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[**Optimizing The Pharmacodynamics And Evaluating Cardiogenic Effects Of The Injectable Anesthetic Alfaxalone In Prairie Rattlesnakes (*Crotalus viridis*)**](https://doi.org/10.1638/2021-0056)

Webb JK, Keller KA, Chinnadurai SK, Kadotani S, Allender MC, Fries R

**ABSTRACT:** North American vipers are commonly housed in zoological institutions or studied as free-ranging populations. Because of their venomous predatory and defensive mechanism, sedation or anesthesia is frequently employed to facilitate safe handling and medical procedures, especially of the head. A new formulation of alfaxalone with proprietary preservatives was recently approved and indexed for 28-d use post-vial puncture. Pharmacodynamic effects of alfaxalone in its prior formulation have been researched in nonvenomous species, but the optimal dose and route of administration in vipers have not been reported. In part one, 10 prairie rattlesnakes (*Crotalus viridis*) participated in a complete four-route crossover study evaluating 20 mg/kg alfaxalone administered intracoelomically (ICo), SC cranial to the heart, IM cranial to the heart, and IV in the ventral coccygeal vein. HR significantly decreased from baseline during IV (*P*= 0.024), IM (*P*= 0.024), and SC (*P*= 0.028) administration. Respiratory rate significantly decreased following alfaxalone delivered IV (*P* = 0.027). Time to first effects was significantly faster in IV compared with IM (*P*= 0.01), SC (*P*= 0.001), and ICo (*P*= 0.036). All IV and IM administrations resulted in deep sedation, but 70% of the IV and 10% of the IM sedation events resulted in apnea and required intermittent positive ventilation via endotracheal tube. Fifty percent of the ICo sedation events and 10% of the SC sedation events did not result in sedation. One successful SC sedation event resulted in apnea. In part two, echocardiograms were performed in the same rattlesnakes at baseline and at maximum effect of sedation with 20 mg/kg alfaxalone administered IM. Cardiac contractility and output were unaffected. Administration of alfaxalone at 20 mg/kg IM cranial to the heart should facilitate safe handling and minimally invasive procedures in prairie rattlesnakes and related species.

**Background:**

* Alfaxalone= neuroactive steroid GABAA agonist
  + Evaluated previously at 10-30 mg/kg via various routes in other snakes
  + Paucity of literature on the optimal dose and route of administration in viperids
  + May lead to cardiovascular/respiratory depression; recommend anesthetic monitoring

**Key Points:**

* Alfaxalone 20mg/kg IM cranial to heart resulted in complete sedation
  + 90% of animals retained spontaneous ventilation with no significant differences in RR
  + No significant changes in contractility or output based on echocardiography
* Alfaxalone 20mg/kg IV also resulted in complete sedation
  + HOWEVER, HR and RR significantly decreased when administered IV
    - 70% required assisted ventilation
  + Time to loss of muscle tone is faster with IV but does not produce longer sedation
  + Tail, head tongue movement noted prior to return of righting reflex or muscle tone
    - Possibly unsafe recovery and increases risk of accidental envenomination
* SC and IC administration did not result in consistent sedation
  + Manual restrain may have overridden the sedative effects of IC injection
* If administering alfaxalone 20mg/kg or greater IV, recommend being prepared to intubate

**TLDR:** Alfaxalone 20 mg/kg the IV or IM produces reliable sedation in prairie rattlesnakes, without changes in echocardiographic parameters, but WITH significant decreases in HR and RR if given IV

**Related Articles:**

* Kane LP, Chinnadurai SK, Vivirito K, Strahl-Heldreth D, Allender MC. Comparison of isoflurane, sevoflurane, and desfluroane as inhalant anesthetics in prairie rattlesnakes (*Crotalus viridis*). J Am Vet Med Assoc. 2020;257(9):945–949
* Vincent EC, Fries R, Allender MC. Effect of body position on echocardiographic parameters in prairie rattlesnakes (*Crotalus viridis*). J Zoo Wildl Med. 2021;52(2):742–748

*AJVR* 2021 83(3):212-217

[**Neuraxial administration of morphine combined with lidocaine induces regional antinociception in inland bearded dragons (*Pogona vitticeps*)**](https://doi.org/10.2460/ajvr.21.08.0104)

Fink DM, Ferreira TH, Mans C

**ABSTRACT:**

**Objective:**To assess the antinociceptive efficacy and safety of neuraxial morphine in inland bearded dragons (*Pogona vitticeps*).

