DICLOFENAC AND THE ASIAN VULTURE CRISIS

Dr Mark Taggart (ERI-UHI)

International workshop on poisoning and vultures in the European-African bird migration flyway: What is the situation in Africa and how can Europe help? April 8-11th, 2014, Ronda - Spain



Confirmed in 2004 (India) for wild birds – supported by experiments in South Africa and Spain



Figure 1. (a) Unic acid and (b) alarine transferase (ALT) concentrations in plasma measured before and after oral treatment of values with 0.8 mg lg^{-1} of dickferae. Lines connect data for the same bird. Results are shown for two dickefenta-dosed (filled squares) and two sham-treated (open squares) Gygs africanse, and for three dickefenac-dosed G, falsus (filled diamonds).



Griffon vulture (*Gyps fulvus*) – Least Concern – increasing.







African white-backed vulture (*Gyps africanus*) – Endangered - decreasing.

Highly likely that all 8 *Gyps* species are susceptible.

ered - decreasing.



Swan et al., 2006, Biol Letts, 2, 279-282.

Diclofenac now known to be highly toxic to Gyps

G. fulvus and *G. africanus* treated with 0.8 mg kg⁻¹ diclofenac – <u>all birds died within 48 hours.</u>

Estimated LD₅₀ for <u>*G. bengalensis*</u>: 0.1-0.23 mg kg⁻¹.

LD₅₀ in rats: strychnine = 16 mg kg⁻¹, K arsenite = 14 mg kg⁻¹; passerines: carbofuran = 0.4 mg kg⁻¹.

Persecution



Swan et al., 2006, Biol Letts, 2, 279-282; Oaks et al., 2004, Nature, 427, 630-633.

Munir-Virani

Diclofenac exposure pathway in the wild



Since 2004, extensive, India wide carcass surveys have been undertaken to assess potential diclofenac exposure (n = 6207 samples tested to date).

Taggart et al., 2007, Env. Poll., 147, 60-65; Taggart et al., 2007, Env. Int., 33, 759-765; Taggart et al., 2009, ES&T, 43, 4561-4566.

Carcass surveys undertaken across India



Liver tissue samples are collected, extracted for NSAIDs and analysed using <u>liquid chromatography - triple quadrupole mass spectrometry</u>, and, by ELISA.

Taggart et al., 2007, Env. Poll., 147, 60-65; Taggart et al., 2007, Env. Int., 33, 759-765; Taggart et al., 2009, ES&T, 43, 4561-4566.

Carcass surveys undertaken across India



Liver tissue samples are collected, extracted for NSAIDs and analysed using liquid chromatography - triple quadrupole mass spectrometry, <u>and, by ELISA</u>.

Saini et al., 2012, Env. Poll., 160, 11-16.

Survey work indicated that in 2004-2006, ~1:10 carcasses available to vultures contained diclofenac



Fig. 1. Prevalence of dickdynae in biom of domestic angulate carcaves from hulos by enter dones, Utunterchal and Meghalays were carveyed but careples were consultable. Nates show to white some not surveyed, limit may above the sampler of samples collected per state and the mamber of sizes then which they were influented to brackers. <u>Survey 1</u> – May 04 to July 05 n = 1848 – <u>10.1%</u> Mean in all +ve's – 352ppb <u>Survey 2</u> – Apr 06 to Dec 06 n = 1488 – <u>11.1%</u> Only <u>0.13-0.77%</u> need contain a lethal dose of DICLOFENAC to drive the observed decline

rate.



Taggart et al., 2007, Env. Int., 33, 759; Taggart et al., 2009, ES&T, 43, 4561; Green et al., 2004, J. App. Ecol. 41, 793.

Survey work indicated that in 2004-2006, ~1:10 carcasses available to vultures contained diclofenac

Detailed models suggest that "*diclofenac is* the main, if not the only cause of the widespread declines in vulture populations" seen on the Indian subcontinent.



Green et al., 2004, J. App. Ecol. 41, 793; Green et al., 2006, J. Appl. Ecol. 43, 949.

Finding an alternative to diclofenac that was "vulture safe" became an urgent priority

Table 2. Evidence for NSAID toxicity on vultures, raptors and other scavenging birds indicating the number of birds that died with gout and/or renal failure and total number of birds treated, the ratio of COX-1/COX-2 inhibition in human, equine and canine blood, and the presence of either an -NH, -COOH or both -NH and -COOH groups in the molecular structure. (Data on COX-1/COX-2 ratios come from Brideau et al. (2001) and Lees et al. (2004).)

drug	toxicity	died/total
aspirin	no	0/3
ketoprofen	<u>no</u>	0/20
meloxicam	no	0/739
carprofen	yes	73/40
diclofenac	yes	28/36
flunixin	yes	7/24
ibuprofen	yes.	1/1
phenyibutazone	ves	1/1



Collated zoo, veterinary, rehabilitation centre data on 870 scavenging birds from 79 species - <u>MELOXICAM</u> had been used in a large number of birds/species (including *Gyps*).

Proven experimentally in S.Africa and India using 3 *Gyps* species and 4 other scavenging avian species.



With an alternative *"vulture safe"* drug available, to protect vultures, India, Pakistan and Nepal essentially banned <u>veterinary</u> diclofenac in 2006 (and Bangladesh also followed in 2010).

Munir Virani

Is the ban working?

TABLE 1 Number of brands of bolus and injectable formulations of NSAIDs and the combined total number from a survey of 11 Indian states during 2007–2010. Numbers in parentheses indicate the number of brands in which paracetamol was a secondary active ingredient.

