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Safety of meloxicam to critically endangered *Gyps* vultures and other scavenging birds in India

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Abstract

Widespread veterinary use of the non-steroidal anti-inflammatory drug diclofenac is responsible for the population collapse of three species of *Gyps* vulture in south Asia; these species are now critically endangered. Vultures die when they consume carcasses of livestock that contain lethal residues of diclofenac. National and international conservation organizations have urgently recommended that diclofenac be banned and replaced with alternative drugs that are relatively safe to *Gyps* vultures and other scavenging birds. We tested the safety of the NSAID meloxicam on the oriental white-backed vulture, long-billed vulture and a range of other scavenging birds in India (Egyptian vulture *Neophron percnopterus*, cattle egret *Bubulcus ibis*, house crow *Corvus splendens*, large-billed crow *Corvus machrorhynchos* and common mynah *Acridotheres tristis*). Meloxicam was administered by oral intubation [at 0.5 and 2.0 mg kg^{-1} vulture body weight (bw)], or through feeding with muscle or liver tissue (at 0.3 to 2.1 mg kg^{-1} vulture bw) from meloxicam-treated buffalo *Bubalus bubalis*. We estimate that 2.0 mg kg^{-1} bw is the maximum likely exposure in the wild. All 31 *Gyps* vultures and the 20 other scavenging birds given meloxicam survived. Feeding behaviour remained normal and there were no significant differences between the treated and control groups in body mass, or the blood haematology and biochemistry parameters monitored, including those known to be affected by diclofenac (uric acid levels and alanine transferase activity). Meloxicam is used to treat a wide range of livestock ailments and is licensed and manufactured in India. We recommend that meloxicam be introduced as rapidly as possible across the Indian sub-continent as an alternative to diclofenac.

Introduction

The major role played by the veterinary drug diclofenac in the population collapse of *Gyps* vulture species endemic to south Asia is now well supported by several lines of evidence (Green *et al*., 2004; Oaks *et al*., 2004; Shultz *et al*., 2004). Diclofenac, a non-steroidal anti-inflammatory drug (NSAID), is routinely used in India, Nepal and Pakistan for the management of pain and inflammation in injured and diseased livestock (Oaks *et al*., 2004). Vultures are exposed to diclofenac when they consume the carcasses of livestock that were dosed with the drug shortly before death. Consumption by vultures of diclofenac-contaminated tissues results in renal failure, and they die within days of exposure with clinical signs of extensive visceral gout. These clinical signs and residues of diclofenac have been found in a high proportion of vultures found dead in the wild, as well as in experimentally dosed vultures (Oaks *et al*., 2004; Shultz *et al*., 2004; Swan *et al*., 2006*a*). Population modelling demonstrates that just 0.1–0.8% of carcasses need to contain lethal levels of diclofenac to have caused the observed decline in vulture numbers, and that the proportion of dead vultures showing post-mortem evidence of diclofenac poisoning is consistent with it being the sole or major cause of the observed population declines (Green *et al*., 2004). In 2003, populations of three *Gyps* vulture species, which used to number tens of millions, had collapsed to less than 5% of their levels in the early 1990s (Gilbert *et al*., 2002; Prakash *et al*., 2003; Green *et al*., 2004), and continue to decline at 22–48% a year (Green *et al*., 2004). The three affected species [oriental white-backed vulture (OWBV) *Gyps bengalensis*, long-billed vulure *Gyps indicus* and slender-billed vulture *Gyps tenuirostris*] are all now listed as critically endangered (IUCN, 2004).