**Animals:**10 healthy adult bearded dragons.

**Procedures:**Animals were sedated with alfaxalone (15 mg/kg) SC prior to neuraxial injections. In a randomized, blinded, placebo-controlled, crossover design, animals received preservative-free morphine (0.5 mg/kg) combined with lidocaine (2 mg/kg) or lidocaine (2 mg/kg) only (control treatment). For both treatments, saline (0.9% NaCl) solution was used for dilution to a total volume of 0.3 mL/kg. If the initial injection did not result in motor block of the pelvic limbs or cloaca relaxation within 10 minutes, a second injection was performed. Measurements consisted of bilateral mechanical stimulation of the limbs and at 25%, 50%, and 75% of the trunk's length as well as cloacal tone to assess spread and duration of motor block. Pelvic limb withdrawal latencies in response to a thermal noxious stimulus were measured over a 48-hour period to assess antinociception.

**Results:**Success rate following the first injection was 90% (18/20 injections) and increased to 100% following a second injection. Motor block occurred within 5 minutes with both treatments. Pelvic limb withdrawal latencies were significantly prolonged following neuraxial morphine versus control treatment for at least 12 hours after injection. By 24 hours, no effect of morphine on pelvic limb latencies was detectable.

**Clinical relevance:**These results demonstrated that neuraxial administration of morphine results in regional antinociceptive effects for at least 12 hours and has no clinically relevant adverse effects in healthy bearded dragons. This technique has potential for providing regional analgesia in this species.

**Background:**

* μ-opioid agonists have most consistently resulted in analgesia in lizards and chelonians
* Prior studies in bearded dragons evaluated neuraxial 2mg/kg lidocaine and 1 mg/kg bupivacaine
  + Both had regional effects caudally and minimal adverse effects
  + Brief onset of action (< 5 min) but brief duration (48 min lidocaine, 68 min bupivacaine)

**Key Points:**

* Preliminary study of 0.1, 0.2, and 0.5 mg/kg morphine combined with 2 mg/kg lidocaine
  + At 0.1 and 0.2 mg/kg antinociceptive effects were inconsistent and lasted <8 hr
* Success rate following the first injection was 90%
* No difference in sedation parameters (righting reflex, head position) or duration of motor block
  + Lidocaine alone lasted only 20 min vs. previous study 48 min
  + Possibly difference in lidocaine concentration
* Both treatments: time of onset 5 min
* 9/10 had sensory block up to 25% of caudal trunk, 4-5/10 had cranial spread up to 75% of trunk
  + 2/10 individuals had motor block up to forelimbs
  + Higher volume had more consistent cranial spread vs. lower volume in past study
  + Reducing dilution volume may reduce unwanted cranial spread of motor/sensory block
* Thermal withdrawal latency was longer with morphine vs lidocaine alone up to 12 hr, not at 24 hr
* HR significantly decreased for both (more with morphine) but was WNL
  + Initial transient increase in HR at 5 min after lidocaine alone, resolved by 10 min
  + No change in RR

**TLDR:** Neuroaxial morphine (0.5 mg/kg) with lidocaine (2 mg/kg) can provide at least 12 hr of regional antinociceptive effects in healthy bearded dragons with no clinically relevant adverse effects

**Related Articles:**

* Ferreira TH, Mans C. Evaluation of neuraxial anesthesia in bearded dragons (*Pogona vitticeps*). *Vet Anaesth Analg.* 2019;46(1):126–134
* Ferreira TH, Fink DM, Mans C. Evaluation of neuraxial administration of bupivacaine in bearded dragons (*Pogona vitticeps*). *Vet Anaesth Analg.* 2021;48(5):798–803

Evaluation of subcutaneous administration of alfaxalone-midazolam and dexmedetomidine-midazolam for sedation of ball pythons (Python regius).

Yaw, T.J., Mans, C., Johnson, S., Bunke, L., Doss, G.A. and Sladky, K.K.

*Journal of the American Veterinary Medical Association*, 2020;256(5):573-579.

OBJECTIVE To evaluate SC administration of alfaxalone-midazolam and dexmedetomidine-midazolam for sedation of ball pythons (Python regius).

ANIMALS 12 healthy juvenile ball pythons.

