Osmotic pump maintains plasma concentrations of meloxicam for 6 days after orthopedic surgery in pigeons (*Columbia livia*)

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OBJECTIVE
To determine the plasma concentration of meloxicam delivered via an osmotic pump in pigeons undergoing orthopedic surgery and if an osmotic pump is a suitable alternative to repeated oral administration of this drug.

ANIMALS
16 free-ranging pigeons presented for rehabilitation with a wing fracture.

PROCEDURES
An osmotic pump filled with 0.2 mL of 40 mg/mL meloxicam injectable solution was implanted subcutaneously in the inguinal fold of 9 pigeons under anesthesia for orthopedic surgery. The pumps were removed 7 days postsurgery. Blood samples were collected before pump implantation (time 0) and 3, 24, 72, and 168 hours after pump implantation in 2 pigeons in a pilot study then at 12, 24, 72, and 144 hours in the 7 pigeons of the main study. The blood of 7 other pigeons receiving meloxicam at 2 mg/kg, PO, every 12 hours was also sampled between 2 to 6 hours after the last meloxicam administration. Plasma meloxicam concentrations were measured via high-performance liquid chromatography.

RESULTS
The plasma concentration of meloxicam was maintained at significant levels from 12 hours to 6 days after osmotic pump implantation. Median and minimum plasma concentrations in implanted pigeons were maintained at the same or higher level than those measured in pigeons that received meloxicam at a dose known to be analgesic in this species. No adverse effects attributable to either osmotic pump implantation and removal or meloxicam delivery were observed in this study.

CLINICAL RELEVANCE
Plasma concentrations levels of meloxicam in pigeons implanted with osmotic pumps were maintained at a similar concentration or higher than the suggested analgesic meloxicam plasma concentration in this species. Thus, osmotic pumps could represent a suitable alternative to the frequent capture and handling of birds for analgesic drug administration.

Medication can be challenging in avian patients especially in zoos or wildlife rehabilitation centers, requiring frequent capture and handling resulting in stress that can impact recovery and welfare. For this reason, there is a need to seek alternative methods for treatment delivery that can significantly reduce the frequency of these negative events for birds. Potential alternatives previously studied in birds include sustained-release or long-acting drug formulations,1–5 use of poloxamer hydrogels,6,7 and osmotic pumps.8 Osmotic pumps are miniature cylindrical implants able to deliver any liquid drug formulation present in its reservoir at a constant infusion rate by using the osmotic pressure difference between the patient’s interstitial fluid and the osmotic agent present in the pump.9 Osmotic pumps are commercially available in a range of sizes based on drug reservoir...
volume, pump rate, and duration. As a main drawback of this device, the osmotic pump needs to be implanted and removed under general anesthesia at the end of its expected duration. However, this is a minor problem in wildlife rehabilitation centers and zoos, as anesthesia is usually required for most procedures requiring handling and the act of implantation and removal represents a minor surgical act.

To date, the use of an osmotic pump has only been studied in a clinical setting in birds, in common peafowl (Pavo cristatus) for the administration of butorphanol. That study showed that the osmotic pump was able to maintain a steady state of plasma butorphanol concentration in common peafowl at or above the reported efficient analgesic concentrations within 24 hours of pump implantation and for at least 7 days before pump removal. However, further studies using other drugs in other species are needed to extend the potential for the therapeutic use of this device in a clinical setting.

Pigeons (Columba livia) are common in clinical practice including companion animals, zoological institutions, or wildlife rehabilitation settings. In addition, this species is much smaller than the common peafowl allowing the evaluation of whether osmotic pumps can be used without complications in a smaller bird species.

