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CASE REPORT

Accidental intravenous overdose of meloxicam in a Cape Vulture (*Gyps coprotheres*)

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Many species of vulture are under threat from man-made inventions; this has led to wounded and sick vultures presenting for veterinary treatment and in need of pain management. Following the devastating effect of diclofenac on vultures in South Asia, meloxicam was found to be very safe for vultures, as a treatment as well as through ingestion of meat from treated animals. Many studies investigated the safety of meloxicam, and all found it to be safe up to 2 mg/kg, which was deemed the maximum likely exposure through treated carcasses. All studies exposed the birds either through oral dosing, treated meat or intramuscular administration, no instances of toxicity where recorded and all birds remained healthy. In this case the bird was exposed to a single dose of 2 mg/kg, intravenously, with no signs of toxicity. This appears to be the first recorded instance of accidental intravenous administration of meloxicam in a vulture.

Keywords: meloxicam, *Gyps coprotheres,* Cape Vulture, intravenous, accidental overdose

Introduction

The Cape Vulture (*Gyps coprotheres)* is listed as "Vulnerable" by the IUCN Red List; with a decreasing population trend, it is estimated there are between 9 600 and 12 800 adults remaining. Major threats to this species include: collisions with powerlines and wind turbines, poisoning, poaching and climate change (IUCN 2021). Vultures play an integral role in the maintenance of ecosystems by speeding up the removal of carcasses, preventing the buildup of diseases and contributing to overall biodiversity (Henriques et al. 2018). Increasing numbers of sick, grounded or injured vultures are presented for veterinary care, bringing about the need for a nonsteroidal anti-inflammatory drug (NSAID) that is safe to use in vultures as a method of pain management following injury or surgery. Following the devastating effect of diclofenac on vultures in South Asia that led to a population collapse (Swarup et al. 2007), meloxicam was found to be a safe alternative both for treatment of vultures but also for ingestion of meat from animals treated with meloxicam (Naidoo, Wolter et al. 2008). NSAIDs act via the inhibition of cyclo-oxygenase (COX) 1 and 2, which mediates the inflammatory process and cascade as well as homeostatic functions. COX-2 is responsible for pain and inflammation while COX-1 is responsible for "homeostasis" such as regulation of blood flow to the kidneys. Meloxicam is a NSAID that selectively inhibits COX-2, therefore having more of an effect on inflammation than on homeostatic functions, making it safer (Schattenkirchner 1997). COX-selectivity however, is species-specific and the importance of COX-1 and COX-2 receptors may vary among animals (Chandrasekharan & Simmons, 2004).

Several studies have been performed testing the safety of meloxicam in vultures, mostly in the Cape Vulture (*Gyps coprotheres)* and African White-Backed Vulture (*Gyps africanus)*, both through oral dosing and the feeding of carcasses from animals treated with meloxicam prior to death. In the study performed by Naidoo (2008) it was found that the maximum likely level of exposure is 2 mg/kg. This was calculated from liver samples of cattle treated with meloxicam at double the recommended dose (i.e. 1 mg/kg) for five days prior to death and extrapolated based on the maximum meal size of a vulture should it consume just liver tissue, which contains the highest concentration of meloxicam (Naidoo, Wolter et al. 2008). The recommended therapeutic dose of meloxicam in vultures is 0.2 to 0.5 mg/kg (Swan et al. 2006) indicating that the maximum likely exposure of 2 mg/kg is well above the therapeutic range. All birds in the study that received oral doses of meloxicam up to 2 mg/kg showed no adverse effects, no change in feeding behaviour and no significant changes in body mass, biochemistry such as uric acid and alanine transaminase (ALT) or haematology parameters (Swarup et al. 2007).

Excretion of nitrogenous waste in birds occurs mainly via uric acid in the kidneys; as such it is a reliable measure of kidney function. An increase can reflect renal damage or dehydration. A more reliable evaluation however, is the urea to uric acid ratio, where an increase indicates pre-renal azotaemia, such as dehydration or hypoperfusion, while a decrease suggests renal damage (Naidoo, Diekmann et al. 2008). ALT is present in the liver tissue as well as in various other tissues throughout the body. Consequently, an elevated ALT level is not a definitive indicator of liver damage. Creatine kinase (CK), an enzyme that is predominately found in skeletal muscle, heart muscle and brain, will be elevated in the serum when muscle damage is evident. Therefore, if ALT is elevated but CK remains normal, liver damage may be present (Naidoo, Diekmann et al. 2008).