**PROCEDURES** In a randomized crossover study, each snake was administered a combination of **alfaxalone (5 mg/kg [2.3 mg/lb]) and midazolam (0.5 mg/kg [0.23 mg/lb])** and a combination of **dexmedetomidine (0.05 mg/kg [0.023 mg/lb]) and midazolam (0.5 mg/kg)**, **SC**, with a washout period of at least 7 days between protocols. Respiratory and heart rates and various reflexes and behaviors were assessed and compared between protocols. Forty-five minutes after protocol administration, sedation was reversed by SC administration of flumazenil (0.05 mg/kg) alone or in combination with atipamezole (0.5 mg/kg; dexmedetomidine-midazolam protocol only). Because of difficulties with visual assessment of respiratory effort after sedative administration, the experiment was repeated for a subset of 3 ball pythons, with plethysmography used to assess respiration.

RESULTS Both protocols induced a similar level of moderate sedation with no adverse effects aside from transient apnea. Cardiopulmonary depression was more profound, but time to recovery after reversal was significantly shorter, for the dexmedetomidine-midazolam protocol than for the alfaxalone-midazolam protocol. Plethysmographic findings were consistent with visual observations and suggested that snakes compensated for a decrease in respiratory rate by increasing tidal volume amplitude.

CONCLUSIONS AND CLINICAL RELEVANCE Results indicated that both protocols induced clinically relevant sedation in ball pythons and should be useful for minor procedures such as venipuncture and diagnostic imaging. However, caution should be used when sedating snakes with compromised cardiopulmonary function.

Background

* Alfaxalone: neuroactive synthetic steroid
  + Enhances neuronal cell membrane chlorine ion transport via interaction with cell surface y-aminobutyric acid A receptors to induce sedation and anesthesia
  + Apnea and prolonged recovery with high doses in reptiles, reactive to stimulation with low doses

Key Points

* Attempted intubation and blood collection at 30 min, reversed at 45 min
* Subset of 3 snakes: respiration evaluated with plethysmography in airtight chamber
* No adverse effects, no tissue damage at injection sites
  + SC allowed larger volume with comparable induction time to IM
* Both AM and DM: similar depth of sedation, successful intubation and blood draw, HR and RR decreased significantly
* AM:
  + shorter time to first effect and loss of jaw tone
  + longer duration of loss of righting reflex (no antagonist)
  + longer time to recovery
  + More snakes were reactive to superficial pain stimulation
  + Majority had spontaneous mouth opening/chewing behavior
* DM:
  + greater decrease in HR and RR
  + Increase in tidal volume - possibly compensating for decreased RR
  + Transient periods of apnea

Conclusions

* SC alfaxalone (5 mg/kg) + midazolam (0.5 mg/kg) or dexmedetomidine (0.05 mg/kg) + midazolam (0.5 mg/kg) resulted in sufficient sedation for tracheal intubation and blood sample collection in healthy juvenile ball pythons
  + Self-limiting apnea
  + Both protocols induced significant decreases in RR and HR, more profound with DM
  + DM can be reversed - faster recovery

Table

Description automatically generated

Evaluation of the effects of a dexmedetomidine-midazolam-ketamine combination administered intramuscularly to captive red-footed tortoises (*Chelonoidis carbonaria*)

Eshar D, Rooney TA, Gardhouse S, Beaufrère H

*AJVR* 2021 82(11):858-864

OBJECTIVE: To evaluate the effects of a dexmedetomidine-midazolam-ketamine (DMK) combination administered IM to captive red-footed tortoises (*Chelonoidis carbonaria*).

**ANIMALS**: 12 healthy adult red-footed tortoises.

**PROCEDURES**: In a prospective experimental study, DMK (0.1, 1.0, and 10 mg/kg, respectively) was administered IM as separate injections into the right antebrachium. Atipamezole (0.5 mg/kg, IM) and flumazenil (0.05 mg/kg, SC) were administered into the left antebrachium 60 minutes later. Times to the first treatment response and maximal treatment effect after DMK administration and time to recovery after reversal agent administration were recorded. Vital signs and reflexes or responses to stimuli were assessed and recorded at predetermined intervals.

RESULTS: DMK treatment produced deep sedation or light anesthesia for ≥ 20 minutes in all tortoises. Induction and recovery were rapid, with no complications noted. Median times to first response, maximum effect, and recovery were 4.5, 35, and 14.5 minutes, respectively. Two tortoises required additional reversal agent administration but recovered < 20 minutes after the repeated injections. Mean heart and respiratory rates decreased significantly over time. All animals lost muscle tone in the neck and limbs from 35 to 55 minutes after DMK injection, but other variables including palpebral reflexes, responses to mild noxious stimuli (eg, toe pinching, tail pinching, and saline ([0.9 NaCl] solution injection), and ability to intubate were inconsistent.