Meloxicam is an NSAID commonly used to treat pain in birds. Its pharmacokinetic properties have been evaluated in the pigeon but only by the IV route. Its pharmacodynamic properties have also been studied in pigeons but were not associated with a pharmacokinetic study. Therefore, an efficient dose of PO administration is known in pigeons but has not been transposed into an effective plasma concentration of meloxicam in this species. Such an effective plasma concentration has only been reported in avian species such as Hispaniolan Amazon parrots (Amazona ventralis), cockatiels (Nymphicus hollandicus), and emus (Dromaius novaehollandiae) to date. However, most of these studies focused on the anti-inflammatory properties of meloxicam in relation to its specific inhibitory effect on proinflammatory factors, while only the study in Hispaniolan Amazon parrots focused on its analgesic effect. Potential toxic effects of various doses of meloxicam have been studied in multiple avian species including pigeons, and no adverse effects have been reported even at high dosages in American kestrels (Falco sparverius). However, in 1 recent study, evidence of renal acute tubular injury and gout was observed in chickens.

The objective of the present study was to evaluate the ability of an osmotic pump to maintain plasma meloxicam concentration likely adequate to achieve analgesia over a 1-week period in pigeons presented for rehabilitation with a wing bone fracture based on a previous pharmacodynamic study of meloxicam in pigeons with femoral fracture undergoing surgical repair. To answer this objective, a secondary objective was to determine plasma meloxicam concentration in pigeons with the same treatment regimen as in the previously cited pharmacodynamics study to compare those concentrations to the ones achieved using an osmotic pump over time.

**Materials and Methods**

**Animals**

Nine adult free-ranging pigeons (Columbia livia) (mean ± SD body weight, 287 ± 28 g) presented to the Chuv Faune Sauvage rehabilitation center at the Ecole Nationale Vétérinaire d’Alfort for inability to fly due to appendicular wing fracture were included in this study. After admission to the rehabilitation center, the fracture was diagnosed by the veterinarian on site and an initial stabilization using a figure-of-eight bandage was performed. The bird received first care as required by its condition on arrival before transfer at the CHV Frégis for fracture management and inclusion in the study. Those first care included SC or IV lactate Ringer solution (B. Braun) at a dose or rate depending on clinical assessment of the dehydration status of the bird, force-feeding using a convalescence diet (Emerald Intensive Care Omnivore; EmerAid) at a dose of 25 mL/kg 3 times a day if anorectic, and opioid analgesia using tramadol at the dose of 10 mg/kg, PO, every 12 hours (Topaigic; Sanofi-Inventis). No meloxicam was administered to any bird at any time between admission and orthopedic surgery. The use of animals in this study was approved by Ecole Nationale Vétérinaire d’Alfort ethical committee (Comité d’Ethique en Recherche Clinique) file No. 2019-04-27.

**Osmotic pump and dosage calculation**

Osmotic pumps used in this study are 3 cm in length, 0.7 cm in diameter, and weigh 1.1 g (Azlet 2001 pump; Durect Corp). Each pump has a 0.2-mL volume reservoir and is able to deliver medication at the manufacturer-specified rate of 1 µL/h for 7 days. These pump characteristics are based on osmolality and body temperature for mammals. Calculations to better fit the physiology of avian species were obtained by use of an equation given by the manufacturer (Table 1) resulting in an adjusted pump rate for pigeons estimated at 1.2 µL/h using the Azlet 2001 pump.

Table 1—Equations used to estimate meloxicam solution concentration necessary to fill the osmotic pump with to reach target meloxicam plasma concentration in pigeons.

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<td>Equation 1</td>
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<td>Equation 2</td>
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<td>Equation 3</td>
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BW = Body weight with a mean of 287 g in the subjects used. e = Base of natural logarithm. MSPRM = Manufacturer-specified pump rate for mammals. Osm = Osmolality reported at 335 mosmol/kg in pigeons. T = Body temperature defined as 40°C for pigeons.
The target meloxicam plasma concentration and clearance were used to calculate the infusion rate. At this point of the study, the analgesic meloxicam plasma concentration was not available in pigeons; therefore, the concentration of 3.45 µg/mL that has been shown to be analgesic in Hispaniolan Amazon parrots was used for the calculation purposes at this stage. Clearance of 39 mL/kg/h was taken based on the results of a pharmacokinetic study evaluating IV administration of meloxicam in pigeons. Taking those data into account, an infusion rate of 134.6 µg/kg/h was calculated following the second equation in Table 1.

