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Author(s): Samanta Waxman , DVM, PhD, Ana Paula Prados , DVM, Julio de Lucas , DVM, PhD, Manuel Ignacio San Andres , DVM, PhD, Juan Carlos Sassaroli , DVM, Marcela Orozco , DVM, PhD, Hernán Argibay , DVM, and Casilda Rodriguez , DVM, PhD

Source: Journal of Avian Medicine and Surgery, 27(3):180-186. 2013.
Published By: Association of Avian Veterinarians
DOI: http://dx.doi.org/10.1647/2012-022
URL: http://www.bioone.org/doi/full/10.1647/2012-022

Journal of Avian Medicine and Surgery 27(3):180–186, 2013

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Abstract: To determine the dosage of enrofloxacin in southern crested caracaras (*Caracara plancus*), plasma concentrations of enrofloxacin were measured by high-performance liquid chromatography after intravenous (IV) (5 mg/kg) and intramuscular (IM) (10 mg/kg) administration. This compound presented a relatively high volume of distribution (2.09 L/kg), a total body clearance of 0.24 L/kg·h, and a long permanence as shown by an elimination half-life of 7.81 hours after IV administration and a terminal half-life of 6.58 hours after IM administration. The areas under the concentration-time curves (AUC) were 21.92 and 34.38 μg·h/mL for IM and IV administration, respectively. Enrofloxacin was rapidly absorbed after IM administration with a time to reach maximum concentration of 0.72 hours and bioavailability of 78.76%. After IM administration, the peak drug concentration (C_{max}) was 3.92 μg/mL. Values of minimum inhibitory concentration (MIC), C_{max}, and AUC have been used to predict the clinical efficacy of a drug in treating bacterial infections, with a C_{max}/MIC value of 10 and an AUC/MIC ratio of 125–250 associated with optimal bactericidal effects. By using the study data and a MIC breakpoint of 0.25 μg/mL, values of C_{max}/MIC were 13.74 and 15.94 and for AUC/MIC were 90.73 and 139.63, for the IV and IM routes respectively. For the treatment of infectious diseases caused by microorganisms with MIC $\leq$0.25 μg/mL, the calculated optimal dosages were 7.5 and 9.5 mg/kg q24h by the IV and IM routes, respectively. For less susceptible bacteria, a dose increase should be evaluated. To treat caracara by the IV route against microorganisms with MIC $\leq$0.25 μg/mL, the dose should be higher than the 5 mg/kg used in our study, but possible side effects derived from an increase in the IV dose and efficacy in sick birds should be assessed.

Key words: enrofloxacin, fluoroquinolones pharmacokinetics, pharmacodynamics, southern creasted caracars, *Caracara plancus*

Introduction

One of the most challenging problems for birds of prey in captivity is bacterial infection. The fluoroquinolone antibiotics have several favorable properties, such as excellent bioavailability, good tissue penetrability, and a relatively low incidence of adverse and toxic effects.[1] These agents have been extensively used in avian medicine because of their broad antimicrobial spectrum, which includes most gram-negative bacteria, some gram-positive bacteria (including staphylococci), some mycoplasma, and chlamydiae,[2,3] as well as their bactericidal activity and relative lack of adverse effects. Enrofloxacin is one of the most common drugs within this group used in birds. Because of its antimicrobial properties, enrofloxacin has advantages for use in birds in treating common infectious

From the Pharmacology Department, FCV, University of Buenos Aires, Chorroarin 280, 1427, Argentina (Waxman, Prados); Pharmacology Department, Universidad Complutense de Madrid, Av. Puerta de Hierro s/n, 28040, Spain (Lucas, Andres, Rodriguez); Reserva Ecológica Costanera Sur, T. A. Rodriguez 1550, 1107, Buenos Aires, Argentina (Sassaroli); Ecoepidemiology Laboratory, FCEN, UBA, C. Universitaria,1428, Buenos Aires, Argentina (Orozco); and Ecological Park "El Puma", MEYRNR, Candelaria, 3308, Misiones, Argentina (Argibay).

diseases, such as *Mycoplasma* infection, colibacillosis, and pasteurellosis.[4]