National and international organizations agree that a rapid ban on the veterinary use of diclofenac within the Indian sub-continent is essential to prevent the extinction of these species (Anon., 2006). To help facilitate a ban on veterinary diclofenac, it is necessary to identify alternative NSAIDs that are relatively non-toxic to vultures and can be used to replace diclofenac for the treatment of livestock. The results of questionnaire surveys of zoo and veterinarians on the clinical treatment of vultures identified the NSAID meloxicam as a suitable potential alternative, with 39 birds from six species of *Gyps* vulture known to have been treated with this drug (Cuthbert *et al.,* in press). In a phased programme of safety testing on the closely related African white-backed vulture *Gyps africanus*, meloxicam was administered to vultures by oral dosing or through the consumption of tissues from meloxicam-dosed cattle (Swan *et al*., 2006*b*). A total of 43 birds were treated and 40 birds received meloxicam doses that were higher than the maximum levels of exposure they would theoretically be exposed to in the wild. There were no mortalities after dosing with meloxicam, and levels of alanine transferase (ALT) and uric acid in the blood, which increase in diclofenac treated birds before death (Swan *et al*., 2006*a*), remained constant throughout the trials (Swan *et al*., 2006*b*). To confirm the safety of meloxicam to Asian vulture species, the final phase of testing treated *G. bengalensis* and *G. indicus* within India: and again, all birds survived (Swan *et al*., 2006*b*).

With the decline in vulture numbers across Asia, there are increased feeding opportunities for other scavengers. Livestock carcasses in India now attract large numbers of feral dogs, leading to an increase in their population (Anon., 2006), where formerly *Gyps* vultures would have dominated (Houston, 1983). Excluding *Gyps* vultures, raptors and other scavenging bird species observed on carcasses include cinereous vulture *Aegypius monachus*, Egyptian vulture *Neophron percnopterus*, red-headed vulture *Sarcogyps calvus*, steppe eagle *Aquila nipalensis*, black kite *Milvus migrans*, cattle egret *Bubulcus ibis*, house crow *Corvus splendens*, jungle crow *Corvus machrorhynchos* and common mynah *Acridotheres tristis*. Two of these species (Egyptian vultures and red-headed vultures) have recently undergone rapid population declines, possibly as a result of diclofenac poisoning (Cuthbert *et al*., 2006). Other scavenging species within the region that may also potentially come into contact with contaminated carcasses include greater and lesser adjutants *Leptoptilos dubius* and *Leptoptilos javanicus*, which are both globally threatened. As a consequence, and because there is inter-specific variation in the toxicity of NSAIDs (Anderson, Piper & Swan, 2005), it is vital that any alternative to diclofenac is safe, at the likely exposure levels, to *Gyps* vultures and also safe, or of low toxicity, to other scavenging birds.

In this study, we present the results of safety testing of meloxicam on critically endangered *Gyps* vulture species and other scavenging birds within India. Data on clinical observations and survival of *G. bengalensis* and *G. indicus* after oral treatment with meloxicam have already been presented in Swan *et al*. (2006*a*,*b*). Here, we present further information on blood haematology and biochemistry of meloxicam-treated birds and also on the safety of meloxicam to scavenging species other than *Gyps* vultures, namely: Egyptian vultures, cattle egrets, large billed crows *C. macrorhynchos* and house crows and common mynahs. Lastly, in order to replicate the natural route of exposure and to ensure that there are no toxic meloxicam metabolites produced by livestock, we fed *G. bengalensis* and *G. indicus* muscle and liver tissues from buffalo *Bubalus bubalis* that had been dosed with double the highest normal veterinary dose of meloxicam before slaughter.

Materials and methods

Experimental design

The trials were held at the Vulture Conservation Breeding Centre (VCBC), Haryana State, India. Meloxicam testing was undertaken over three phases between June 2005 and April 2006. Safety testing was undertaken on OWBV and long-billed vultures permanently held captive at the VCBC. Individuals from the five other scavenging species were captured from the wild and held at the centre for the duration of the trials. All individuals spent a minimum of 5 days in captivity before testing.