The concentration of meloxicam solution needed to fill each 0.2-mL osmotic pump was then calculated using the previously calculated infusion rate and adjusted pump rate for pigeons resulting in a required meloxicam solution concentration of 32.2 mg/mL (third equation in Table 1). Meloxicam injectable solution at 40 mg/mL (40 mg/mL Metacam; Boehringer) was used in osmotic pumps without dilution for all individuals in this study to simplify the procedure and avoid potential phase separation inside the pump with diluent.

**Study procedures**

Once admitted at CHV Frégis, each pigeon was anesthetized with isoflurane via a face mask to perform orthogonal radiographic views of the affected wing and orthopedic surgery was planned for the following day. The osmotic pump was primed overnight before the surgery day as recommended by the manufacturer. Briefly, the pump was aseptically filled with 0.2 mL of 40 mg/mL meloxicam solution and left in sterile 0.9% NaCl solution at 37°C overnight (Figure 1).

The following day, the bird was premedicated with a combination of midazolam 0.5 mg/kg and 1 mg/kg butorphanol injected intramuscularly before induction with isoflurane via face mask. All birds were intubated using a 2.5 mm uncuffed endotracheal tube. The bird was then placed on dorsal recumbency, and the inguinal area was aseptically prepared for insertion of the osmotic pump subcutaneously. Under aseptic conditions, a small skin incision (approx 1 cm) was made on the inguinal fold to allow insertion of the pump after gentle subcutaneous dissection cranially. Once the pump was placed, the incision was closed with 1 or 2 single interrupted stitches (PDS 4-0). Orthopedic surgery was then performed using the most appropriate internal fixation technique considering the fractured bone and the fracture characteristic with the aim of recovery of full flight ability. Birds were then kept for 1 week at CHV Frégis for daily monitoring and blood sampling for plasma meloxicam dosages. After surgery, tramadol (10 mg/kg per, PO, q 12 h for 4 days; Topalgic; Sanofi-Inventis) was used for analgesia management, and antibiotic coverage (oxytetracycline at 40 mg/kg, IM, q 24 h for 7 days; Terramycine; Zoetis) was prescribed to prevent infection risk from fracture site considering the free-ranging origin of the bird and the multiple surgical procedures performed. A figure-of-eight bandage was maintained for wing support and to restrict movement in the immediate week postoperatively, but it was reapplied every 48 h allowing surgical wound care. The site of pump insertion was monitored daily for any sign of infection, inflammation, or dehiscence. After 1 week, the birds were again anesthetized with isoflurane via face mask for the first radiographic follow-up and removal of the osmotic pump. The inguinal region where the pump was inserted was again aseptically prepared, sutures were removed, and as there was only partial or little healing of the insertion site, the pump was easily retrieved. The incision was then again closed using 1 or 2 single interrupted stitches (PDS 4-0). The birds were then returned to the rehabilitation center for the rest of the rehabilitation process.
Establishment of analgesic meloxicam plasma concentration

To establish if an osmotic pump achieves analgesic meloxicam plasma concentration in the pigeons of the present study, this concentration has to be estimated since it is not available to date in the literature. However, a pharmacodynamic study previously showed that meloxicam given PO at the dosage of 2 mg/kg every 12 hours achieved analgesia in pigeons after orthopedic surgery for all the intervals between 2 administrations. Therefore, 7 additional pigeons receiving meloxicam at 2 mg/kg PO, every 12 hours for other pathological conditions at the rehabilitation center were recruited. A blood sample (1 mL) was obtained from the ulnar or metatarsal vein between 2 and 6 hours after meloxicam administration for plasma meloxicam assay. The blood was collected in EDTA microtubes and centrifuged within 10 minutes after sampling. Plasma was then isolated and kept frozen at −18°C until the meloxicam level was analyzed (shipped on ice to the laboratory in the next few weeks after collection).