Enrofloxacin was the first fluorinated quinolone compound used in veterinary medicine. Ciprofloxacin, its primary metabolite, is also a very potent antibacterial. Data on their pharmacokinetics have been published for different domestic and wild avian species,[2,4–8] and their pharmacokinetic behavior vary widely among species. After extravascular administration, enrofloxacin is well absorbed. This drug has been shown to achieve high concentrations in tissues, and it is partly metabolized and excreted, mainly by the kidneys. Metabolism of enrofloxacin is variable in animal species, and the extent of ciprofloxacin formation is less than 10% in ducks,[9] ostriches (*Struthio camelus*),[7] and turkeys.[4]

One concern with the intramuscular injection is that it can produce irritation at the injection site, which is problematic because birds have a limited muscle mass.[10] Quinolone-induced arthropathy has been observed after a single large dose or after several moderately large doses in juvenile animals of multiple species. Previous studies showed condrotoxicity after a high dose of quinolones in nestling pigeons (*Columba livia*) and chickens.[11] However, treatment with a therapeutic dose of enrofloxacin for a period exceeding the recommended duration of therapy does not cause arthropathy in growing chickens.[12]

The aim of this study was to investigate the plasma concentrations of enrofloxacin and its active metabolite ciprofloxacin in southern crested caracaras (*Caracara plancus*) to establish pharmacokinetic and pharmacodynamic relationships and the optimal dose for single intravenous (IV) and intramuscular (IM) administration of enrofloxacin.

Materials and Methods

Animals

This study was approved by the Institutional Animal Care and Use Committee (Comite Institucional de Cuidado y Uso de Animales de Laboratorio) of the Veterinary Sciences School, University of Buenos Aires (authorization reference number 2008/19).

Four healthy adult southern crested caracaras with a mean weight of 1.33 ± 0.06 kg were used. The birds were held in the recovery area of a local reserve (Reserva Ecologica Costanera Sur, Buenos Aires, Argentina). The birds were housed in large pens, fed a standard diet for the species, and had access to water ad libitum. Criteria for selection of healthy animals were based on routine acceptance of daily meals, maintenance of body weight, and results of a complete physical examination and hematologic testing.

Materials

Ofloxacin, enrofloxacin, and ciprofloxacin analytical standards were purchased from Sigma-Aldrich (Sigma-Aldrich, Madrid, Spain). Stock standard solutions (1 mg/mL) were prepared from the reference standards, dissolved in 0.1 N formic acid in water, and stored at –80°C. The mobile phases were prepared daily using high-performance liquid chromatography (HPLC) grade solvents (Sigma-Aldrich; Scharlau Chemie S.A., Barcelona, Spain). The product administered to the animals was a commercial 5% enrofloxacin injectable solution (Baytril, Bayer, Isando, South Africa).

Experimental design

Enrofloxacin was administered to all birds at a dose of 5 mg/kg IV into the brachial vein. After a 4-week washout period, enrofloxacin was administered at a dose of 10 mg/kg IM into the right pectoral muscles.

Blood samples (0.6 mL at each time point) were collected from the metatarsal veins with a 27-gauge needle attached to a 1-mL heparinized syringe at 0, 5, 15, and 35 minutes and at 1, 2, 4, 6, 8, 10, 12, 24, 29, and 34 h after IV administration; and at 0, 10, 20, and 40 minutes and at 1, 2, 4, 6, 8, 10, 12, 24, 29, and 34 h after IM injection. For each experiment the total sample volume did not exceed 10% of the blood volume of the animal. Plasma was separated immediately in a refrigerated centrifuge and frozen at –80°C until analyzed.

Sample processing

The sample processing methodology was slightly modified from a previously published method.[5] A volume of 200 μL of plasma was placed into 15-mL screw-capped tubes. Fifty microliters of the internal standard solution (ofloxacin, 2.5 μg/mL in formic acid 0.1 N) and 3 mL of trichloromethane were added. After being agitated for 10 minutes in a horizontal agitator, the samples were centrifuged at 3200*g* for 7 minutes and the organic layer transferred to another tube from where it was evaporated under vacuum at 40°C. The samples were re-dissolved in 125 μL of mobile phase. The mean recoveries of enrofloxacin and ciprofloxacin from plasma samples were 95.15% ± 4.67% and 88.09% ± 9.80%, respectively.

