knowledge and awareness on AMR is not high

Summary

- Factors associated with use of important human antimicrobials
 - Veterinary clinics with high knowledge and awareness of antibiotics have a low proportion of important antibiotics for human use
 - The frequency of use of important antibiotics is high in clinics that prioritize the cost and ease of use of antibiotics.
- Antimicrobial resistance stewardship
 - Use the benchmark
 - Defined daily dose used
 - In the UK , the proportion of important antibiotics used declined by 23.5% for dogs and by 39.0% for cats in 6 months
 - Education
 - Continuing education and outreach programs for veterinarians are effective
 - Stewardship towards owners is also important in building trust
- Limitation
 - Important antibiotic use per consultation is unknown
 - Monitoring of clinical data and prescriptions can be used as objective indicators