Plasma meloxicam concentration

Chemical reference analytes of meloxicam and the internal standard (IS) piroxicam were purchased from Sigma-Aldrich. A peak area ratio of the drug to the IS was used for quantitation. Each standard solution was accurately weighed and diluted in methanol using the sodium form of meloxicam correcting for the sodium weight to allow this dissolution in methanol. The final calibration curve contains concentrations ranging from 10 to 0.2 μg/mL in the mobile phase. Quality control samples were performed every 6 samples at 1 μg/mL with an accuracy of 100.9% and a variation coefficient of 4.4% to assess its precision.

Plasma samples were prepared as follows: to an aliquot of 0.25-mL plasma sample in a 10-mL glass tube, 25 μL of IS solution (10 μg/mL solution) and 5 mL acetonitrile were added and vortex-mixed for 1 min, followed by centrifugation at 3,500 rpm for 5 min. Next, the upper clear layer solutions were transferred in a new tube and evaporated to dryness under nitrogen in a water bath at 45°C. Then, the samples were dissolved in 0.25 mL mobile phase, and 75 μL was injected by the autosampler.

Liquid chromatography was performed in an Agilent 1260 affinity and a G7117C Diode array detector (Agilent Technologies) at 355 nm. The analytical column was a Nucleosil C18 particle size of 5 μm, 150 (length) X 4.6 mm (inner diameter) (Macherey-Nagel). The mobile phase consisted of a mixture of acetonitrile (solvent A) and 0.2% formic acid in deionized water (solvent B), eluted at a flow rate of 1 mL/min using a gradient elution of 30 to 80% of solvent A in 6 min.

Blood sampling: pilot study

A pilot study was first performed on 2 pigeons to allow further adjustment to the blood sampling timetable if necessary. A blood sample (1 mL) was obtained from the ulnar or metatarsal vein during the first anesthesia for the radiographs (time = 0 hours), and additional samples were collected at 3 hours, 24 hours, 3 days, and 7 days after. The blood samples were handled and analyzed as previously described.

Blood sampling: main study

Considering the very low plasma concentration in the 2 pigeons from the pilot study at 3 hours and 7 days after surgery, those time points were replaced by samples at 12 hours and 6 days after surgery for the 7 birds of the main study. The blood samples were handled and analyzed as previously described.

Data presentation

For data analysis, pigeons from the pilot and main studies were considered together given they differed only by 2 sampling times without any other alteration in the experimental protocol so with no reason to suppose differences in result for common sampling times (T0, T + 24 h, and T + 3 days). Considering the small number of subjects and the fact that not all times were measured in all subjects, data are presented using median, minimum, and maximum values. All data manipulations and graphs were made using Excel 2019 (Microsoft Corporation).

Results

Outcomes

Of the 9 pigeons included in this study, 3 went through the entire rehabilitation process and were released without complication, 2 died accidentally due to predation in the outdoor rehabilitation aviary a few days before their release (an unknown predator managed to create a hole in the aviary at night, which was then repaired without any further similar incident reported afterward), and 3 were euthanized for reasons unrelated to the meloxicam administration with the osmotic pump (1 developed severe neurologic signs consistent with paramyxovirus infection 1 month after surgery at the end of its rehabilitation process, 1 presented a severe shoulder ankylosis after removal of its humeral surgical device 3 weeks after surgery and did not improve after 1 week of physical therapy, and 1 presented with surgical device failure on follow-up radiographs 1 week after surgery and would not be releasable). Finally, 1 bird died 3 days after surgery and osmotic pump insertion, and thus the blood sample was not available 6 days after pump implantation in this bird. A complete postmortem examination was performed in this case and macroscopic examination revealed diffuse white deposits on serosal surfaces of the heart, liver, and the rest of coelomic viscera. There were no other macroscopic abnormalities. Histopathological examination revealed findings consistent with acute infection (but without any specific agent seen) with secondary severe dehydration and visceral gout. Overall, no complications were associated with the procedure of pump insertion or removal throughout the study, and all inguinal wounds created for
Establishment of analgesic meloxicam plasma concentration

The results of the plasma concentration of meloxicam measurements in pigeons having received 2 mg/kg, PO, of meloxicam are presented (Table 2) with a median and minimum concentration of 2.1 µg/mL and 0.36 µg/mL, respectively.