Analytical assay

Plasma concentrations of enrofloxacin and its active metabolite ciprofloxacin were quantified by using HPLC/UV, according to a previously published method.[5] The extracted samples were injected directly into the HPLC/UV system, where separation was accomplished by an ion-pairing reverse-phase column (PR C-18 5 μm 150 · 4.6 mm) with a precolumn (PR C-18 5 μm 15 · 4.6 mm). The mobile phase consisted of buffer pH 2.7:methanol: acetonitrile:acetic acid:triethylamine (74:20:4:1:1, v/v/v/v/v). The buffer pH 2.7 was a 0.4% aqueous solution of tetrabutylammonium hydrogensulphate (p/v) and diammonium hydrogenphosphate (p/v). The UV detection wavelength was 279 nm, and the flow rate was 1 mL/min. The limit of quantification (LOQ) was 0.025 mg/L for enrofloxacin and 0.05 mg/L for ciprofloxacin, and the method was linear up to 10 mg/L. No chromatography interferences were observed in the retention time of analyzed analytes. The calibration curve was linear over the selected concentrations (0.025–10 ug/mL, r^2>0.99 for both drugs). Precision was calculated as the coefficient of variation of the average value found for each concentration, being intra-day precision 5.68% ± 3.11% and 3.57% ± 3.06% and inter-day precision 8.81% ± 1.57% and 8.22% ± 3.01% for enrofloxacin and ciprofloxacin, respectively. Accuracy ranged between 82.4%–119.1% and 83.52%–118.5%, for enrofloxacin and ciprofloxacin, respectively.

Pharmacokinetic and statistical analysis

Plasma levels of enrofloxacin after IV and IM administration were subjected to compartmental and noncompartmental analysis by using a nonlinear least-squares regression analysis using PCnonlin V4.0 software package (Statistical Consultants, Lanexa, VA, USA), Akaike's Information Criterion (AIC), residual sum of squares (Rs), and analysis of residuals plots were used to discriminate between models. The area under curve (AUC), area under first moment curve (AUMC), and mean residence time (MRT) were calculated using the trapezoidal rule with extrapolation to infinity (∞). The extrapolated areas did not exceed 4%. The absolute bioavailability (F) was calculated as F (%) = (AUC_∞IM/ AUC_∞IV) × (dose IV/dose IM) × 100. The descriptive statistical analysis was performed using the SPSS 17.0 software package (SAS, Armonk, NY, USA).

To calculate efficacy parameters, minimum inhibitory concentration (MIC) and mutant prevention concentration (MPC) values were used. The derived pharmacokinetic/pharmacodynamic (PK/PD) indices selected were the AUC/MIC ratio (AUC_∞/MIC), the peak drug concentration/MIC ratio (C_{max}/MIC), the time that the concentrations were above the MIC (T > MIC), the time that the concentrations were above the MPC (T > MPC), and the time that the concentrations were within the mutant selection window (T_{MSW}). It has been observed that selective amplification of spontaneous drug-resistant mutants is more pronounced within the range of antimicrobial plasma concentrations between the MIC of the wild bacterial population and the MPC, defined as T_{MSW}. The PK/PD indices were calculated using AUC values obtained by adding both enrofloxacin and ciprofloxacin AUC values and C_{max} values that are a result of considering the point at which the addition of enrofloxacin and ciprofloxacin concentrations reaches the maximum value. Because MIC and MPC data of isolates from caracaras are not available, MIC and MPC values of wild isolates of *Escherichia coli* and *Campylobacter jejuni* and gyrA first-step resistant mutants have been included in our study.[13,14] However, those values were calculated for isolates from chickens, a species in which the selection pressure is probably high because of the intensive use of these kind of antimicrobials and, consequently, MIC values in populations with first-step mutation are high. Therefore, to determine the optimal dose of enrofloxacin in caracaras, we also calculated some PK/PD indices with a MIC breakpoint of 0.25 μg/mL. Because we consider it to be a more realistic scenario, this breakpoint was chosen on a basis of the susceptibility of isolates from other bird species in which most susceptible bacteria have MIC < 0.25 μg/mL.[15] With these data, the optimal dose of enrofloxacin in southern crested caracaras was then calculated by means of the following equation[9]: [dose = (AUC/MIC * Cl * MIC) / (F * 24 h)].