Signs of NSAID toxicity following various exposures are well documented for diclofenac, which include: head drooping, depression, reluctance to move, increases in serum uric acid and elevated serum ALT, with vultures typically dying within two days of exposure (Swarup et al. 2007). Similar signs were observed in a vulture that died from a carprofen overdose. There was a 27-fold increase in uric acid and a 15-fold increase in ALT (Naidoo et al. 2018). Ketoprofen has been found to be similar to diclofenac in

terms of its toxicity (Fourie et al. 2015). Meloxicam thus appears to be the safest NSAID for use in vultures. Carprofen, however, has the potential for toxicity, especially if the vulture consumes meat from the injection site. (Naidoo et al. 2018). The same is true for flunixin and phenylbutazone (Fourie et al. 2015). The safety of NSAIDs in vultures appears to be related to the drug's half-life and the potential for accumulation (Fourie et al. 2015).

Meloxicam has a relatively short half-life and rapid elimination in vultures, which may contribute to its safety. The half-life was found to be 0.5 hours ± 0.0 hours (Adawaren et al. 2019). This suggests that meloxicam could be completely eliminated from a vulture's system within five to seven hours (Naidoo, Wolter et al. 2008) and for accumulation to occur, 2 mg/kg will need to be given every hour. The reason for the rapid elimination is unknown but it is hypothesised that vultures have a different pathway or route of metabolism versus mammals (Adawaren et al. 2019). Further studies are needed in this area as variations in tolerance and metabolism have been documented within species and between species (Naidoo et al. 2018).

Case history

An adult male Cape Vulture was presented to the Wildlife Section of the Onderstepoort Veterinary Academic Hospital, with a complaint of being grounded and unable to fly. Upon presentation the animal was found to have a body weight of 6.3 kg (normal is 7–11 kg) and reduced mobility in the right wing. Radiography revealed a dislocation of the humerus and ulna. Whitening of the radiograph around the injury indicated significant soft tissue opacity, suggesting a degree of chronicity. Blood samples were collected, revealing a uric acid level of 0.81 mmol/L. This value exceeds the normal reference range of 0.15–0.65 mmol/L (Fourie 2014), possibly indicating a degree of dehydration. All other parameters were unremarkable. The vulture was administered intravenous fluids (Lactated Ringer's Injection, USP; Fresenius Kabi, [Pty] Ltd) at a maintenance rate of 2 mL/kg/hour. Preoperative meloxicam (Metacam®, 5 mg/mL; Boehringer Ingelheim Animal Health, RSA) was administered intramuscularly at a dose of 0.5 mg/kg into the pectoral muscle.

The following day (Day 1), closed reduction was initially attempted to improve the chances of returning the bird to flight. However, the procedure was unsuccessful due to the presence of connective tissue formation and malalignment of the joints. As a result, open reduction was chosen, and the joint was surgically opened to remove the fluid accumulation and loosen the formed connective tissue. During the procedure pieces of cartilage from the joint were found to be loose and were removed. Realignment of the joint was attempted, but could not be fully corrected. Therefore, an external fixator was applied with the aim of stabilising the joint and facilitating joint fusion. Twenty-four hours after the first dose of meloxicam, the vulture was accidentally given meloxicam intravenously (Metacam®, 20 mg/ml, Boehringer Ingelheim Animal Health, RSA). Not only was the route of administration incorrect, but an accidental fourfold overdose of 2 mg/kg was also administered (instead of 0.5 mg/kg). As a precaution all NSAID treatment was stopped, and the intravenous fluid rate increased to 2.5 times the maintenance rate, to maintain perfusion to the kidneys and assist in flushing out toxic metabolites that could have accumulated. The vulture was monitored for signs of toxicity, such as depression, head drooping and reluctance to move, but none were noticed. The vulture was returned to a rehabilitation facility six days later. Fourteen days post-overdose (Day 14), a follow-up examination was conducted to evaluate the wound. Blood samples were also collected for a subsequent uric acid level analysis, which was found to be 0.18 mmol/L, within the reference range (0.15–0.65 mmol/L [Fourie 2014]). All other haematological parameters were unremarkable.