Table 2—Plasma meloxicam concentrations (in µg/mL) in 7 pigeons at 1 time point between 2 and 6 hours after administration of 2 mg/kg, PO, of meloxicam.

<table>
<thead>
<tr>
<th>Plasma meloxicam concentration (µg/ml)</th>
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<tbody>
<tr>
<td>5.34</td>
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<tr>
<td>2.10</td>
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<tr>
<td>1.13</td>
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<tr>
<td>3.11</td>
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<tr>
<td>0.85</td>
</tr>
<tr>
<td>5.24</td>
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<tr>
<td>0.36</td>
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</table>

Plasma meloxicam concentration

The results of the plasma concentration of the meloxicam measurements in pigeons with osmotic pump are presented (Table 3 and Figure 2). All pigeons had concentrations below the limit of quantification before osmotic pump implantation. After

Table 3—Plasma meloxicam concentrations (in µg/mL) in 9 pigeons (pigeons 1 and 2 are from the pilot study) at different time after implantation of the osmotic pump filled with 0.2 mL of 40 mg/mL meloxicam solution.

<table>
<thead>
<tr>
<th>Time</th>
<th>Pigeons</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>0 0 0 0 0 0 0 0 0</td>
</tr>
<tr>
<td>T + 3 h</td>
<td>0.29 &lt; 0.2 NM NM NM NM NM NM NM</td>
</tr>
<tr>
<td>T + 12 h</td>
<td>NM NM 1.94 2.42 1.99 0.7 2.48 2.09 5.22</td>
</tr>
<tr>
<td>T + 24 h</td>
<td>3.08 1.92 2.49 2.19 3.3 1.34 2.91 5.08 4.48</td>
</tr>
<tr>
<td>T + 3 d</td>
<td>3.19 2.64 4.08 1.82 2.12 1.36 2.6 1.29 5.85</td>
</tr>
<tr>
<td>T + 6 d</td>
<td>NM NM 3.15 2.01 2.68 2.04 1.1 NM 2.25</td>
</tr>
<tr>
<td>T + 7 d</td>
<td>&lt; 0.2 0.2 NM NM NM NM NM NM NM</td>
</tr>
</tbody>
</table>

0 = Less than the limit of detection. < 0.2 = Less than the limit of quantification. NM = Not Measured.

Pigeons from the pilot and main studies were regrouped in the same table explaining why some time points are missing for some pigeons.

Figure 2—Box plot of plasma concentration of meloxicam in 7 pigeons 2 to 6 hours after receiving 2 mg/kg meloxicam, PO (left) and in 9 pigeons with subcutaneously implanted osmotic pump containing 0.2 mL of 40 mg/mL meloxicam solution for 1 week. Each point represents a pigeon. Median (red line) and minimum (dashed red line) plasma concentration of meloxicam from the 7 pigeons PO is reported on the right for comparison.
implantation, despite a rather high variability, the median and minimum concentrations in pigeons with osmotic pumps were respectively, equal to or higher, from 12 hours to 6 days after implantation, than the median and minimum concentrations found in pigeons that received 2 mg/kg of meloxicam, PO. The maximum concentration in pigeons with the osmotic pump was below the minimum concentration in pigeons that received 2 mg/kg meloxicam PO at 3 hours and at 7 days after pump implantation.