Results

The mean (±SD) enrofloxacin and ciprofloxacin plasma concentration-time curves after IV and IM administration are shown in Figures 1 and 2, respectively. Data obtained after IV administration were best fitted to a 2-compartment open model with first-order output. Data from the IM administration and ciprofloxacin concentrations were analyzed by the noncompartment model. Pharmacokinetic parameters are presented in Table 1. The PK/PD indices are shown in Table 2.

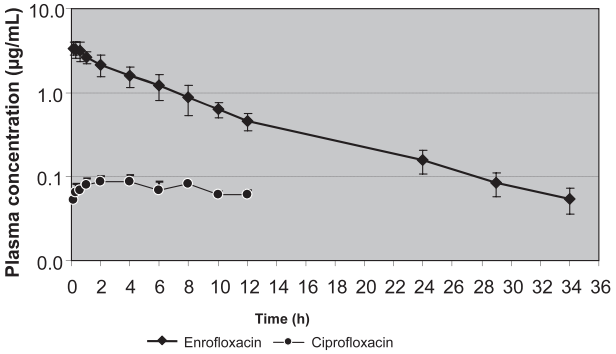

Figure 1. Enrofloxacin and ciprofloxacin concentration-time profile (mean ± SD) after intravenous administration of enrofloxacin (5 mg/kg) in southern crested caracaras (n = 4).

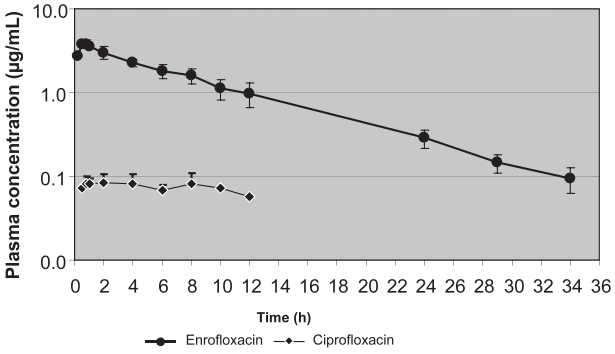

Figure 2. Enrofloxacin and ciprofloxacin concentration-time profile (mean ± SD) after intramuscular administration of enrofloxacin (10 mg/kg) in southern crested caracaras (n = 4).

In southern crested caracaras, enrofloxacin presents a volume of distribution at steady-state (V_{ss}) of 2.09 ± 0.48 L/kg and total plasma clearance (Cl) of 0.24 ± 0.05 L/kg·h. Its distribution half-life after IV administration is $t_{½\alpha} = 2.25$ ± 0.65 h. It has a long elimination and terminal half-life ($t_{½\beta} = 7.81 \pm 0.19$ h and $t_{½\lambda} = 6.58 \pm 0.69$ h after IV and IM administration, respectively).

Pharmacokinetic parameters did not show significant differences ($P > .05$) between both routes of administration. Enrofloxacin was rapidly absorbed after IM administration with a time to reach maximum concentration (T_{max}) of 0.72 ± 0.31 h; the bioavailability (F) was 78.76 ± 4.83%. Although quinolones are reported to produce tissue irritation in other species, signs of pain or lameness were not observed after IM administration of enrofloxacin in southern crested caracaras. No adverse effects were detected during IV and IM injections or for up to 7 days after administrations.

The most relevant efficacy parameters against microorganisms with MIC ≤ 0.25 µg/mL were $C_{max}/MIC = 13.74 \pm 2.51$ and 15.94 ± 1.59 and AUC/MIC = 90.73 ± 18.37 and 139.63 ± 25.84 for IV and IM administrations, respectively. The efficacy parameters against *E coli* and *C jejuni* are shown in Table 2.

The optimal dose of enrofloxacin in southern crested caracaras, estimated by means of an equation previously suggested[16] for the treatment of infections against microorganisms with MIC = 0.25 µg/mL[15] (and target AUC/MIC = 125 h), would be 7.5 and 9.5 mg/kg per day by IV and IM routes, respectively.