Details of the numbers of birds treated and the experimental schedule for the three phases of safety testing are presented in Table 1. Birds in phases I and II were administered meloxicam 0.5% (Melonex, each millilitre containing Meloxicam BP 5 mg; marketed by Intas Pharmaceuticals Ltd, Ahmedebad, India) as a single dose by oral gavage, with the gavage tube flushed with 2 mL of water. In phase I, doses of meloxicam administered by gavage were 0.5 or $2\,mg\,kg^{-1}$. In phase II, all birds were dosed at $2\,mg\,kg^{-1}$. A dose of $2\,mg\,kg^{-1}$ meloxicam was selected for safety testing, as this is the estimated maximum likely exposure in the wild (see Swan *et al*., 2006*b*). To minimize the risk to the birds in phase I, meloxicam dosing was staggered, with injured non-releasable birds treated first. The initial two non-releasable birds were first treated at the lowest dose of $0.5\,mg\,kg^{-1}$, along with one sham-dosed control bird (treated with distilled water). After 48 h, no apparent ill effects of the treatment were observed, and hence, a further three birds were dosed at $0.5\,mg\,kg^{-1}$, and two non-releasable birds were given a $2\,mg\,kg^{-1}$ dose. After another 48 h, the last three birds were also dosed at $2\,mg\,kg^{-1}$ (along with two final control birds).

In phase III of safety testing, vultures were given tissues from buffalo treated with a course of meloxicam. To ensure that vultures received tissues with high meloxicam levels, buffalo were administered a 5-day course of meloxicam with daily subcutaneous injections at a dosage of $1.0\,mg\,kg^{-1}$ body weight (bw), which is twice the highest normal veterinary dose. Two animals were slaughtered 8 h after the last dose, when meloxicam concentrations in liver and muscle tissues were likely to be the highest. Two entire livers were collected along with samples of muscle tissue from throughout the body of both animals. Muscle samples were not

Table 1 Experimental schedule for meloxicam safety testing indicating the phase of study, species, treatment, dose administered, route of administration and the sample size of birds. Species treated are: Oriental white-backed vulture *Gyps bengalensis*, long-billed vulture *Gyps indicus*, Egyptian vulture *Neophron percnopterus*, cattle egret *Bubulcus ibis*, crow species (house *Corvus splendens* and large-billed crow *Corvus macrorhynchos*) and common myna *Acridotheres tristis*

Phase	Species	Treatment	Dose mg kg^{-1} bw	Route	*n* birds
I	*G. bengalensis*	Meloxicam	0.5	Oral gavage	3
I	*G. bengalensis*	Meloxicam	2.0	Oral gavage	3
I	*G. bengalensis*	Control	–	Oral gavage	2
I	*G. indicus*	Meloxicam	0.5	Oral gavage	2
I	*G. indicus*	Meloxicam	2.0	Oral gavage	2
I	*G. indicus*	Control	–	Oral gavage	3
II	*N. percnopterus*	Meloxicam	2.0	Oral gavage	5
II	*N. percnopterus*	Control	–	Oral gavage	4
II	*B. ibis*	Meloxicam	2.0	Oral gavage	5
II	*B. ibis*	Control	–	Oral gavage	4
II	*Corvus* sp.	Meloxicam	2.0	Oral gavage	5
II	*Corvus* sp.	Control	–	Oral gavage	5
II	*A. tristis*	Meloxicam	2.0	Oral gavage	5
II	*A. tristis*	Control	–	Oral gavage	5
III	*G. bengalensis*	Meloxicam	0.3–0.5	Treated muscle	12
III	*G. bengalensis*	Meloxicam	0.5–2.1	Treated liver	7
III	*G. bengalensis*	Control	–	Control muscle	5
III	*G. indicus*	Meloxicam	0.5	Treated muscle	2

Data in phase I are also reported in Swan *et al.* (*2006b*), bw; body weight.

taken from around the meloxicam injection site. Single samples of muscle, liver and kidney tissue were taken from each of the two slaughtered buffalo for meloxicam analysis. Treated buffalo liver and muscle tissues were fed to seven and 14 vultures, respectively. The seven birds given liver (which contained meloxicam levels over six times higher than those found in muscle; see 'Results') were all non-releasable individuals, and included the three non-releasable birds used in phase I of testing. These seven birds were habituated to feeding on uncontaminated (NSAID-free) liver for 1 week before the experiment, to ensure that they were used to consuming liver tissue. Birds fed buffalo tissues were housed in aviaries holding three and four birds (fed liver), and five and nine birds (fed muscle). In order to ensure that all birds had access to food and to quantify the amount taken, muscle and liver tissue was cut into small pieces between 20 and 30 g in mass (mean mass = 26.3 ± 2.6 g, $n = 100$). Feeding was filmed so that the number of pieces consumed and mass of liver ingested could be estimated for each bird. Vultures given muscle tissue were observed during feeding and the crops of all birds (in both treatments) were observed after feeding to ensure that they had taken a meal. A further five vultures were fed a whole skinned goat *Capra hircus* to serve as a control group. Goats are kept by VCBC for 7 days before slaughter to ensure that they are free from diclofenac or other NSAIDs (M. Taggart, unpubl. data).