Active ingredient	Bolus	Injectable	Total
Meloxicam	19 (12)	31 (13)	50 (25)
Diclofenac	16 (8)	26	42 (8)
Aceclofenac	1 (1)		1 (1)
Analgin	9 (1)	6 (1)	15 (2)
Flunixin		1	1
Ibuprofen	8 (2)		8 (2)
Ketoprofen		6	6
Mefenamic acid		2 (2)	2 (2)
Nimesulide	27 (22)	2	29 (22)
Paracetamol	1	1	2
Phenyl butazone ²	2	5 (1)	7 (1)
Piroxicam	1	2 (1)	3 (1)
Total with paracetamol as secondary compound	46	18	64

^bTwo bolus and three injectable brands of analgin were formulated with phenyl butazone

³One brand of injectable phenyl batazone was formulated with sodium salicylate (aspirin)

• Poor regulation

- Illegal sales
- Misuse of human formulations
 - Cost



In 2007-10, diclofenac was still very prevalent in the Indian market place – 16 bolus brands, 26 injectable.

Cuthbert et al., 2011, ORYX, 45, 420-426.

By rapidly disposing of livestock carcasses, vultures provide(d) an invaluable <u>ECOSYSTEM SERVICE</u>...

Now almost completely lost - populations of these keystone species are unlikely to rebound to previous levels.

Vultures potentially helped control disease by disposing of infected animals rapidly:

Anthrax, brucellosis, tuberculosis

unir Virar







Dog populations are increasing on/near carcass dumps, significantly increasing the risk of rabies infections in humans (increased by >7 million between 1992 and 2003).

India is No.1 in the world for rabies infections already, dog bites being the main source.





Historically, carcasses were a valuable resource, providing hide for tanning, and CLEAN stripped bone for fertiliser. If India has to switch to burial/incineration, both resources are potentially lost, and disposal costs will be huge (10's of millions of carcasses/year).







Vultures are very large, very impressive, enigmatic raptors - their loss in itself holds high value (biodiversity, tourism, etc.).



The FUTURE



- <u>CONSERVATION BREEDING AND RELEASE</u> 3 breeding centres in India, 1 in Nepal, 1 in Pakistan – more to follow
- <u>VULTURE SAFE ZONES</u> creation of zones that are "safe" for vultures (diclofenacmeloxicam swapping, education, safe food provision, etc.)
- <u>CONTINUED ADVOCACY</u> remove diclofenac from the market (large vial human formulations especially) – promote meloxicam
- <u>CONTINUED RESEARCH</u> NSAID safety work, population monitoring, carcass surveys, tracking

Some lessons learned (perhaps)?

- CONSERVATION BREEDING critical for long term plans
- Effective ADVOCACY has been critical throughout in particular, getting the attention of "*big players*" (large conservation bodies like RSPB are very good at this!)
 - RESEARCH has been critical peer reviewed, International, quality, high profile (Nature!) publications are important (at least in Asia)
 - Having a PLAN the SAVE consortium Recovery Blueprint is very important going forward – signed up to by many stakeholders (conservation, science, government!)

IUCN Red List status

- ECOSYSTEM SERVICES aspect has, to date, been somewhat overlooked potentially extremely important leverage
 - BASELINE data was/is critical in Asia often lacking
 - SECURING/TRANSPORTING SAMPLES for research is/has been significant barrier to progress (extent of problem, analysis required)
 - SAFETY TESTING has simply been too slow (for other NSAIDs)





TO SUM UP

Diclofenac

- Declines this fast, on this scale are virtually unprecedented
 - Driven by one rather unremarkable compound
 - Critical that diclofenac is removed from the vet market significant progress made with the ban far more to do
 - That it is not replaced by another equally problematic NSAID
- A combination of social, economic and ecological factors have come together to cause this "*Perfect Storm*"



THE Perfect Storm (Prof. Pat Redig)



Superabundance







Valuable – old age



Toxicity

GROWTH IN DRI

說

Ξ

1974

In 2004, 52% of vet-NSAID use was with diclofenac - 2007-10, still cheapest

THEE.

1981

Extended half-life





TO SUM UP



- Declines this fast, on this scale are virtually unprecedented
 - Driven by one rather unremarkable compound
 - Critical that diclofenac is removed from the vet market significant progress made with the ban far more to do
 - That it is not replaced by another equally problematic NSAID
- A combination of social, economic and ecological factors have come together to cause this "*Perfect Storm*"
- Case has highlighted how little we know about the potential effects of pharmaceuticals in the terrestrial environment
- On a possible POSITIVE note vulture populations "may" now be turning a corner



Turning a corner? Changes in population indices of the oriental white-backed vulture Gyps bengalensis, from 6 years of repeat surveys of a large number of road transects in India. Vertical lines show 95% confidence limits derived by bootstrapping: the curve shows the cubic log-linear trend for 2000 to 2011. The y axis has a logarithmic scale.



Acknowledgements



People

RSPB: Richard Cuthbert, Rhys Green, Debbie Pain, Toby Galligan, Chris Bowden Wildlife Institute of India: Yadvendradev Jhala BNHS: Vibhu Prakash, Kalu Ram Senacha, Asad Rahmani IVRI: Devendra Swarup, Mohini Saini, Suchitra Upreti University of Pretoria: Gerry Swan, Vinny Naidoo AND MANY MORE.....

Further information:

http://www.save-vultures.org/