Conclusion

The safety of meloxicam in vultures is well documented, when given both orally and intramuscularly. However, to the authors' knowledge, there are no reports on the (unintended) intravenous administration of this drug. While the dose was in line with the maximum doses in other publications, this case showed that the intravenous administration of meloxicam at four times the typical therapeutic dose produced no clinical signs of toxicity after therapeutic intervention with intravenous fluid administration. No adverse reactions were noticed and serum uric acid levels following the exposure were well within the reference interval. Two weeks after the initial overdose, the vulture was still in good health. Perhaps more serial uric acid levels as well as the U:UA ratio and ALT levels could have been evaluated to provide a more in-depth assessment as to whether there was any organ damage.

This case appears to be the first recorded instance where meloxicam was accidentally administered intravenously in a vulture. This case report further supports the safety of meloxicam and its use according to the recommended doses and route of administration.

Conflict of interest

The authors declare they have no conflicts of interest, directly or indirectly related to the research.

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Ethical approval

Ethical approval was obtained from the following ethical review board: University of Pretoria, Research Ethics Committee (REC150-23).

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References

Adawaren, E.O., Mukandiwa, L., Chipangura, J., et al., 2019, Percentage of faecal excretion of meloxicam in the Cape vultures (Gyps corprotheres), *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology* 215, 41-6. https://doi.org/10.1016/j.cbpc.2018.10.001.

Chandrasekharan, N.V., Simmons, D.L., 2004, The cyclooxygenases, *Genome Biol* 5(9), 241. https://doi.org/10.1186/gb-2004-5-9-241.

Fourie, T., Cromarty, D., Duncan, N., et al., 2014, The safety of carprofen, flunixin and phenylbutazone in the Cape Vulture (Gyps coprotheres)-a pilot study, *University of Pretoria*. https://doi.org/10.1371/journal.pone.0141419.

Fourie, T., Cromarty, D., Duncan, N., Wolter, K., and Naidoo V., 2015, The safety and pharmacokinetics of carprofen, flunixin and phenylbutazone in the Cape Vulture (Gyps coprotheres) following oral exposure, *PLOS One* 10, e0141419. https://doi.org/10.1371/journal.pone.0141419

Henriques, M., Granadeiro, J.P., Monteiro, H., et al., 2018, Not in wilderness: African vulture strongholds remain in areas with high human density, *PLOS One* 13, e0190594. https://doi.org/10.1371/journal.pone.0190594.

IUCN. 2021. Available from: https://www.iucnredlist.org/species/22695225/197073171. Accessed 05 June 2024.

Naidoo, V., Diekmann, M., Wolters, K., et al., 2008, Establishment of selected baseline blood chemistry and hematologic parameters in captive and wild-caught African White-Backed Vultures (Gyps africanus), *Journal of Wildlife Diseases* 44, 649-54. https://doi.org/10.7589/0090-3558-44.3.649.

Naidoo, V., Taggart, M.A., Duncan, N., et al., 2018, The use of toxicokinetics and exposure studies to show that carprofen in cattle tissue could lead to secondary toxicity and death in wild vultures, *Chemosphere* 190, 80-9. https://doi.org/10.1016/j.chemosphere.2017.08.167.

Naidoo, V., Wolter, K., Cromarty, A.D., et al, 2008, The pharmacokinetics of meloxicam in vultures, *Journal of Veterinary Pharmacology and Therapeutics* 31, 128-34. https://doi.org/10.1111/j.1365-2885.2007.00923.x.

Schattenkirchner, M., 1997, Meloxicam: a selective COX-2 inhibitor non-steroidal anti-inflammatory drug, *Expert Opin Investig Drugs* 6, 321-34. https://doi.org/10.1517/13543784.6.3.321.

Swan, G., Naidoo, V., Cuthbert, R., et al., 2006, Removing the threat of diclofenac to critically endangered Asian Vultures, *PLOS Biology* 4, e66. https://doi.org/10.1371/journal.pbio.0040066.

Swarup, D.P.R.C., Patra, R.C., Prakash, V., et al., 2007, Safety of meloxicam to critically endangered Gyps vultures and other scavenging birds in India, *Animal Conservation* 10, 192-98. https://doi.org/10.1111/j.1469-1795.2006.00086.x.