CONCLUSIONS AND CLINICAL RELEVANCE: DMK administration produced deep sedation or light anesthesia with no adverse effects in healthy adult red-footed tortoises. At the doses administered, deep surgical anesthesia was not consistently achieved. Anesthetic depth must be carefully evaluated before performing painful procedures in red-footed tortoises with this DMK protocol.

Background:

* Dexmedetomidine-midazolam-ketamine (DMK) previously reported in chelonian species
  + In African spurred tortoises, SC DMK produced moderate to deep sedation
    - Suitable for cloacal endoscopy; recovery was rapid after reversal
  + In red-eared slider turtles, SC DMK produced moderate to deep sedation
    - Suitable for cloacal endoscopy/intrathecal injection; recovery rapid

Key Points:

* Anesthesia protocol administered IM in a forelimb:
  + 0.1 mg/kg dexmedetomidine + 1.0 mg/kg midazolam + 10 mg/kg ketamine
  + Reversal: 0.5 mg/kg atipamezole IM & 0.05 mg/kg flumazenil SC
* Resulted in a rapid deep sedation or light anesthesia for ≥ 20 min in all tortoises
  + Lasted approximately 40 min in more than half of the tortoises
  + After 55 min, all tortoises had complete muscle relaxation; 6 of 12 could be intubated
  + No apparent adverse effects
* Low respiratory rates observed in tortoises in this study
  + Respiratory depression is a common effect of α2-adrenoceptor agonists in reptiles
  + Lower RR was consistent with findings in other studies using medetomidine
* Tortoises had a slight but nonsignificant increase in cloacal temp
  + Cloacal temp continued to increase after reversal
  + Possible advantage of this DMK protocol for short durations
* Variable preservation of reflexes and responses suggested DMK protocol can produce deep sedation or light anesthesia, but not a consistent surgical plane of anesthesia

Conclusions: DMK produced deep sedation/light anesthesia, but not surgical anesthesia, in red-footed tortoises

Karklus, Alyssa A., Kurt K. Sladky, and Stephen M. Johnson. "Respiratory and antinociceptive effects of dexmedetomidine and doxapram in ball pythons (Python regius)." *American Journal of Veterinary Research* 82.1 (2021): 11-21.

OBJECTIVE: To determine the effects of dexmedetomidine, doxapram, and dexmedeto- midine plus doxapram on ventilation ( ̇Ve), breath frequency, and tidal vol- ume (Vt) in ball pythons (Python regius) and of doxapram on the thermal antinociceptive efficacy of dexmedetomidine.

ANIMALS 14 ball pythons.

PROCEDURES Respiratory effects of dexmedetomidine and doxapram were assessed with whole-body, closed-chamber plethysmography, which allowed for estimates of  ̇Ve and Vt. In the first experiment of this study with a complete crossover design, snakes were injected, SC, with saline (0.9% NaCl) solution, dexmedetomidine (0.1 mg/kg), doxapram (10 mg/kg), or dexmedetomidine and doxapram, and breath frequency,  ̇Ve, and Vt were measured before and ev- ery 30 minutes thereafter, through 240 minutes. In the second experiment, antinociceptive efficacy of saline solution, dexmedetomidine, and dexme- detomidine plus doxapram was assessed by measuring thermal withdrawal latencies before and 60 minutes after SC injection.

RESULTS Dexmedetomidine significantly decreased breath frequency and increased Vt but did not affect  ̇Ve at all time points, compared with baseline. Doxapram significantly increased  ̇Ve, breath frequency, and Vt at 60 minutes after injection, compared with saline solution. The combination of dexmedeto- midine and doxapram, compared with dexmedetomidine alone, significantly increased  ̇Ve at 30 and 60 minutes after injection and did not affect breath frequency and Vt at all time points. Thermal withdrawal latencies significantly increased when snakes received dexmedetomidine or dexmedetomi- dine plus doxapram, versus saline solution.

CONCLUSIONS AND CLINICAL RELEVANCE

Concurrent administration of doxapram may mitigate the dexmedetomidine-induced reduction of breathing frequency without disrupting thermal antinociceptive efficacy in ball pythons. (Am J Vet Res 2021:82:11–21)

-   Opioids are effective analgesics in turtles and lizards but inconsistent in snakes.