Blood sampling and analysis

NSAIDs act rapidly and *Gyps* vultures treated with diclofenac died within 2 days of treatment (Swan *et al.*, 2006*a*). Consequently, observations on toxicity and blood biochemistry were measured 48 h after dosing. For birds in phases I and II, blood samples were taken before dosing (at 0 h) and at 48 h following treatment by oral gavage. In phases I and II, body mass was recorded at 0 h (to the nearest 0.1 kg), and retaken at 7 days and 48 h, respectively. In phase III, blood samples and body mass were only taken at 48 h, as it was highly likely that the disturbance from handling would have stopped the birds from feeding. No blood samples were taken from common mynahs as their small size did not allow sufficient blood to be collected for blood haematology and biochemistry analysis. In all three phases, birds were observed for a period of 7 days for signs of toxicity and abnormal feeding behaviour. Blood samples were collected by direct veno puncture from the brachial or median metatarsal veins. The blood haematology and biochemistry parameters quantified were as follows: total erythrocyte count (TEC), packed cell volume (PCV), haemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), total leucocyte count (TLC), % heterocytes and % lymphocytes as per the standard methods (Jain, 1986). Uric acid (Span Diagnostics, Surat, India), creatinine (Technopharmachem, M.I.E., Haryana, India), total protein (Qualigens Diagnostics, Mumbai, India), albumin (Qualigens Diagnostics), ALT (Span Diagnostics) and aspartate transferase (AST) (Span Diagnostics) were estimated spectrophotometrially (ECIL Model UV5704SS) using standard kits.

Extraction of meloxicam from tissues/plasma was achieved using 0.5 g of sample extracted using 2 mL of HPLC-grade acetonitrile (MeCN). The sample was weighed into a new glass test tube, MeCN was added and the mixture was homogenized for 30 s using an Ultra Turrax IKA T8

Homogenizer (IKA Labortiehnik, Germany). The mixtures were then centrifuged at $1000 \times \boldsymbol{g}$ for 5 min and the supernatant was filtered using disposable PTFE/PE syringe filter units of 0.45 μm. The filtered extract was then stored in crimp top LC vials at $-20\,^{\circ}C$ until analysis. Meloxicam levels were determined by LC–ESI/MS (liquid chromatography–electrospray ionization mass spectrometry) using an Agilent 1100 series instrument 1946D (Agilent, Santa Clara, CA, USA). The instrument was calibrated using six standards ranging from 25 to 1000 $\mu g\,L^{-1}$ in meloxicam concentration, generated using meloxicam sodium salt (Sigma-Aldrich, St Louis, MO, USA, M3935). The calibration was linear across this range, with an r^2 value of at least 0.99. Meloxicam was monitored by the MS at the mass/charge ratio of 352 in the positive ion mode. Chromatographic separation was achieved on the LC using a Waters Xterra (Waters Xterra, Milford, MA, USA) MS C18 column (3.9 mm $\times$ 150 mm, 5 μm). Samples and standards (20 μL) were subjected to a binary gradient elution profile using 0.1% acetic acid in water and 100% MeCN. The flow rate was set at $0.7\,mL\,min^{-1}$. The limit of quantification (LOQ) for this technique (back calculated to wet tissue/plasma concentration) was found to be $7\,\mu g\,kg^{-1}$.