Discussion

Data on the pharmacokinetics of enrofloxacin in birds of prey are scarce, and no specific pharmacokinetic information has been documented for southern crested caracaras.

After IV administration, the pharmacokinetic behavior of enrofloxacin in southern crested caracaras was similar to that described for other bird species. Elimination half-life (7.81 h), clearance (0.24 L/kg·h), mean residence time (7.97 h), and volume of distribution at steady state (2.09 L/kg) in caracaras were consistent with values found in houbara bustards (*Chlamydotis undulata*) ($t_{½\beta}$ = 5.63 h, Cl = 0.34 L/kg·h, MRT = 8.13 h, V_{ss} = 2.98 L/kg)[2], turkeys ($t_{½\beta}$ = 6.64 h, Cl = 0.4 L/kg·h, MRT = 8.96 h, V_{ss} = 3.57 L/kg),[4] and broiler chickens ($t_{½\beta}$ = 10.96 h, Cl = 0.25 L/kg·h, V_{ss} = 2.92 L/kg)[6]. However, other bird species like ratites showed a faster elimination and, consequently, a shorter permanence of the drug in the body ($t_{½\beta}$ = 2.66 and 0.78 h, Cl = 3.95 and 4.56 L/kg·h, MRT = 1.23 and 0.7 h, and V_{ss} = 5.01 and 3.4 L/kg for *Rhea* species and ostriches, respectively).[5,7]

Intramuscular bioavailability of enrofloxacin in southern crested caracaras (78.76%) was relatively high, similar to that found in other birds of prey, such as red-tailed hawks (*Buteo jamaicensis*) (87%),[8] and slightly smaller than that reported for ostriches (91%)[7] and houbara bustards (97.3%).[2]

Previously published reports suggest that optimum bactericidal effect of fluoroquinolones are associated with values of the efficacy parameters C_{max}/MIC and AUC/MIC ≥10 and ≥125–250, respectively. These values would allow clinical success to be predicted. High C_{max}/MIC ratios also have been associated with a lower incidence of resistance development.[17,18] However, some authors suggest that, in immunocompetent patients, values of AUC/MIC <125 are also likely to be effective.[10] The efficacy parameters against micro-

Table 1. Pharmacokinetic parameters (mean ± SD) of enrofloxacin and its metabolite ciprofloxacin after single enrofloxacin intravenous (5 mg/kg) and intramuscular (10 mg/kg) administrations in southern crested caracaras (n = 4).

	Intravenous (5 mg/kg)		Intramuscular (10 mg/kg)	
Parameter[a]	Enrofloxacin	Ciprofloxacin	Enrofloxacin	Ciprofloxacin
α (h^{-1})	0.34 ± 0.13			
β (h^{-1})	0.089 ± 0.002			
$t_{½\alpha}$ (h)	2.25 ± 0.65			
$t_{½\beta}$ (h)	7.81 ± 0.19			
$t_{½\gamma}$ (h)			6.58 ± 0.69	
V_{ss} (L/kg)	2.09 ± 0.48			
Cl (L/kg·h)	0.24 ± 0.05			
AUC_{∞} (μg·h/mL)	21.92 ± 4.42		34.38 ± 6.32	
MRT_{∞} (h)	7.97 ± 1.12		8.95 ± 0.64	
AUC_t (μg·h/mL)	21.41 ± 4.43	0.76 ± 0.24	33.48 ± 6.06	0.53 ± 0.39
MRT_t (h)	7.09 ± 0.63	4.84 ± 1.29	8.04 ± 0.45	3.51 ± 1.61
C_{max} (μg/mL)		0.085 ± 0.022	3.92 ± 0.37	0.094 ± 0.023
T_{max} (h)		5.25 ± 4.72	0.72 ± 0.31	2.55 ± 1.88
F (%)			78.76 ± 4.83	

