Effect of non-steroidal anti-inflammatory drugs on the blood profile in the green iguana (*Iguana iguana*)

S. Trnkova, Z. Knotkova, A. Hrda, Z. Knotek

Faculty of Veterinary Medicine, University of Veterinary and Pharmaceutical Science, Brno, Czech Republic

ABSTRACT: A total of 20 healthy green iguanas (14 males and six females with body weight ranging from 280 to 720 g) were divided into three groups and used for the experiment. Carprofen (2.0 mg/kg, *i.m.*) was administered to seven iguanas for 10 days, five were treated with meloxicam (0.2 mg/kg, *i.m.*) for the same period, and eight iguanas received the same volume of saline solution (0.04 ml/kg). All iguanas were blood sampled on Day 1 and 11 to obtain haematological and biochemical parameters. Comparing the values within particular groups, a decrease in haemoglobin concentration and packed cell volume accompanied by an increase in azurophils ($P < 0.05$) was observed in iguanas treated with carprofen. Decreased values of haemoglobin and packed cell volume were also found in control iguanas ($P < 0.05$). Increased ALT levels ($P < 0.01$) were found in all three groups of iguanas. A decrease in the concentration of Ca ($P < 0.01$) was observed both in meloxicam-treated iguanas and in the control ones. Mean ALT values of carprofen-treated iguanas (2.42 ± 0.52 μkat/l) were considerably higher ($P < 0.01$) than those in iguanas treated with meloxicam (0.49 ± 0.18 μkat/l) or saline (0.43 ± 0.13 μkat/l). Repeated doses of carprofen induced higher levels of AST (0.82 ± 0.26 μkat/l) compared with saline ($P < 0.01$, 0.31 ± 0.16 μkat/l) or meloxicam ($P < 0.05$, 0.38 ± 0.16 μkat/l). All blood parameters of green iguanas following the 10-day intramuscular administration of both carprofen and meloxicam were within the physiological reference values of this species.

Keywords: meloxicam; carprofen; reptiles; haematology; plasma chemistry

The underestimation of painful conditions in reptiles may result in serious health deterioration or even in the death of patients in the perioperative and postoperative period. Commonly occurring painful conditions in lizards include pododermatitis, periodontal inflammation, arthritis, spondylitis, osteomyelitis, and articular gout (Redrobe, 2004). Recent references stress a need for the pain control in reptiles in addition to anaesthesia (Redrobe, 2004; Kirchgessner, 2006; Schumacher and Yelen, 2006). Many sources dealing with surgery, anaesthesia and analgesia in reptiles mention substances commonly used in mammalian species (Bennett, 1998; Carpenter et al., 2001; Girling and Raiti, 2004; Redrobe, 2004; Wellehan and Gunkel, 2004; Kirchgessner, 2006; Schumacher and Yelen, 2006) such as non-steroidal anti-inflammatory drugs (NSAIDs), i.e. carprofen (1.0–4.0 mg/kg) and meloxicam (0.1–0.3 mg/kg), for the control of chronic painful conditions including metabolic skeletal disorders, gout and neoplasia (Schumacher and Yelen, 2006). Some authors reported the risk of the use of NSAIDs in patients with liver and kidney diseases (Wellehan and Gunkel, 2004). Special attention should be paid to this risk because disorders of these organs occur frequently in captive reptiles (Boyer et al., 1996; Ball et al., 1999; Antinoff, 2000; Divers and Cooper, 2000). When selecting a suit-

Partially supported by the Internal Grant of the University of Veterinary and Pharmaceutical Sciences, Brno (Grant No. 29/2007).

able combination of analgesics and anaesthetics, it is therefore necessary to monitor the liver and kidney function using techniques including diagnostic imaging, haematology and plasma chemistry (Boyer et al., 1996; Knotek et al., 2002; Hernandez-Divers et al., 2005).

The objective of this study was to evaluate and compare the effects of repeated administration of non-steroidal anti-inflammatory drugs, meloxicam and carprofen, on the blood profile of green iguanas kept under captive experimental conditions.