Statistical analysis

In phases I and II, the effect of meloxicam dosing on each blood haematology and biochemistry parameter was analysed by two-way ANOVA, with Treatment (meloxicam or control) and Period (pre- and post-dosing) as the main effects and Treatment $\times$ Period as an interaction effect. In phase III, where blood parameters for the three groups (liver, muscle, control) were only measured at 48 h, the results were analysed by one-way ANOVA. Because of the large number of variables measured, we used a Bonferroni correction to set an appropriate P value for exploratory data analysis. In total, 15 haematological and blood biochemistry variables were analysed for OWBV, Egyptian vultures and cattle egrets. Values for PCV, MCV and MCHC could not be obtained for crows at 48 h because of the small blood volume available for analysis, and 12 variables were analysed for crows. We had an a priori expectation that uric acid and ALT levels would increase and body mass would decline if meloxicam had toxic effects similar to diclofenac (Swan *et al.*, 2006*a*), and as a result we did not apply the Bonferroni correction and used $P = 0.05$ as the significance level for these parameters. For the remaining variables, P was set at 0.00384 (0.05/13) for OWBV, Egyptian vultures and cattle egrets and 0.005 (0.05/10) for crows. We compared the survival of *Gyps* vultures in these experiments with *G. bengalensis* dosed with diclofenac administered either by oral gavage or through feeding on tissues of livestock treated with a veterinary course of the drug (Oaks *et al.*, 2004).

Results

Over the course of all three phases of the study, a total of 51 birds were dosed with meloxicam, administered either by oral gavage at doses of $0.5\,mg\,kg^{-1}$ ($n = 5$) and $2.0\,mg\,kg^{-1}$ ($n = 30$), or through feeding on muscle tissue ($n = 14$) or liver tissue ($n = 7$) taken from buffalo dosed with meloxicam. The two slaughtered buffalo had meloxicam tissue residues of 12.79 and $6.97\,mg\,kg^{-1}$ in the liver, 17.09 and $12.03\,mg\,kg^{-1}$ in the kidney and 1.82 and $1.16\,mg\,kg^{-1}$ in muscle tissue. Vultures given liver consumed an average of 0.41 ± 0.21 kg of liver tissue (range 0.21–0.83 kg), exposing birds to an estimated mean meloxicam dose (using the average of the two liver values) of $1.00 \pm 0.52\,mg\,kg^{-1}$ bw, with minimum and maximum doses ranging from 0.5 to $2.1\,mg\,kg^{-1}$ bw for individual birds. The two groups of five and nine vultures given muscle tissue consumed on average 0.76 and 1.49 kg, respectively, and were exposed to an average meloxicam dose of 0.3 and $0.5\,mg\,kg^{-1}$ bw.

No adverse reaction to the drug was observed in any of the six species treated with meloxicam, and all 51 birds remained alive and healthy throughout the 7-day-experimental period. For the *Gyps* vultures treated in phases I and III, the survival of all individuals treated with meloxicam is a statistically significant difference from the result of treating *G. bengalensis* with diclofenac (0 death from 31 exposures for meloxicam versus 16 deaths from 24 exposures for diclofenac; the two-tailed Fisher exact test, $P < 0.0001$). The difference in survival is significant regardless of the route of administration (feeding tissues from treated livestock, 0/21 deaths for meloxicam vs. 13/20 deaths for diclofenac, the two-tailed Fisher exact test $P < 0.001$; by gavage, 0 deaths from 10 exposures for meloxicam vs. three deaths for four exposures for diclofenac; the two-tailed Fisher exact test, $P = 0.051$). The ten meloxicam-dosed vultures from phase I ($6 \times$ *G. bengalensis* and $4 \times$ *G. indicus*) were still alive 11 months after dosing, suggesting no long-term deleterious effect of a single meloxicam dose on survival. All 20 experimental and 18 control birds of the four other scavenging species (phase II) were successfully released into the wild 21 days after the end of the trial, providing a total period of 4 weeks of observation following dosing with meloxicam. Feeding behaviour of all meloxicam-dosed birds remained normal throughout the 7 days of post-dose observation for all three phases of the study. There was no significant change in body mass for any meloxicam-dosed birds in phases I and II (ANOVA for Treatment $\times$ Period; phase I, *Gyps* vultures, $F_{2,29} = 0.00$, $P = 0.998$; phase II, Egyptian vulture, $F_{1,17} = 0.00$, $P = 0.978$; cattle egret, $F_{1,17} = 0.19$, $P = 0.670$; crows, $F_{1,19} = 0.02$, $P = 0.897$; common mynah $F_{1,19} = 0.85$, $P = 0.370$).