-    NSAIDs have minimal efficacy

-    Alpha2 reported to provide analgesia in ball pythons (at least 8 hours)

o   Alpha2-adrenoreceptors can cause inhibition of breathing

o   Respiratory depression may alter arterial blood gas and reduce hypoxic ventilatory responses, leading to hypoxemia and tissue hypoxia

-    **Doxapram is a potassium channel blocker that acts on the central respiratory centers and peripheral chemoreceptors to stimulate breathing**

M&M

-    14 ball pythons

-    Dexmed 0.1mg/Kg, doxapram 10mg/Kg (based on alligators) Crossover study

-    Dexmed, doxapram, dexmed+doxapram, saline

-    Evaluation of Ve (ventilation), Vt (tidal volume), TWL (thermal withdrawal latency)

Results:

* Dexmedetomidine significantly decreased breath frequency and increased Vt but did not affect  ̇Ve at all time points, compared with baseline.
* Doxapram significantly increased  ̇Ve, breath frequency, and Vt at 60 minutes after injection, compared with saline solution. The combination of dexmedetomidine and doxapram, compared with dexmedetomidine alone, significantly increased  ̇Ve at 30 and 60 minutes after injection and did not affect breath frequency and Vt at all time points.
* Thermal withdrawal latencies significantly increased when snakes received dexmedetomidine or dexmedetomi- dine plus doxapram, versus saline solution.

Discussion

-    Dexmed decreased breath frequency, but Ve remains the same from baseline possibly due to fast sedation (Ve increased in saline group)

-    Snakes and other reptiles have an active inspiration, active expiration, and a breath-holding period

o   Dexmed changed pattern: Vt irregular, inspiration and expiration varied in duration and amplitude

§  Could have negative consequences for healthy and sick snakes

§  Breathing disruptions ay cause fluctuation son PaCO2 and PaO2. Episodic breaths lead to increase in CO2 and leading to acidemia

-    Hypoxia and hypoxemia induce compensatory hypothermia and reduced metabolic rate. When supporting for heat, be careful not to over do it as may lead to increased respiratory rate, oxygen uptake, Ve and metabolic rate

-    Doxpram did increase Ve and Vt, but not respiratory rate

o   Effects for 60 minutes (vs mammals 5-15 minutes)

-    Doxapram counteracts  effects of dexmed on breathing, but did not affect analgesic effects

-    Doxapram is associated with decreased cerebrall blood flow in dogs, and increased ccardiac work.

Take home: Doxapram counteracts respiratory effects of dexmedetomidine in ball pythons, but did not counteract analgesic effects.

Related articles:

Bunke, Laura G., Kurt K. Sladky, and Stephen M. Johnson. "Antinociceptive efficacy and respiratory effects of dexmedetomidine in ball pythons (Python regius)." *American journal of veterinary research* 79.7 (2018): 718-726.

Attitudes of Brazilian Veterinarians Towards Anesthesia and Pain Management in Reptiles Vanessa N. Gris1,3, Mario A. Ferraro1, Andressa F. K. T. Lima1, Silvia R. G. Cortopassi1, Adriano B. Carregaro2

Abstract: Veterinarians’ perceptions regarding anesthetics and pain management in reptiles are understudied. We conducted an internet-based survey of Brazilian practitioners to assess their knowledge and attitudes towards the use of anesthetics, as well as recognition and treatment of pain, in reptiles. The most commonly cited anesthesia-related complications were prolonged recovery periods and respiratory depression. Difficulty in recognizing pain was the main impeding factor for providing analgesics. Tramadol (88.2%) and meloxicam (97%) were the most commonly used analgesics, and ketamine (88.2%), midazolam (88.2%), and isoflurane (94.5%) were the most common anesthetic agents. In conscious patients, the assessment of pain was performed mainly by observation of behavioral changes. Only 32.7% of the respondents considered their knowledge of anesthesia and analgesia in reptiles to be adequate. More women than men considered their knowledge to be insufficient (P , 0.0068), whereas age of the practitioner had no effect. Nevertheless, all respondents believe that reptiles can feel pain, and 82% provide analgesia to most of their patients. Understanding the criteria, choice, and timing of drug administration, as well as opinions on pain and anesthesia, provides information on the current practices and might assist in targeting areas where more research and development is needed to ensure reptile welfare.