MATERIAL AND METHODS

The study was performed using a group of green iguanas (*Iguana iguana*) kept under experimental conditions at the Avian and Exotic Animal Clinic, Faculty of Veterinary Medicine, University of Veterinary and Pharmaceutical Sciences in Brno. A total of 20 healthy green iguanas (14 males and six females with body weight ranging from 280 to 720 g) were included in the experiment. The lizards were manually restrained for intramuscular injections every morning of the 10-day experimental period. Group A iguanas received carprofen (2.0 mg/kg Rimadyl inj. a.u.v., Pfizer), group B iguanas were applied meloxicam (0.2 mg/kg Metacam inj. a.u.v., BASF) and group C lizards saline (0.02 ml sodium chloride 0.9% in water for injection, SIFRA, Italy). Injection sites were alternated daily using the muscles of the front legs. Blood collection on Day 1 and 11, and laboratory processing and examination of samples were performed in accordance with previously published methods (Knotkova et al., 2006). The mean values of studied parameters were computed using Excel (XP, Office, Microsoft). A paired *t*-test was employed to evaluate the effect of 10-day administration of drugs within individual groups. Differences between individual groups were assessed by analysis of variance using the Scheff method of contrasts (Matouskova et al., 1992). Statistical significance was determined as $P < 0.05$ or $P < 0.01$.

RESULTS

There were no changes of clinical importance in haematological parameters of green iguanas following the 10-day intramuscular administration of both carprofen and meloxicam. Comparing the values within individual groups, a decrease in the concentration of haemoglobin and PCV accompanied by an increase in the percentage of azurophils was observed in carprofen-treated green iguanas ($P < 0.05$). A decrease in haemoglobin and PCV ($P < 0.05$) was also observed in iguanas in the control group. Lizards in all three groups showed rising levels of ALT ($P < 0.01$). Decreased levels of Ca ($P < 0.01$) were found in meloxicam-treated iguanas as well as in controls. The mean levels of ALT in carprofen-treated green iguanas (2.42 ± 0.52 μkat/l) were considerably higher ($P < 0.01$) than both in meloxicam-treated iguanas (0.49 ± 0.18 μkat/l) and in controls (0.43 ± 0.13 μkat/l). Repeated doses of carprofen induced higher levels of AST (0.82 ± 0.26 μkat/l) than saline ($P < 0.01$, 0.31 ± 0.16 μkat/l) or meloxicam ($P < 0.05$, 0.38 ± 0.16 μkat/l). Blood parameters of both experimental groups of iguanas were within physiological reference values of healthy green iguanas (Pejrilova et al., 2004; Knotkova et al., 2005, 2006). The mean values of haematological and biochemical parameters of experimental green iguanas are shown in tables (Table 1 and 2).

DISCUSSION

Various combinations of anaesthetics have been recommended for surgical procedures in reptiles (Lumb and Jones, 1984; Mosley et al., 2003a,b, 2004; Mauthe von Degerfeld, 2004). However, the establishment of effective analgesic regimens in reptiles is still problematic (Heard, 2001; Machin, 2001; Read, 2004; Redrobe, 2004; Schumacher and Yelen, 2006). A suitable analgesic regime should be selected in conjunction with an assessment of the unique metabolic and pharmacokinetic processes that occur in reptiles (Tuttle et al., 2006). It is also imperative to consider the possible adverse effects of NSAIDs on the gastric mucosa, kidney function and blood coagulation (Tuttle et al., 2006). The evaluation of peripheral blood parameters is essential for monitoring the health and more specifically the organ function in reptiles. Accordingly, haematological and biochemical profiles prior to and after the 10-day intramuscular administration of two non-steroidal anti-inflammatory drugs were evaluated. Neither carprofen nor meloxicam induced any clinically serious changes in haematological parameters in the green iguana. A rise in the ALT level was found in experimental animals;

Table 1. The biochemical plasma profile of green iguanas prior to and after the 10-day intramuscular administration of non-steroidal analgesics

Group	Day		TP (g/l)	Glucose (mmol/l)	UA (μmol/l)	ALP (μkat/l)	ALP (μkat/l)	AST (μkat/l)	Ca (mmol/l)	P (mmol/l)
Meloxicam (n = 7)	1	$\bar{x}$	43.99	10.13	108.34	0.79	0.20*	1.71	3.22*	2.04
		SD	7.77	1.22	26.13	0.28	0.19	2.51	0.22	1.00
	11	$\bar{x}$	47.29	9.52	103.23	0.76	0.49[b]*	0.38[e]	2.80*	1.55
		SD	10.97	1.44	42.21	0.30	0.18	0.16	0.09	0.16
Carprofen (n = 5)	1	$\bar{x}$	49.64	10.34	162.64	0.69	0.42*	0.78	3.28	2.14
		SD	7.63	1.46	70.44	0.29	0.27	0.40	0.40	0.65
	11	$\bar{x}$	48.06	9.08	148.66	0.74	2.42[a]*	0.82[c]	2.86	1.60
		SD	6.63	1.20	53.11	0.30	0.52	0.26	0.15	0.25
Control (n = 8)	1	$\bar{x}$	44.31	10.30	90.70	0.80	0.26*	0.31	3.14*	1.99
		SD	6.37	1.23	28.33	0.32	0.06	0.19	0.15	0.45
	11	$\bar{x}$	45.45	10.81	112.66	0.81	0.43[b]*	0.31[d]	2.70*	1.72
		SD	3.98	0.78	18.74	0.28	0.13	0.16	0.17	0.31

