Reply to: Letter to the Editor from Malik et al: Acute kidney injury following subcutaneous meloxicam administration

Authors

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Abstract: no abstract

We thank Malik et al. for their letter regarding our recent publication (Krekis, King et al. 2024). The focus of the letter is our reporting of the case of one cat that experienced an IRIS grade II acute kidney injury (AKI) postoperatively. This letter offers an opportunity to discuss important points of the study. A statement on the incidence of acute kidney injury (AKI) was initially included in the abstract, but removed during the manuscript submission to fit the 200 word limit imposed by the journal. The reference to AKI has been reinstated in the abstract.

Cat 53# was a Domestic Short Hair cat, 1.2 years old and weighing 3.26 kg at the time of the surgery (03/09/2012). Baseline plasma creatinine was 1.4 mg/dL [i-STAT-1 reference range: 1.0-2.2 mg/dL]. Meloxicam 0.2 mg/kg was given subcutaneously at induction. Anaesthesia lasted 53 minutes. Intra-operative Doppler blood pressure was between 80 and 110 mmHg (10 minutes recording at 80-84 mmHg).

Cat #53 was examined at the 3 days visit and had been normal at home (eating and drinking well, no vomiting or diarrhoea). This cat had not been given postoperative nonsteroidal anti-inflammatory drugs (NSAIDs) at home. A blood sample was taken at the Day 3 visit (for the purpose of the research, under the Animal Scientific Procedures Act); the plasma creatinine concentration was 2.0 mg/dL. Repeat evaluation of the same sample gave a value of 2.2 mg/dL (Table 1). Thus, the within-day variability is substantial with these cartridges, as results are given as tenth of integers (i.e. 2.0, 2.1, 2.2…).

As the increase of plasma creatinine was not associated with any clinical abnormality, the owners were informed of the result by telephone, given a subsequent appointment for a blood sample and advised to bring the cat back to the clinic if they had any concerns. The cat underwent a veterinary examination at 10 days, was clinically well and the plasma creatinine was 1.81 mg/dL [Catalyst Dx Chemistry Analyser, reference range 0.84-2.4 mg/dL]. The owner is registered with the same practice and cat #53 has not presented with kidney problems over the last 10 years.

Table 1: Biochemistry data available for Cat #53:

Variable	Reference Range	Pre-anaesthesia (catheter placement)	2h post-extubation	3 days First test	3 days Repeated test
Test	ISTAT (enzymatic method)				
Na^+ (mmol/L)	147-155	153	153	155	152
K^+ (mmol/L)	3.0-4.6	3.2	3.7	4.1	4.0
Cl^- (mmol/L)	115-125	124	125	126	125
Ionised Ca^{2+} (mmol/L)	1.20-1.32	1.26	1.27	1.26	1.25
tCO_2 (mmol/L)	17-26	16	16	19	19
Glucose (mg/dL)	56-163	91	146	93	91
BUN (mg/dL)	18-39	32	28	28	27
Creatinine (mg/dL)	1.0-2.2	1.4	1.2	2.0	2.2
Haematocrit (%)	25-47	35	34	38	41
Haemoglobin (g/dL)	8-16	11.9	11.6	12.9	13.9
Serum protein (g/L, refractometer)		64	64	72	
USG		1.050	1.050		

tCO_2 = Total Carbon Dioxide, BUN = blood urea nitrogen; USG = urine specific gravity

Plasma meloxicam concentrations in cat #53 were 309.1 ng/mL at extubation (48 mins after injection) and 619.3 ng/mL at 2h post-extubation (207 mins after injection, past the Tmax), which are in line with the concentrations reported by Lehr et al. (Lehr, Narbe et al. 2010) after a 0.2mg/kg subcutaneous dose. This confirms that this cat did not have an exceptionally low meloxicam clearance.

It is possible that, in this cat, meloxicam facilitated a reduction in glomerular filtration rate (GFR) in response to anaesthesia by inhibiting tubuloglomerular feedback, although this is not necessarily associated with acute tubular damage in a well hydrated cat. As we do not have any data on markers of tubular damage or stress, we cannot say for sure whether this functional effect on GFR which would have led to elevated creatinine for a few days (due to the slow response of serum creatinine to changes in GFR) or is indicative of injury leading to loss of nephrons. Normalisation of creatinine within 10 days seems to suggest a functional change in GFR that was not accompanied by death of nephrons and compensatory hypertrophy of the remaining functioning nephrons (which can take up to three months following experimental renal mass reduction). It is important to stress that we do not have data to support either of these hypotheses.

The risk of withholding NSAID analgesia should also be considered. Inadequate pain relief post-operatively could result in the cats not eating or drinking properly in the immediate post-

operative period. Would this lead to more risk of kidney damage (mild AKI) resulting from the anaesthetic plus poor hydration post-operatively than the NSAID treatment, which allows the cats to eat and drink more quickly in the post-operative period? No one has done that study but we feel cats should receive analgesia.

Although our data are more than 10 years old, we judged they were still important to publish despite the recent improvements in veterinary medicine, including in the fields of AKI diagnosis and pain recognition in cats. Indeed, this discussion initiated by Malik et al. 2024 is testament to the relevance of our data today.

Krekis, A., J. N. King, D. D'Arcy-Howard, N. Stapleton, J. Elliott and L. Pelligand (2024). "Effect of meloxicam or robenacoxib administration timing on renal function and postoperative analgesia in cats undergoing ovariohysterectomy: A randomized, blinded, controlled clinical trial." J Vet Pharmacol Ther.

Lehr, T., R. Narbe, O. Jöns, C. Kloft and A. Staab (2010). "Population pharmacokinetic modelling and simulation of single and multiple dose administration of meloxicam in cats." J Vet Pharmacol Ther **33**(3): 277-286.