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Effect of Butorphanol on Anaesthesia Induction by Isoflurane in the Green Iguana (*Iguana iguana)*

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Abstract

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A total of 10 clinically healthy green iguanas (5 males and 5 females, body weight ranging from 1 350 to 2 770 g) were given butorphanol by intramuscular injection following 24 h fasting. Inhalation anaesthesia was administered by mask (5% isoflurane with oxygen, 1.0 l/min), once reactions to external stimuli had decreased (15.45 ± 1.54 min later). Tracheal intubation was performed as soon as the iguanas exhibited complete tolerance to mechanical stimuli. A second study was performed 4 weeks later using the same green iguanas with no pre-medication. Marked individual reactions to masking were observed during both experiments. Some iguanas exhibited breath holding which prolonged anaesthetic induction. Physical stimulation was used in these cases in order to stimulate spontaneous breathing. The mean anaesthetic induction time was similar in both groups of green iguanas (4.34 ± 0.47 and 4.93 ± 0.88 min). There was also a comparable interval from masking to safe tracheal intubation in both experimental groups (15.21 ± 4.26 and 14.31 ± 1.39 min). In view of the results, pre-medication with butorphanol cannot be considered an effective method of anaesthetic induction in green iguanas.

Analgesia, opioids, induction time, reptiles

In reptiles, anaesthesia is not only necessary for surgical procedures, but also indicated for many diagnostic procedures (Lumb and Jones 1984; Mosley et al. 2003a, 2003b; Mauthe von Degerfeld 2004; Mosley et al. 2004). Ideally, the induction and recovery periods should be as short as possible (Redrobe 2004). With respect to minimising side effects, the technique of choice is inhalation anaesthesia (Heard 2001). In the green iguana, inhalation anaesthesia may be administered by either mask or tracheal intubation, or a combination of both. Due to animals struggling or difficulties with restraint, injectable anaesthetic combinations may be preferred (Girling and Raiti 2004). Injectable agents may, however, prolong the recovery phase (Schumacher and Yelen 2006). It appears that the administration of opioid agents reduces the anaesthetic induction time in reptiles (Hernandez-Divers et al. 2005). An endogenous opioid system exists in reptiles (Liang and Terashima 1993; Machin 2001) with differences in numbers and types of individual opioid receptors in different taxonomic groups. Historically, the analgesic effects of morphine and its derivatives have been studied with subsequent reports on the use of substances blocking the activity at the neuromuscular junction (Brazenor and Kaye 1953; Brisbin 1966; Kanui et al. 1990; Kanui and Hole 1992; Machin 2001). It is supposed that most of these drugs (e.g., gallamine, succinylcholine or d-tubocurarine chloride) are only able to induce immobilization or even paralysis in reptiles without effective analgesia.

Opioid analgesics such as butorphanol and buprenorphine have recently been considered (Read 2004). Butorphanol is considered disadvantageous due to its short-term effect (Bistner et al. 2000) and doubts concerning its analgesic action. Other authors, however,

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highlight its positive effect ensuring a calm induction of inhalation anaesthesia in reptiles (Hernandez-Divers et al. 2005). Despite the fact that the use of the combination of butorphanol and isoflurane for calm induction of anaesthesia seems very practical in reptiles, there are a limited number of studies dealing with this method. The aim of this project was to evaluate the use of the opioid analgesic butorphanol as an effective anaesthetic induction agent in green iguanas.

Materials and Methods

The study was performed using 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 Brno, Czech Republic. A total of 10 clinically healthy green iguanas (5 males and 5 females, body weight ranging from 1 350 to 2 770 g) were used for the study. The animals were fasted for 24 h before anaesthesia.