Abbreviations: α indicates distribution rate constant; β, elimination rate constant; $t_{½\alpha}$, distribution phase half-life; $t_{½\beta}$, elimination phase half-life; $t_{½\gamma}$, terminal half-life; V_{ss}, volume of distribution at steady-state; Cl, total plasma clearance; AUC_{∞}, area under the plasma concentration-time curve; AUC_t, area under the plasma concentration-time curve from time zero to last time (34 h); MRT_{∞}, mean residence time; MRT_t, mean residence time from time zero to last time (34 h); C_{max}, peak drug concentration; T_{max}, time to C_{max}; F, bioavailavility.
[a] AUC values used to calculate pharmacokinetic/pharmacodynamic indices were obtained by adding both enrofloxacin and ciprofloxacin AUC and C_{max} values are a result of considering the point at which the addition of enrofloxacin and ciprofloxacin concentrations reaches the maximum value.

organisms with MIC values ≤0.25 μg/mL were $C_{max}/MIC = 13.74 \pm 2.51$ and 15.94 ± 1.59 and $AUC/MIC = 90.73 \pm 18.37$ and 139.63 ± 25.84 for IV and IM administrations in caracaras, respectively. Therefore, with the administration of 10 mg/kg IM of enrofloxacin, the current recommended minimum values of PK/PD indices could be reached. However, clinical and experimental studies indicate that suboptimal antibiotic dosage regimens may be a significant risk factor for the emergence of resistance.

Optimizing dosages is important, not only to achieve a therapeutic effect but also with respect to minimize development of resistance. Although MIC allows determining the susceptibility of most of the cells of a bacterial population, MPC provides information about the sensibility of small resistant subpopulations. The MPC is a pharmacodynamic parameter that may be a useful tool to guide the dosage of antibiotics to reduce the emergence of bacteria with decreased antibiotic susceptibility. The range of antimicrobial plasma concentrations between the MIC of the wild bacterial population and the MPC is defined as the MSW. It has been observed that selective amplification of spontaneous drug-resistant mutants is more pronounced within the MSW. The time that the concentrations are above the MIC (T > MIC) and the time that the concentrations are above the MPC (T > MPC) are used to calculate the time that the concentrations are within the T_{MSW}. Therefore, to minimize resistance development, high values of T > MPC are desirable in order to maximize T_{MSW}.

It has been suggested that the single pharmacodynamic index that shows the least variation and, therefore, best predicts the prevention of resistance emergence is AUC/MPC.[19] Thus, an AUC/MPC value of 35 was sufficient to prevent the growth of the resistant single mutant, whereas the next lowest tested AUC/MPC value of 14 was insufficient. Also, T_{MSW} appeared to be a good predictor of the prevention of resistance for values <20%–30% for high inoculum size. The results obtained by these authors suggest that the value of the PK/PD indices AUC/MPC and T_{MSW} that prevents the selection of resistant mutants may also depend on inoculum size or the size of the bacterial population at the beginning of the treatment. High MPC for a given strain could be related to resistant subpopulations in the initial inoculum.[19,20] Taking into account these preliminary indices, which have not yet been established for enrofloxacin in birds, our results suggest that enrofloxacin at the administered dose in caracaras could have a therapeutic effect and avoid resistance against wild strains of *E coli* with MIC < 0.039 and MPC < 0.175 μg/mL. With high therapeutic doses, MPC of

Table 2. Efficacy indices obtained after intravenous and intramuscular administrations of enrofloxacin in southern crested caracaras (n = 4). Data are presented as mean ± SD.