* Aim: investigate the attitudes and opinions of vets towards anesthesia and analgesia in reptiles through an online questionnaire
* More females than males filled the surgery out
* All vets believed that reptiles feel pain
* More than half the participants said that their knowledge about reptile anesthesia and analgesia is insufficient; with women being more common to say this than men
* Practitioner age had no effect\
* Older people were more confident in recognizing pain- but only half had confidence in ability to recognize out of the entire population surveyed
* 82% were classified as analgesic users
* Half felt confident in their ability to anesthetize reptiles
* Many users said their limited use of analgesics was due to difficulty in recognizing pain followed closely by lack of knowledge about appropriate therapy.
* Meloxicam most common NSAID cited and Tramadol most common opioid (Dipyrone and morphine were also frequently used)
* There was no significant difference between confident and noncnfident practitioners and their respective use of analgesics
* Most frequently used pain in reptiles: keeping eyelids closed for prolonged periods and mouth gapping (facial/grimace is hard and unknown); change in behavior continue to be the main indicator of pain in Brazil
* Butorphanol= good in corn snakes
* Morphine= Nile crocs, red-eared sliders, bearded dragons, ad tegus
* Fentanyl- good skin penetration but not effective in pythons
* Xylazine is the most common alpha -2 used but their use is MUCH lower.
* Propofol was the agent of choice for induction
* Inhalant drugs are commonly used for maintenance
* Peer review papers was one of the main sources for knowledge in brazil followed by wildlife textbooks and then case discussion with colleagues

Fentanyl Overdose after Cystic Ovarian Tumor Removal Surgery in a Hermaphrodite Green

Anaconda (Eunectes murinus)

Lana Krol, Freeland Dunker

Abstract: A 27-yr-old female green anaconda (Eunectes murinus) presented with coelomic distention in the posterior half of its body. On examination with imaging diagnostics, a fluid-filled cavity that seemed to be related to reproductive tissue was discovered. Diagnostics of this fluid confirmed cystic fluid, and a fine-needle aspirate of the mass determined that it was ovarian tissue. Ovariectomy and mass removal surgery was performed. During surgery, there was discovery of an additional unrecognized organ near the reproductive tract. Histopathology revealed an ovarian cystic neoplasm consistent with a granulosa cell tumor, and biopsy of the unknown structure was identified as a testis. Postoperatively, the green anaconda was administered fentanyl transdermal patches for analgesia and developed a severe adverse reaction, which improved after administration of the opioid reversal agent naltrexone. This is the

first report of hermaphroditism in a snake as well as suspected negative side effects of transdermal fentanyl in a snake.

* There has been limited evidence of positive nociceptive changes despite confirmed bioavailability of drugs after administration
* Reptiles have opioid receptors but the use of opiates for pain have varied results
* 27 year old female green anaconda- turgid swelling in posterior coelom
* 7 fentanyl patches placed post surgery (2.8 ug/kg/hr- LOWER dose, rec 5 ug/kg/hr) and12 hours later= snake was lateral, mouth agape, little jaw tone, flaccid tongue, and no movement or responses to touch and manipulation
  + Patches were removed
  + 0.1 mg/kg naltrexone was given IM and daily fluid therapy
  + Four days after incident- back to normal
* Snake probed after the fact- phenotypical male BUT cloacal probing prior to arrival to park was female
* Unilateral cystic granulosa cell tumor of the ovary
* Efficacy of midazolam given in this study (dose and frequency is unknown)- it was published of no reported analgesia in ball pythons
* Fentanyl- studies show appropriate plasma concentrations but no statistical difference in withdrawal from noxious stimulus between treated and control snakes
* Fentanyl is excreted in the urinary tract so daily fluids might have been the biggest role in clearing it from the snakes system

**Comparison of Ketamine–Dexmedetomidine–Midazolam Versus Alfaxalone–Dexmedetomidine–Midazolam Administered Intravenously to American Alligators (Alligator mississippiensis).** J. of Herpetological Medicine and Surgery, 31(2):132-140 (2021). Jessica Aymen, Patricia Queiroz-Williams, Chiara C. E. Hampton, Jeannette Cremer, Chin-Chi Liu, Javier G. Nevarez. - Review by LEM

