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THE EFFICACY OF INTRACOELOMIC FOSPROPOFOL IN RED-EARED SLIDERS (*TRACHEMYS SCRIPTA*)

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Abstract

Intravenous anesthetic delivery in reptiles can be challenging; current injectable techniques have varied induction/recovery times and anesthetic quality. This study hypothesized that intracoelemic administration of a new anesthetic, fospropofol, in turtles would result in dose-dependent anesthesia and respiratory depression. A two-part prospective trial using adult red-eared slider turtles (*Trachemys scripta*) weighing 764 ± 17 g was conducted to 1) determine an effective anesthetic dose, and 2) evaluate the anesthetic quality, duration and respiratory effects of an efficacious dose. In Part 1, six turtles were randomly administered 25 mg kg^{-1} (low dose: LD) and 50 mg kg^{-1} (high dose: HD) fospropofol in a cross-over design. Respiratory rate, immobility and muscle relaxation scores were evaluated for 180 minutes. In Part 2, eight turtles were administered HD fospropofol. Immobility and muscle relaxation (front and hind limb) scores, and time to endotracheal intubation/extubation were evaluated until scores returned to baseline. In Part 1, the LD group had significantly lower immobility and muscle relaxation scores versus the HD group over time (both $P < 0.05$); scores were significantly elevated from baseline for 20–120 minutes and 15–180 minutes, respectively (all $P < 0.05$). Although not significantly different between groups ($P > 0.05$), respiratory rate was significantly decreased from baseline from 10–120 minutes (all $P < 0.05$). In Part 2, HD fospropofol decreased respiratory rate from $21.5 \pm 2.9 \text{ breaths min}^{-1}$ to $0.1 \pm 0.1 \text{ breaths min}^{-1}$, similar to the results in Part 1. Maximal reductions in immobility, front and hind limb motor tone occurred at 39.0 ± 4.1 , 30.8 ± 3.6 , and 24.0 ± 3.6 minutes, respectively. Intubation in 7/8 turtles occurred at 45.7 ± 5.4 min and extubation at 147.0 ± 23.2 min. However, 2/8 turtles showed prolonged anesthetic effects, requiring resuscitative efforts for recovery. Due to the unpredictable quality and duration of anesthesia with intracoelemic fospropofol, it should be used with caution for general anesthesia in red-eared sliders at the doses and administration route investigated.

Keywords

Anesthesia; fospropofol; intracoelemic; red-eared slider turtle; respiratory rate; *Trachemys scripta*

INTRODUCTION

The successful anesthetic induction and recovery of reptiles can be challenging due to a number of factors, including a lack of easily accessible vasculature. A number of injectable anesthetics and anesthetic combinations is extensively described for chelonians and other reptilian species and includes alfaxalone, medetomidine, ketamine, and xylazine.^{4,5,6,12,13,14,32,34} However, these anesthetic combinations can yield unpredictable anesthetic depth and can be associated with significant negative cardiovascular and respiratory effects.^{5,6,14,34} Volatile anesthetics are of little more utility when used alone as they are associated with unpredictable and prolonged induction and recovery times in reptiles.^{3,15,25} Thus, the use of propofol has gained favor among practitioners performing anesthesia in reptiles, with 43% of veterinarians performing injectable anesthetic techniques in reptiles utilizing propofol.²⁹

Propofol (2,6-diisopropylphenol) is formulated in a lipid-based emulsion due to the limited water solubility of the parent molecule. The lipid emulsion of propofol can be associated with adverse effects such as rhabdomyolysis, hyperlipidemia, bacterial growth, and pain on injection.^{26,28,35} Despite these untoward effects, propofol has a neutral pH and isotonicity and inadvertent perivascular administration rarely results in undesirable effects.¹⁷ However, adverse events associated with extravascular injection of propofol as well as with a similar lipid-free product, Cleofol®, have been reported including venous thrombosis, tissue necrosis, and thrombophlebitis.^{7,30,31,36} Thus, formulations with fewer complications if injected perivascularly where intravascular access can be difficult to attain would be advantageous in veterinary medicine.