**Discussion**

Although high variability was noted, the use of the osmotic pump allowed maintenance of plasma meloxicam concentration at levels above 1 µg/mL from 12 hours to 6 days after pump implantation, which is above the reported efficient concentration in most mammalian species. Efficient plasma meloxicam concentration in pigeons is not reported to date but a pharmacodynamic study performed on pigeons in postoperative period of orthopedic surgery reported analgesic efficacy of meloxicam at 2 mg/kg, PO, every 12 hours. In that study, analgesia was reported at each time points between meloxicam administrations. In an attempt to approximate an efficient plasma concentration of meloxicam in pigeons, it was measured in the 7 pigeons receiving meloxicam at the same dosing regimen as in that pharmacodynamic study. Despite great variability in these measurements, it demonstrates that the osmotic pump maintained plasma meloxicam concentrations similar or higher than those found using oral dosing of meloxicam at 2 mg/kg, PO, every 12 hours. This dosage had been shown to provide analgesia in the pharmacodynamic study in pigeons. Based on those findings, the authors suggest that osmotic pumps used in this study filled with 0.2 mL of 40 mg/mL meloxicam solution are able to provide adequate analgesia in pigeons from 12 hours to 6 days after pump implantation at least for the postoperative period of orthopedic surgery. The analgesic effect in our cohort could not be formally evaluated and compared because all pigeons were presented with different types of fracture, have undergone different procedures, and have unknown backgrounds before presentation; therefore, further study would be required to formally confirm the analgesic effect of meloxicam in pigeons using osmotic pumps as used in the present study.

The plasma meloxicam concentration was still low and below the minimum plasma concentration found in pigeons with the PO dosage regimen 3 hours after implantation of the osmotic pump. This finding suggests that, despite priming of the osmotic pump performed according to the manufacturer’s recommendations, several hours were still required to allow the pump to achieve a steady-state plasma meloxicam concentration. Practically, a first dose of meloxicam at 2 mg/kg, PO, as it has been shown to provide analgesia in pigeons for at least 12 hours could be considered at the time of osmotic pump implantation to provide appropriate analgesia during this postimplantation period. However, the potential for adverse effects associated with this protocol given the cumulative effects with the osmotic pump is not known at this time and further study would be needed.

Overall, the performances of the osmotic pump in this study were below expectations in terms of plasma concentration achieved, as well as the duration of osmotic pump apparent drug delivery when using the data made available by the manufacturer. The initially targeted meloxicam plasma concentration was never achieved except in 2 pigeons at 3 time points despite the fact that the drug concentration used to fill the pump reservoir was 25% higher than the concentration required using the equations recommended by the manufacturer. This could be explained by the inadequacy of some parameters used in these equations such as clearance based on IV administration, which was the only value available at the time of the study in pigeons, or the inaccurately calculated adjusted pump rate secondary to the difference between the theoretical temperature and/or osmolality values reported in literature and the true values in the pigeons of the present study, which had been a potentially very different physiologic state (e.g., dehydration, inflammation due to fracture, and surgery) than their healthy counterparts.

Another point of note was the duration during which the osmotic pump was able to maintain significant plasma meloxicam concentrations. The manufacturer states 7 days of working time for the osmotic pump model used in the present study. However, the results of our study indicate that significant plasma concentrations were only achieved for 6 days. This discrepancy can be explained by the fact that the adjusted pump rate for pigeons (1.2 µL/h) is 20% higher than the stated infusion rate set by the manufacturer for mammals (1 µL/h); therefore, given the pump reservoir capacity is 200 µL according to the previously mentioned pump rate, the expected duration of pump delivery would be 6.9 days in birds and 8.3 days in mammals, which is also consistent with our results showing an arrest of the pump function between 6 and 7 days taking into account the 12 hours of priming before implantation. Thus, it was expected that the pump will stop delivering the drug sooner than stated by the manufacturer. It is also consistent with the fact that the pumps removed at 7 days were observed to have an empty reservoir. However, this reduction effect in duration was not observed in the study in common peafowl but a different bigger model was used in that study.