Abstract: Crocodilians often require chemical immobilization for safe restraint and veterinary procedures, but there is a paucity of anesthetic studies for these species. The aim of this study was to compare the ability of ketamine (5 mg/kg) versus alfaxalone (5 mg/kg), in combination with dexmedetomidine (50 µg/kg) and midazolam (1 mg/kg) (KDM, ADM), to provide a loss of reflexes and safe orotracheal intubation without producing apnea in American alligators (Alligator mississippiensis). Six 22-month-old captive-hatched American alligators (4.75 ± 0.48 kg and body length of 111.1 ± 9.9 cm) were administered KDM and ADM in the lateral occipital venous sinus in a randomized, crossover design with a 72–80 h washout period between treatments. Physiologic parameters (heart rate, respiratory rate, esophageal and cloacal temperatures, end-tidal CO2) and reflexes (palpebral, cloacal, corneal, righting, withdrawal) were serially assessed throughout the anesthetic episode. Alligators were intubated, and assisted ventilation was provided to apneic animals. Intubation was safely performed within 10 min of administration of ADM and KDM. Respiratory rate was the only physiological parameter to differ between ADM and KDM. The majority (5/6, 83.3%) of alligators administered KDM maintained spontaneous ventilation (P = 0.016) and withdrawal reflexes (P = 0.031), and all alligators (6/6, 100%) given ADM became apneic and lost their withdrawal reflexes in all four limbs. Palpebral, cloacal, and righting reflexes were consistently lost in all animals with both combinations. Recovery time ranged from 5 to 35 min following administration of the reversal agents. Although KDM and ADM both permitted orotracheal intubation, KDM produced less apnea and a lighter plane of anesthesia compared to ADM.

Background:

* Benefits of chemical over physical restraint in gators: reduces altered behaviors (i.e. decreased appetite), limits the metabolic consequences (i.e. hyperlactatemia, acidosis)
* Alfaxolone = neuroactive steroid with anesthetic properties that can be administered IM or IV; can produce CV and respiratory depression in mammals
* Ketamine = dissociative anesthetic with analgesic properties; historically high doses (110 mg/kg IM) have been associated with death in crocodilians

Methods: compare ketamine vs. alfaxalone in combo IV immob protocols for American alligators

* **Ketamine**-dexmed-midazolam vs. **alfaxalone**-dexmed-midazolam
* Administered in lateral occipital venous sinus of subadult American alligators (n=6)
* Randomized crossover design with 72-80h washout period
* Intubated, supplied PPV if apneic; procedure times - 55 min ADM, 70 min KDM (with 150-minute cut-off; if not awake by then received reversal)

Key Points:

* Induction in all animals lacked excitation and allowed for successful intubation
* Intubation was safely performed within 10 min of administration of KDM and ADM
* HR, RR (when spontaneously breathing), ETCO2 and esophageal temp did not differ between tx
* HR decrease over time, esophageal and cloacal temps increased over time
* **Majority of KDM gators maintain spontaneous ventilation and withdrawal reflexes**
  + **⅙ developed apnea** and this was the only gator that developed bradycardia
  + Not a surgical plane of anesthesia
* **All ADM gators (6/6) became apneic and lost withdrawal reflex in all four limbs**
  + **Adequate surgical plane of anesthesia**
  + *Confusing because discussion says ⅚ but regardless more apnea with ADM*
* Palpebral, cloacal, righting reflexes consistently lost in all animals with both combos
* ADM gators remained anesthetized for >60 min, KDM gators for 150 min
* Recovery time ranged from 5-35 minutes after antagonist administered
  + Two gators that received KDM did not require reversal; all others did
  + All gators that received reversals did NOT need a second dose
  + All animals fully recovered by 3 hours from end of anesthetic episode
* One ADM gator died - lost spontaneous ventilation 10 min after ADM admin; provided PPV while apneic, other physiologic parameters remained stable until ~70 min when EtCO2 was lost, received two rounds of reversals which were unsuccessful; euthanized with pentobarb IV
  + Determined to be chronically ill on necropsy/not ideal anesthetic candidate
* **KEY: KDM and ADM both provided anesthesia adequate for orotracheal intubation**
  + **KDM had less apnea and lighter plane of anesthesia compared to ADM**

**Evaluation of the Safety of Multiple Intramuscular Doses of Ketoprofen in Bearded Dragons (Pogona vitticeps).** J. of Herp Medicine and Surgery, 32(2):123-129 (2022). Annabelle Vigneault, Stéphane Lair, Carolyn Gara-Boivin, Guy Beauchamp, Claire Vergneau-Grosset. - Review by LEM