Butorphanol group

Green iguanas were manually restrained and injected with 2.0 mg/kg butorphanol (Torbugesic, Fort Dodge Animal Health, Iowa, USA) using the proximal muscles of the thoracic limb. Lizards were kept separately in cardboard boxes (26 × 33 × 56 cm) after injection. Once the response to external stimuli had decreased, inhalation anaesthesia was induced by masking (5% isoflurane - Isofluran Nicholas Piramal, Nicholas Piramal India Ltd., London, UK - with oxygen, 1.0 l/min). The semi-closed anaesthetic system was used. During the procedure lizards were placed upon an electric heating pad (37.5 °C) (Bosch PFP 1031, Bosch CZ). Reactions to external stimuli were evaluated at regular (2 min) intervals. Skin sensitivity was monitored by gently touching the skin on the pelvic limbs while deep sensitivity was judged by the toe-pinch reflex on the right pelvic limb. The time from the start of inhalation anaesthesia to the loss of the righting reflex was recorded as induction time. The time from the loss of the righting reflex (when on back or side, the reptile cannot right itself) to the loss of the toe-pinch reflex was recorded as surgical plane of anaesthesia time: from the early Stage 3 (Plane 1) to Stage 3 (Plane 2) (Lumb and Jones 1984). An endotracheal tube was inserted at the moment of complete loss of reaction to the above-mentioned stimuli and the animals were ventilated manually with pure oxygen only (1.0 l/min) for approximately one minute, after which they were ventilated with air. Upon the onset of spontaneous breathing the animals were extubated and placed back in the terrarium.

Control group

Four weeks later, the same green iguanas were subjected to identical procedures; the only exception being that butorphanol was not administered. To simulate the conditions of the previous procedure, the animals were placed in the cardboard box for a similar time prior to the induction. All other steps of the control study were the same as for the treatment study.

Statistical evaluation

Statistical evaluation of the variables studied was performed using Microsoft Excel. Maximum (max) and minimum (min) values were computed for each of the evaluated variables as well as the mean (x) and standard deviation (SD). Statistical significance of differences between both groups of green iguanas was determined using a paired *t*-test.

Results

Treated iguanas spent a similar period of time in the cardboard box prior to anaesthetic induction compared with the animals used in the control study (15.45 ± 1.54 and 14.73 ± 0.48 minutes, respectively). Despite the mean induction time being shorter in the green iguanas pre-medicated with butorphanol (4.34 ± 0.47 versus 4.93 ± 0.88 minutes), the difference between the two groups was not significant ($p = 0.124$). Both studies resulted in a rather comparable surgical plane of anaesthesia time as well as nearly the same interval from masking to tracheal intubation (10.76 ± 4.27 versus 9.18 ± 1.80 and 15.21 ± 4.26 versus 14.31 ± 1.39 min, respectively). Markedly different individual reactions to masking were observed. Breath holding in some individuals resulted in a longer induction time. The shortest induction time (3.46 min) was observed in green iguana No. 5 which breathed spontaneously and regularly during the entire induction period. On the other hand, the longest induction time (5.14 min) was found in green iguana No. 10 which exhibited marked breath holding. The surgical plane of anaesthesia time was also influenced considerably by breath holding in some of the green iguanas (No. 5 and 10). This problem could partly be solved by encouraging spontaneous breathing using mechanical stimulation, i.e. touching

Table 1. Isoflurane anaesthesia in green iguanas after (or without) induction with butorphanol (2mg/kg i.m.) injection

Iguanas	Introduction		Mask (Isoflurane/O_2)					
			Induction time		Surgical plane of anaesthesia time		Total time	
	butorphanol minutes	control minutes	butorphanol minutes	control minutes	butorphanol minutes	control minutes	butorphanol minutes	control minutes
1	20.00	15.42	5.00	4.56	15.00	9.09	20.00	14.05
2	15.11	15.13	4.07	4.57	13.35	7.10	17.42	12.07
3	15.05	15.08	4.48	4.26	9.53	9.23	14.41	13.49
4	15.20	14.39	4.45	4.40	10.15	12.09	15.00	16.49
5	15.27	15.03	3.46	5.43	17.07	6.49	20.53	12.32
6	14.50	14.11	4.22	3.59	6.15	11.07	10.37	15.06
7	15.15	14.16	4.05	4.51	4.32	11.09	8.37	15.08
8	15.10	14.23	4.50	6.59	5.15	7.16	10.05	14.25
9	14.58	14.49	4.01	6.24	11.51	10.00	15.52	16.24
10	14.58	15.29	5.14	5.12	15.33	8.48	20.47	14.00
min	14.50	14.11	3.46	3.59	4.32	6.49	8.37	12.07
max	20.00	15.42	5.14	6.59	17.07	12.09	20.53	16.49
mean	15.45	14.73	4.34	4.93	10.76	9.18	15.21	14.31
SD	1.54	0.48	0.47	0.88	4.27	1.80	4.26	1.39
t-test	0.150		0.124		0.401		0.601	

the skin of pelvic limbs and toe-pinching. Due to the tendency to hold breath during anaesthetic induction (iguana No. 10) and/or during the stay on the heating pad (iguanas No. 5 and 10) there was a prolongation of the interval from masking to the loss of the toe-pinch reflex (20.53 and 20.47 min).