There was no significant effect of meloxicam on uric acid levels (Figs 1 and 2) during any phase of the study (ANOVA for Treatment $\times$ Period, uric acid $F_{2,20} = 0.13$, $P = 0.879$, for *Gyps* vultures in phase I; and $P > 0.334$ for Egyptian vultures, cattle egrets and crows in phase II). There was no significant difference in serum uric acid and ALT activity at 48 h following feeding with meloxicam-dosed liver, meloxicam-dosed muscle or untreated goat tissues (phase III; One-way ANOVA; uric acid, $F_{2,12} = 0.24$, $P = 0.791$; ALT, $F_{2,9} = 1.50$, $P = 0.274$). Nor was there any significant difference between the route of meloxicam administration

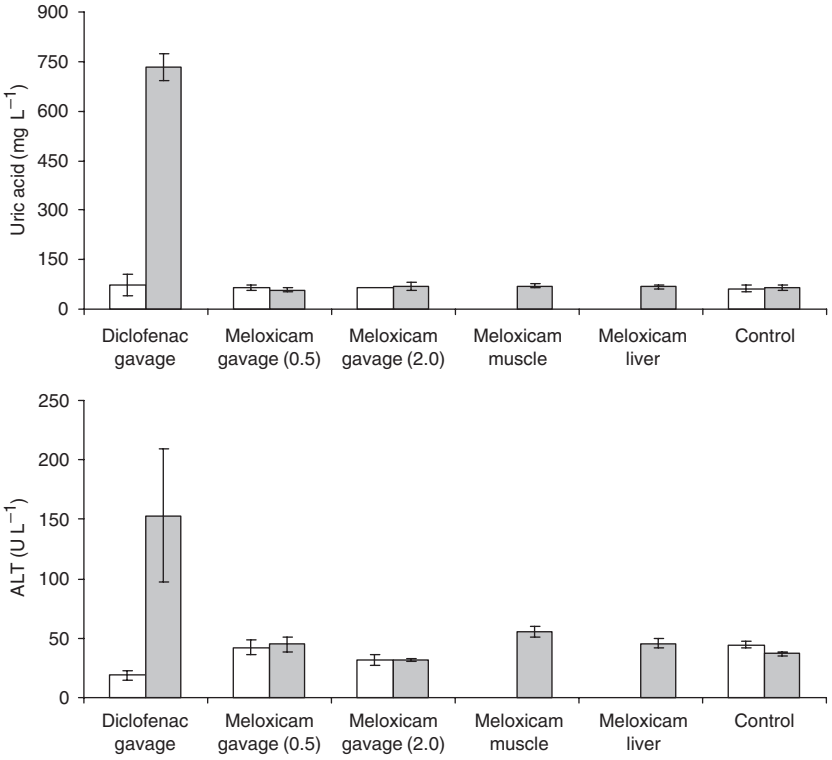

Figure 1 Effect of administration of meloxicam on serum uric acid levels and alanine transferase (ALT) activity in *Gyps bengalensis* for birds dosed with meloxicam by oral gavage at 0.5 and 2.0 mg kg^{-1} (phase I), given muscle and liver tissues from meloxicam-dosed buffalo *Bubalus bubalis* (phase III) with vultures receiving estimated doses of 0.3–0.5 mg kg^{-1} (muscle) and 0.5–2.1 mg kg^{-1} (liver), and for control birds (phase I). Values are arithmetic means ± one standard error for uric acid and ALT measured before dosing (unshaded) and at 48 h after dosing (shaded). Values before dosing are unavailable for birds receiving muscle and liver tissues, and only values at 48 h after dosing are presented. For comparison, data are presented for *G. bengalensis* administered diclofenac by gavage at 0.25–2.5 mg kg^{-1} (Oaks *et al.*, 2004), with uric acid levels measured, before death, at 1 h (unshaded) and 24 h (shaded) after dosing. ALT levels are shown for African white-backed vultures *Gyps africanus* administered diclofenac by gavage at 0.8 mg kg^{-1} (Swan *et al.*, 2006*a*,*b*), measured at 4 h (unshaded) and 24 h (shaded) after dosing.