No complications were observed in this study secondary to the pump implantation or removal, which is consistent with the previous report. Concerning the bird that died during the study, histopathological lesions were consistent with an unknown infectious process resulting in cardiac and renal lesions, which may have been associated with dehydration resulting in visceral gout. Indeed, the renal histopathologic lesions consisted of mild tubular interstitial nephritis (consistent with the infectious systemic disease along with similar lesions in the heart), tubular dilatation with urates (consistent
primarily with dehydration), and nonspecific signs of renal dysfunction (tubular dilatation and mineralizations as well as mineralization of proventricular glands). Meloxicam has recently been reported to cause renal lesions in chickens using high dosages of 5 mg/kg twice a day for 5 days. NSAIDs other than meloxicam such as ketoprofen or diclofenac are reported to cause renal lesions, especially in eiders (Somateria spp) and old-world vulture species (Gyps spp), respectively. However, in all those cases, the main histopathological lesions consisted of renal tubular epithelium degeneration and necrosis associated with the presence of protein casts and the formation of urate tophi, which was not observed in the present pigeon. In this case, the direct cause of death was visceral gout most likely due to severe dehydration secondary to the inability to fly due to the wing fracture along with a likely systemic infectious disease. Furthermore, while renal damage is described in birds with the NSAIDs mentioned above, this has been demonstrated in birds using meloxicam only in 1 study in chickens using a high dosage that was much higher than what was delivered in the present study. In the present case, about 0.1 mL of meloxicam was retrieved from the osmotic pump reservoir after the death of this pigeon; therefore, it received a total dose of 4 mg, eg, 12 mg/kg over 3 days, which represents exactly the recommended dose at present in pigeons (2 mg/kg q 12 h). It seems therefore unlikely that meloxicam played a role in the death of that pigeon but this hypothesis cannot be ruled out completely.

One main limitation of the present study was the low number of cases that resulted in a reduced number of measurements for each time point. However, despite this limitation, the results of this study clearly show (Figure 2) that the use of an osmotic pump allows a plasma meloxicam concentration in pigeons that falls into the range of plasma concentrations when using PO administration at recommended dosages that were shown in a previous study to provide analgesia in this species. Another main limitation was the size of the birds used in this study, which precludes frequent blood sampling and therefore limited the number of time points. This led to a less precise cut-off for the start and end of efficient pump delivery of meloxicam between 3 and 12 hours and 6 and 7 days postpump implantation, respectively. Finally, the interpretation of this study is impaired by the lack of comprehensive pharmacokinetic study in pigeons for meloxicam via routes other than IV and testing the current recommended dose of 2 mg/kg, PO, that is based only on clinical pharmacodynamic data. Establishing the efficient plasma meloxicam concentration in pigeons as was performed in Hispaniolan Amazon parrot would allow for a more precise interpretation of the present study, although the few additional plasma meloxicam concentration measurements performed here already allow confidence in the ability of osmotic pump to achieve efficient plasma meloxicam concentration with the protocol presented in this study. However, further study with proper pharmacokinetic modeling and calculation in more pigeons in tandem with a pharmacodynamic study would be required to fully confirm this interpretation.

Another potential limitation of our study could lie in the apparent contradiction between the main goal of using prolonged drug delivery systems to avoid daily handling of the patient for medication and the fact that we still prescribed other daily medications (oxytetracycline and tramadol) during this study. The choice of these drugs and treatment plan was made to avoid adding more complexity to the study and because the pigeons were to be regularly handled for blood samples. In a field setting, alternative prolonged drug delivery systems could also be used for these treatments. For further analgesia, tramadol could have been replaced by butorphanol also delivered via an osmotic pump and antibiosis could have been also performed using an injectable for IM administration with 5 to 7 days efficiency. In that way, those pigeon cases could have been managed entirely without handling except for the osmotic pumps implantation and removal.

In conclusion, subcutaneously implanted osmotic pumps filled with 0.2 mL of 40 mg/mL meloxicam solution allow maintenance of a presumed analgesic plasma concentration of meloxicam from 12 hours to 6 days after implantation in pigeons without observable side effects. The use of osmotic pumps therefore represents an alternative for the management of analgesia in pigeons that allows a considerable reduction in the frequency of capture and handling, which is very valuable in zoos and wildlife rehabilitation settings. Further studies using different drugs in different species are required to extend the use of the osmotic pump in birds.

Acknowledgments

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