Discussion

The healthy adult green iguana can be a strong and often aggressive patient. In order to ensure handler safety and "trouble-free" surgery, it is desirable to have a reliable and smooth anaesthetic induction. Various combinations of anaesthetics and analgesics have been used in reptiles. It has been found that the use of butorphanol for the pre-medication of inhalation anaesthesia using isoflurane or sevoflurane does not have a detrimental effect (Mosley et al. 2004; Hernandez-Divers et al. 2005). One previous study in green iguanas has shown that 1 mg/kg i.m. of butorphanol does not produce significant isoflurane-sparing effects (Mosley et al. 2003a). As a result of this study Hernandez-Divers et al. (2005) proposed an increased dose for green iguanas of 2 mg/kg i.m. The same dose was used in our study. Until recently, no report described the difference between the quality of induction in reptiles anaesthetized with isoflurane compared with those anaesthetized with isoflurane and pre-medicated with butorphanol. Hernandez-Divers et al. (2005) have not noted a difference in induction quality between iguanas anaesthetized with isoflurane versus butorphanol and isoflurane. Based on our

clinical experience with green iguanas, we expected individual differences in response to butorphanol, therefore the same group of adult healthy green iguanas was used as the control group. When comparing individual anaesthetic protocols, apart from evaluating physical reflexes, vital functions such as the respiratory and heart rate, ECG, blood pressure, temperature, tissue oxygen saturation and concentration of CO_2 in expired gas may also be measured (Bennett 1996, 1998; Wellehan and Gunkel 2004; Hernandez-Divers et al. 2005; Knotek et al. 2006; Knotková et al. 2006). The scope of our study did not include the evaluation of the afore-mentioned indicators.

The inclusion of butorphanol as a premedicant for masked isoflurane induction had no positive effect. Some differences were observed between individual green iguanas. Anaesthesia was induced most quickly in green iguanas that did not hold their breath after masking. Spontaneous breathing enabled a shorter induction time and facilitated endotracheal intubation.

Considering the results obtained in this study, as well as our experience with the use of injection anaesthetics tiletamine-zolazepam and propofol (Knotek et al. 2005, 2006; Knotková et al. 2006), we do not regard pre-medication with butorphanol as an effective method of shortening the anaesthetic induction time in the green iguana.

Vliv butorfanolu na úvod do anestézie isofluranem u leguánů zelených (*Iguana iguana*)

U 10 klinicky zdravých leguánů zelených (5 samců, 5 samic, 1 350 – 2 770 g ž. hm.) byl po 24hodinové hladovce aplikován butorfanol (2,0 mg/kg) intramuskulárně. Po zjištění omezené reakce na vnější podněty (15,45 ± 1,54 min) byla zahájena inhalační anestézie maskou (5% isofluran s kyslíkem 1,0 l/min). V okamžiku, kdy byla potvrzena úplná tolerance na mechanické podněty, byla provedena tracheální intubace. Shodné sledování, ale bez podání butorfanolu, bylo u stejných leguánů uskutečněno za 4 týdny. V obou experimentech byla pozorována výrazně individuální reakce na nasazení masky. Pokud leguáni reagovali na nasazení masky a přívod isofluranu zadržením dechu, došlo k oddálení účinku inhalační anestézie a prodloužení její úvodní fáze. Průměrná hodnota úvodní fáze anestézie byla shodná u obou skupin leguánů zelených (4,34 ± 0,47 vs. 4,93 ± 0,88 min). Spontánní dýchání bylo možno vyprovokovat mechanickými stimulacemi. U obou skupin byl srovnatelný interval od nasazení masky do provedení bezpečné tracheální intubace (15,21 ± 4,26 vs. 14,31 ± 1,39 min). Zařazení butorfanolu do zahájení inhalační anestézie nepřineslo příznivý efekt zkrácení úvodu. Na základě dosažených výsledků nepovažujeme premedikaci butorfanolem za účinnou metodu ke zkrácení úvodní fáze inhalační anestézie maskou před tracheální intubací.

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