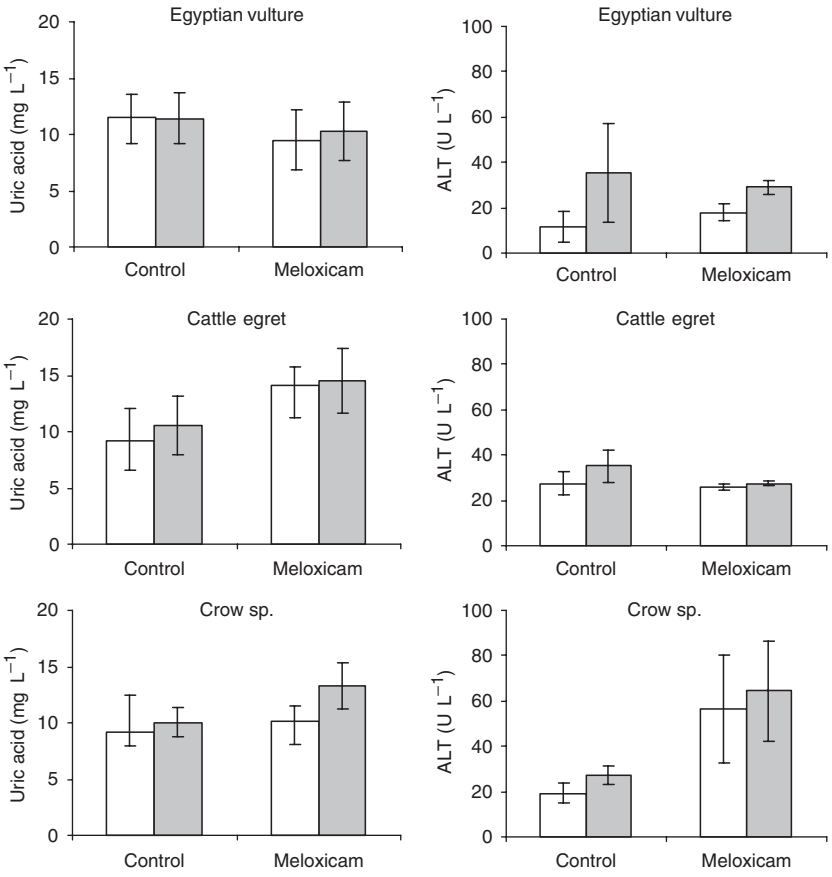

Figure 2 Effect of administration of meloxicam on serum uric acid levels and alanine transferase (ALT) activity in Egyptian vultures *Neophron percnopterus*, cattle egrets *Bubulcus ibis* and crow species (house crow *Corvus splendens* and large-billed crow *Corvus machrorhynchos*) for birds dosed with meloxicam by oral gavage at 2.0 mg kg^{-1} and sham-dosed control birds. Values are arithmetic means ± one standard error for uric acid and ALT measured before dosing (unshaded) and at 48 h after dosing (shaded). There were no significant ($P < 0.05$) Treatment × Period interactions in uric acid and ALT for any species, although there was a significant increase in ALT activity in Egyptian vultures ($P = 0.033$) in both control and meloxicam-dosed groups.