Comparisons between groups: [a–b]($P < 0.01$), [c–d]($P < 0.01$), [c–e]($P < 0.05$)
Comparisons within groups: *($P < 0.01$)

however, there was also an increase in this parameter in the control group. The mean levels of ALT in carprofen-treated green iguanas were significantly higher than those in iguanas treated with meloxicam and saline. Repeated doses of carprofen also induced higher levels of AST than the administration of both meloxicam and saline. The cause of these differences is not known. Carprofen induced

Table 2. The haematological blood profile of green iguanas prior to and after the 10-day intramuscular administration of non-steroidal analgesics

Group	Day		Hb (g/l)	PCV (l/l)	ERY (T/l)	LEU (G/l)	HE (G/l)	EO (G/l)	BA (G/l)	MO (G/l)	AZ (G/l)	LY (G/l)
Meloxicam (n = 7)	1	$\bar{x}$	81.37	0.31	1.14	8.5	2.53	0.01	0.23	0.27	0.59	4.87
		SD	11.21	0.04	0.13	3.01	1.35	0.02	0.11	0.26	0.27	2.15
	11	$\bar{x}$	78.36	0.29	1.06	10.64	3.50	0.03	0.47	0.37	1.41	4.88
		SD	9.71	0.02	0.15	3.98	1.74	0.05	0.38	0.28	1.53	1.58
Carprofen (n = 5)	1	$\bar{x}$	92.25*	0.32*	1.13	7.38	2.67	0.05	0.36	0.22	0.54*	3.55
		SD	9.78	0.03	0.18	3.78	2.38	0.05	0.21	0.27	0.55	1.16
	11	$\bar{x}$	79.13*	0.27*	1.09	11.8	5.97	0.03	0.65	0.38	1.22*	3.55
		SD	14.26	0.05	0.21	5.84	4.86	0.04	0.30	0.27	1.09	2.18
Control (n = 8)	1	$\bar{x}$	81.66*	0.30*	1.14	9.75	3.64	0.07	0.33	0.22	0.93	4.57
		SD	8.90	0.02	0.14	4.13	3.34	0.08	0.30	0.27	0.38	1.50
	11	$\bar{x}$	76.46*	0.28*	1.11	13.19	5.38	0.04	1.00	0.09	1.37	5.32
		SD	4.47	0.01	0.13	7.23	6.09	0.07	0.38	0.20	0.73	3.10

Comparisons within groups: *($P < 0.05$)

a decrease in the haemoglobin level and PCV in green iguanas. The same changes, however, were found in control animals. Decreased levels of Ca were found in meloxicam-treated and control green iguanas. Nevertheless, these levels were within the physiological reference range of healthy green iguanas (Pejrilova et al., 2004; Knotkova et al., 2005, 2006). None of the changes in blood parameters found in green iguanas had any adverse effects on their health state.

Acknowledgments

The authors would like to thank Dr. Robert S.P. Johnson, BVSc, MACVSc, CertZooMed, South Penrith Veterinary Clinic, New South Wales, and Doc. Dr. J. Pikula, Ph.D, University of Veterinary and Pharmaceutical Sciences, Brno for their valuable comments and kind help with translation of the manuscript.

REFERENCES

Antinoff N. (2000): Renal disease in the green iguana (*Iguana iguana*). In: Proceeding of the Association Reptilian and Amphibian Veterinarians, Reno, 61–63.

Ball R.L., Dumonceaux G., MacDonald C. (1999): Hypertrophic osteopathy associated with renal gout in a green iguana *Iguana iguana*. In: Proceeding of the Association Reptilian and Amphibian Veterinarians, Columbus, 5.–9. 10. 1999, 49–50.

Bennett R.A. (1998): Reptile anaesthesia. Seminars in Avian and Exotic Pet Medicine, 7, 30–40.

Boyer T.H., Getzy D., Vap L., Innis C. (1996): Clinicopathologic findings of twelve cases of renal failure in *Iguana iguana*. In: Proceeding of the Association Reptilian and Amphibian Veterinarians, Tampa, 24.–27. 8. 1996, p. 113.

Carpenter J.W., Mashima T.Y., Rupiper D.J. (2001): Exotic Animal Formulary. W.B. Saunders, Philadelphia. 423 pp.

Divers S.J., Cooper J.E. (2000): Hepatic lipidosis. Seminars in Avian and Exotic Pet Medicine, 9, 153–164.