Pathogen	Sensitive wild isolate MIC = 0.039 μg/mL MPC = 0.175 μg/mL		First-step mutation MIC = 1.83 μg/mL MPC = 4.5 μg/mL	
Escherichia coli[a]	Intravenous	Intramuscular	Intravenous	Intramuscular
C_{max}/MIC	196.35 ± 35.84	227.72 ± 22.77	1.88 ± 0.34	2.18 ± 0.22
AUC/MIC	1296.19 ± 262.39	1994.77 ± 369.15	12.40 ± 2.51	19.08 ± 3.53
AUC/MPC (h)	581.62 ± 117.74	895.09 ± 165.64	5.04 ± 1.02	7.76 ± 1.44
T>MIC (h)	44.27 ± 5.44	49.88 ± 4.46	0.36 ± 3.92	5.55 ± 2.05
$(\%)_{24h}$	(>100)	(>100)	(1.50)	23.11
T>MPC (h)	36.70 ± 4.11	42.24 ± 3.73	NA	NA
$(\%)_{24h}$	(>100)	(>100)	–	–
T_{MSW} (h)	0	0	NA	NA
$(\%)_{24h}$	0	0	–	–
	Sensitive wild isolate MIC = 0.40 μg/mL MPC = 1.05 μg/mL		First-step mutation MIC = 0.42 μg/mL MPC = 3.33 μg/mL	
Campylobacter jejuni[b]	Intravenous	Intramuscular	Intravenous	Intramuscular
C_{max}/MIC	8.59 ± 1.57	9.96 ± 1.00	8.18 ± 1.49	9.49 ± 0.95
AUC/MIC	56.71 ± 11.48	87.27 ± 16.15	54.01 ± 10.93	83.12 ± 15.38
AUC/MPC (h)	21.60 ± 4.37	33.25 ± 6.15	6.81 ± 1.38	10.48 ± 1.94
T>MIC (h)	14.72 ± 2.06	20.04 ± 2.07	14.26 ± 2.09	19.58 ± 2.05
$(\%)_{24h}$	(61.33)	83.51	(59.41)	81.58
T>MPC (h)	5.61 ± 3.08	10.84 ± 1.92	NC	NC
$(\%)_{24h}$	(23.36)	45.18	–	–
T_{MSW} (h)	9.11 ± 1.76	9.20 ± 0.99	NC	NC
$(\%)_{24h}$	37.97	38.34	–	–

Abbreviations: C_{max} indicates peak drug concentration; MIC, minimum inhibitory concentration; AUC, area under concentration-time curve; MPC, mutant prevention concentration; T, time; T_{MSW}, mutant selection window time; NA, not available (plasma concentrations <MPC); NC, not calculated (plasma concentrations >3.33 μg/mL ranged between 0 and 45 minutes or 30 and 90 minutes, after intravenous or intramuscular administration, respectively).

[a]MIC and MPC values previously described.[6]

[b]MIC and MPC values previously described.[7]

sensitive isolates (MPC <1.05 μg/mL) or intermediate strains (MPC <4.5 μg/mL) could be attained, whereas the concentrations needed for infections involving isolates with high MPC, especially those containing mutations in *gyrA* and *parC* genes, are practically unlikely to be achievable in vivo. This is especially true when T_{MSW} values are considered, which means not only the need to reach MPC values but also to maintain those concentrations. Taking all these data into account, we could conclude that the dose used in our study does not avoid the selection of resistant mutants for subpopulations with high MPC values and treatment with combinations of antimicrobials should be adopted. Nevertheless, these results should be interpreted very carefully, because MPC values were calculated for isolates from chickens,[13,14] a species in which the selection pressure is probably high because of the intensive use of these kind of antimicrobials.

Although there is no recommended dosage for enrofloxacin in southern caracaras, different values have been reported for other avian species (5–15 mg/kg q12h).[21] The optimal dosage of enrofloxacin in southern crested caracaras for the treatment of infections caused by microorganisms with a MIC = 0.25 μg/mL,[15] calculated according to an equation previously suggested,[16] would be 7.5 and 9.5 mg/kg q24h by the IV and IM routes, respectively. However, because MIC data of isolates from caracaras are not available, these calculations are made using a MIC breakpoint chosen on a basis of the susceptibility of isolates from other bird species.[8,15] The optimal dose calculated for the IM route is similar to that used in our study (10 mg/kg). Therefore, we consider the administration of 10 mg/kg of enrofloxacin by the IM route to be a good choice in crested caracaras against infections caused by microorganisms with MIC values ≤0.25 μg/mL. For less susceptible bacteria, a dose increase should be evaluated. To treat this species

by the IV route, the dose should be higher than the 5 mg/kg dose administered in our study; however, further studies should be conducted to assess possible side effects derived from an increase in the IV dose.

Acknowledgments: This study was performed as part of UBACyT project V603, supported by the Secretaria de Ciencia y Tecnica, Universidad de Buenos Aires. We thank Mr Mariano Diaz-Flores for technical assistance and the staff of the Servicio de Prestamo Interbibliotecario, Facultad de Veterinaria, Universidad Complutense de Madrid, for their invaluable help.

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