(muscle, liver or gavage) and uric acid levels at 48 h (phase I and III; One-way ANOVA, $F_{2,18} = 0.13$, $P = 0.879$). There was a significant increase in ALT activity in Egyptian vultures following dosing ($F_{1,16} = 5.72$, $P = 0.033$); however, this was found in both the meloxicam-dosed and control groups, and there was no significant interaction between Treatment × Period ($F_{1,16} = 1.00$, $P = 0.334$). Analysis of all other haematological and blood biochemistry parameters (with significance levels set at P/k; where k represents number of variables i.e. 13 or 10) found no significant effect of meloxicam treatment for *Gyps* vultures in phases I and III, or for Egyptian vultures, cattle egrets and crows in phase II. Unadjusted P values suggest that for Egyptian vultures, the total leucocyte count increased and the % lymphocytes decreased over the course of the experiment ($F_{1,17} = 8.95$, $P = 0.010$ and $F_{1,17} = 10.76$, $P = 0.005$, respectively), possibly due to the stress (as a result of capture and handling) observed for this species. However, there was no significant interaction between meloxicam treatment and period for these two parameters ($F_{1,17} = 3.03$, $P = 0.104$ and $F_{1,17} = 0.97$, $P = 0.343$, respectively).

Discussion

The results of this study demonstrate the safety of the NSAID meloxicam to India's critically endangered *Gyps* vultures and to several other scavenging bird species. All of the birds dosed with meloxicam survived the trials, and the vultures tested in the first stage of the trials remain alive and healthy nearly one year after treatment. No sub-lethal effects of meloxicam could be detected, with no change observed in feeding behaviour or body mass, or any increase in uric acid and ALT levels related to treatment, as occurred in vultures dosed with diclofenac (Swan *et al.*, 2006*a*). There was an increase in ALT activity in Egyptian vultures for both meloxicam-dosed and control groups, although the observed increase is markedly different from the six-fold increase in ALT following dosing with diclofenac (Figs 1 and 2). While ALT levels do increase following diclofenac dosing causing renal damage (Swan *et al.*, 2006*a*), ALT is generally not considered to be organ specific in birds (Campbell, 2004) and the increase in Egyptian vultures may have resulted through muscular damage, possibly as a result of handling. No detectable differences were found for a wide range of other blood variables that would indicate ill health or damage to liver and/or kidney function. The five species tested in this study are from the orders Falconiformes, Ciconiiformes and Passeriformes, indicating that meloxicam appears to be safe to a taxonomically diverse group of birds. Information from a survey of veterinarians and zoological institutions on the clinical treatment of vultures, raptors and other scavenging birds confirms that meloxicam is of low toxicity to a wide range of birds: over 700 birds from 60 species are known to have been treated with meloxicam and yet there have been no reported instances of mortality (Cuthbert *et al.*, in press). Repeated long-term exposure to meloxicam, as may occur among scavenging birds in the wild, is unlikely to alter these conclusions, as research on six bird species, including Cape griffon vultures *Gyps coprotheres*, indicates that meloxicam is very rapidly metabolized in birds with a half-life of less than one hour and will be completely eliminated within one day (Baert & De Backer 2003; V. Naidoo, pers. comm.). The clinical treatment of vultures and scavenging birds with meloxicam further supports the safety following long-term exposure, with drug treatments lasting between 1 and 120 days and no reported adverse effects (Cuthbert *et al.*, in press).

To be a suitable alternative to diclofenac, it is essential that meloxicam is effective for the treatment of livestock. Meloxicam is a second-generation NSAID with preferential COX-2 inhibition, conferring analgesic, antipyretic and anti-inflammatory properties and a reduced risk of adverse effect on renal functioning (Engelhard *et al.*, 1995; Brater, 2002). Meloxicam is used to treat a variety of veterinary ailments and for cattle, horses and pigs, its use is recommended for the treatment of acute respiratory infection, diarrhoea, lameness, inflammation of acute and chronic musculo-skeletal disorders, and for the treatment of mastitis in combination with antibiotic therapy (EMEA, 2006). Clinical trials demonstrate the efficacy of meloxicam to be similar to or better than other NSAIDs tested (Noble & Balfour, 1996; del Tacca *et al.*, 2002; Deneuche *et al.*, 2004; Friton *et al.*, 2004). Meloxicam is already licensed and manufactured as a veterinary drug in India and Nepal, and is available at an affordable price. Given these factors, we recommend that meloxicam be introduced as rapidly as possible across the Indian sub-continent as an alternative to diclofenac to reduce the risk to *Gyps* vultures and other scavenging birds.

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