Girling S.J., Raiti P. (2004): BSAVA Manual of Reptiles. 2nd ed. BSAVA, Quedgeley. 383 pp.

Heard D.J. (2001): Reptile anaesthesia. Veterinary Clinics of North America: Exotic Animal Practice, 83–117.

Hernandez-Divers S.J., Stahl S., Stedman N.L., Hernandez-Divers S.M., Schumacher J., Hanley C.S., Wilson H., Vidyashankar A.N., Zhao Y., Rumbeiha W.K. (2005): Renal evaluation in the healthy green iguana (*Iguana iguana*): assessment of plasma biochemistry, glomerular filtration rate, and endoscopic biopsy. Journal of Zoo and Wildlife Medicine, 36, 155–168.

Kirchgessner M.S. (2006): Meloxicam. Journal of Exotic Pet Medicine, 15, 281–283.

Knotek Z., Hauptman K., Knotkova Z., Hajkova P., Tichy F. (2002): Haemogram and plasma biochemistry in green iguanas with renal disease. Acta Veterinaria Brno, 71, 333–340.

Knotkova Z., Pejrilova S., Trnkova S., Matouskova O., Knotek Z. (2005): Influence of reproductive season upon plasma biochemistry values in green iguanas. Acta Veterinaria Brno, 74, 515–520.

Knotkova Z., Knotek Z., Trnkova S., Mikulcova P. (2006): Blood profile in green iguanas after short-term anaesthesia with propofol. Veterinarni Medicina, 51, 491–496.

Lumb W.V., Jones E.W. (1984): Veterinary Anesthesia. Lea and Febiger, Philadelphia. 693 pp.

Machin K.L. (2001): Fish, amphibian, and reptile analgesia. Veterinary Clinics of North America, Exotic Animal Practice, 4, 19–34.

Matouskova O., Cigler M., Chalupa K., Hruska K. (1992): STATPlus – Manual (in Czech). 1st ed. Veterinary Research Institute, Brno. 168 pp.

Mauthe von Degerfeld M. (2004): Personal experiences in the use of Association Tiletamine/Zolazepam for anaesthesia of the green iguana (*Iguana iguana*). Veterinary Research Communications, 28, 351–353.

Mosley C.A.E., Dyson D., Smith D.A. (2003a): Minimum alveolar concentration of isoflurane in green iguanas and the effect of butorphanol on minimum alveolar concentration. Journal of American Veterinary Medicine Association, 222, 1559–1564.

Mosley C.A.E., Dyson D., Smith D.A. (2003b): The cardiac anaesthetic index of isoflurane in green iguanas. Journal of American Veterinary Medicine Association, 222, 1565–1568.

Mosley C.A.E., Dyson D., Smith D.A. (2004): The cardiovascular dose-response effects of isoflurane alone and combined with butorphanol in the green iguana (*Iguana iguana*). Veterinary Anaesthesia and Analgesia, 31, 64–72.

Pejrilova S., Knotkova Z., Knotek Z., Vrbas J. (2004) Age-related changes of the haematological profile in green iguana (*Iguana iguana rhinolopha*). Acta Veterinaria Brno, 73, 305–312.

Read M.R. (2004): Evaluation of the use of anaesthesia and analgesia in reptiles. Journal of American Veterinary Medicine Association, 224, 547–552.

Redrobe S. (2004): Anaesthesia and analgesia. In: Girling S.J., Raiti P. (eds): BSAVA Manual of Reptiles. 2nd ed. BSAVA, Quedgeley. 131–146.

Schumacher J., Yelen T. (2006): Anaesthesia and analgesia. In: Mader D.R. (ed.): Reptile Medicine and Surgery. Saunders Elsevier, St. Louis. 442–452.

Tuttle A.D., Papich M., Lewbart G.A., Christian S., Gunkel C., Harms C.A. (2006): Pharmakokinetics of ketoprofen in the green iguana (*Iguana iguana*) following single intravenous and intramuscular injections. Journal of Zoo and Wildlife Medicine, 4, 567–570.

Wellehan J.F.X, Gunkel C.I. (2004): Emergent diseases in reptiles. Seminars in Avian and Exotic Pet Medicine, 13, 160–174.

Received: 2007–05–21
Accepted after corrections: 2007–10–10

Corresponding Author:

Prof. MVDr. Zdenek Knotek, CSc., University of Veterinary and Pharmaceutical Sciences Brno, Faculty of Veterinary Medicine, Avian and Exotic Animal Clinic, Palackeho 1–3, 612 42 Brno, Czech Republic
Tel. +420 541 562 381, fax +420 541 562 381, e-mail: knotekz@vfu.cz