Abstract: Cyclooxygenase (COX) 1 has been shown to increase significantly in inflamed ophidian skin and chelonian muscles. Nonselective COX-1 and COX-2 inhibitors, such as ketoprofen, could therefore reduce inflammation more effectively than preferential COX-2 inhibitors in reptiles. The objective of this study was to evaluate potential adverse effects of ketoprofen in bearded dragons (Pogona vitticeps). Thirteen adult bearded dragons were divided into three groups receiving daily intramuscular injections for 14 days in a blinded randomized study design. Group 1 (n = 5) received saline, Group 2 (n = 4) received ketoprofen at 2 mg/kg (diluted 1:10 with saline) and Group 3 (n = 4) received ketoprofen at 20 mg/kg (undiluted). Biochemical values, fecal occult blood (FOB) tests, and blood clotting time were assessed before and after the 2-wk treatment. Renal, digestive, hepatic, and muscular histopathology was evaluated. Clinically, injection-site reactions were noted in Group 3 only (n = 1/4). No other clinical adverse effects were detected. No changes were detected in plasma biochemical values and clotting times before and after treatments, nor were changes detected between control and treatment groups. No lesion associated with ketoprofen toxicity was detected on histologic examination of the kidney, liver, and gastrointestinal tract. Lesions of muscular necrosis at the injection sites were of higher magnitude in Group 3 compared to Group 1. In conclusion, daily intramuscular administration of diluted ketoprofen at 2 mg/kg for 14 days did not cause adverse effects in a small number of bearded dragons, whereas severe muscular necrosis was detected at 20 mg/kg.

Background:

* NSAIDS → inhibit cyclooxygenase (COX) enzymes → decreased synthesis of prostanoids (prostaglandins, prostacyclins, thromboxanes) → antinociception, anti-inflammatory, antipyretic
* COX-2: generates PG that initiates inflammation and pain in mammals; selective COX2 in mammals often preferred due to less adverse effects
  + COX2 selective = meloxicam, carprofen, firocoxib
* COX-1: generates PG to protect GI in mammals; adverse effects of inhibition include GI ulcers, kidney and liver damage, and decrease clotting function
  + Increased in inflamed muscles of box turtles, inflamed skin of ball pythons
  + Nonselective (ketoprofen, aspirin) may be more effective in these species

Methods: evaluate adverse effects of ketoprofen IM SID q14d in bearded dragons (n=13)

* 3 groups: (1) n=5: saline control, (2) n=4: ketoprofen 2 mg/kg (diluted), (3) n=4: ketoprofen 20 mg/kg
  + Received treatments IM SID x 14d then evaluated biochem, fecal occult blood, blood clotting time and histopath (renal, GI, hepatic, muscle)

Key Points:

* No change in appetite, activity or body weight during 2 wks treatment
* Five animals developed positive fecal occult (2/5 from control, 3/4 from high dose group)
  + Consider anatomy of cloaca; 3 had underlying salpingitis/egg yolk coelomitis
  + None from 2 mg/kg group had positive fecal occult throughout study
  + No GI ulcers on necropsies
* PCV, TP, biochemistry no different between groups (before, during, after treatment)
* Whole blood clotting (evaluated with capillary tubes) was not different between groups nor before vs. after treatments
  + Capillary tube method: tubes were broken every 5 min up to 45 min; first time point to visualize clot was considered clotting time
* Muscle necrosis adverse effect: 2/5 from control and 1/4 from 2 mg/kg had grade mild(1)-moderate(2) muscle necrosis at injection site, all 4 from 20 mg/kg group had grade 3 muscle necrosis
  + Interestingly, no difference in CK concentration despite difference in necrosis
  + 1/4 from 20 mg/kg → black cutaneous lesions at injection site and stiff tricep muscles
* **KEY: ketoprofen 2 mg/kg diluted IM SID q14 days was safe in healthy adult dragons**
  + **Ketoprofen 20 mg/kg caused adverse effects/muscle necrosis but no systemic effects suggesting a wide therapeutic margin**
  + **Ketoprofen should be diluted regardless of dose**

**Related papers:**

Ketoprofen in loggerheads: Harms CA, Ruterbories LK, Stacy NI, Christiansen EF, Papich MG, Lynch AM, Barratclough A, Serrano ME. 2021. Safety of multiple-dose intramuscular ketoprofen treatment in loggerhead turtles (*Caretta caretta*). J Zoo Wildl Med, 52(1):126–132.