Intravenous and intraosseous propofol administration has been described in red-eared sliders,^{8,38} as well as in other reptilian species.^{2,19,21} However, there are circumstances where it is difficult or impractical to achieve intravenous or intraosseous access such as in very small animals or animals that are difficult to restrain adequately. While the chelonian subcarapacial or supravertebral sinus is easily accessible and can be used to deliver anesthetics, a report of inadvertent submeningeal administration of propofol in tortoises suggests drug administration via this sinus may carry more risk than previously thought.²⁷

Administration of propofol via intramuscular and intraperitoneal routes has been examined in rodent species with unfavorable results.^{1,24} Intraperitoneal administration of 100% propofol in rats resulted in little appreciable sedation and was associated with significant tissue inflammation and necrosis; a single large dose of intraperitoneal propofol led to the death of a rat due to respiratory arrest.²⁴ In addition, intramuscular administration did not result in appreciable sedation and evidence of muscle inflammation and necrosis associated with the injection site was evident on histological examination.²⁴ Altogether, these studies suggest that the intraperitoneal or intramuscular routes of administration may not be clinically useful.

Fospropofol (2,6 diisopropylphenoxymethyl phosphate) is a novel prodrug of propofol that offers the advantage of water solubility, eliminating the need for a lipid carrier. The substitution of a noncharged hydroxyl group for a charged phosphate group on the 2,6

diisopropylphenol molecule induces an electronegativity allowing the new molecule to dissolve in water.^{11,20,37} This water-soluble drug is gaining popularity among human physicians for sedation during procedures such as bronchoscopy, colonoscopy, and minor surgical procedures.^{10,11} However, its use in veterinary species has only recently been reported and no reptile studies have been performed.^{18,22,23} Although intended solely for intravenous use, it may be useful after administration via extravascular routes, due to the water solubility of the drug. However, it has not been used studied via this non-labeled route.

The purpose of this study was to investigate the effects of a single dose of fospropofol administered into the cranial coelomic cavity of red-eared slider turtles (*Trachemys scripta*). This study hypothesized that, due to its water solubility, fospropofol administered by an extravascular route would be associated with dose-dependent sedation leading to anesthesia in red-eared slider turtles while reducing respiratory rates similar to those seen with intravenously administered propofol.¹⁹

MATERIALS AND METHODS

All procedures were approved by the Animal Care and Use Committee at the University of Wisconsin's School of Veterinary Medicine. Fourteen adult female red-eared slider turtles (*Trachemys scripta*) weighing 764 ± 17 g (mean $\pm$ SE) were obtained from a commercial supplier (Niles Biological Supply, Sacramento, California 95829, USA). Turtles were kept in 1800-liter open tanks with access to dechlorinated water for swimming, with heat lamps and dry areas for basking. Room temperature was maintained at 27–28°C with light provided for 14 hours per day. Turtles were fed a commercial diet 3–4 times weekly (ReptoMin floating food sticks, Tetra, Blacksburg, Virginia 24060, USA). Animals were considered to be healthy based on history and physical appearance.

Part 1: efficacy study

In Part 1, a crossover experimental design was utilized with six turtles receiving two fospropofol dosages with a seven-day washout period between treatments. Prior to experimental procedures, animals were randomly assigned to receive either 25 mg kg⁻¹ (LD) or 50 mg kg⁻¹ (HD) of fospropofol intracoelomically (Lusedra®, 35 mg ml⁻¹, Eisai Inc., Woodcliff Lake, New Jersey 07677, USA). Doses were considerably higher than human intravenous doses (maximum = 12.5 mg/kg, IV) to account for species and administration route differences. Fospropofol was diluted with 0.9% NaCl accordingly to create equal volume of injectate to maintain blinding of a single investigator who performed all observations (CS). To avoid potential renal uptake, drug injection was performed into the cranial coelomic cavity through the pectoral girdle using a 27g, ½ inch needle. Following aspiration free of blood, air, or lymph, the drug was injected. Injections were performed on the left side for the first treatment and on the right side for the second treatment.

Baseline respiratory rate, immobility and muscle tone scores (1–4; Table 1) were obtained and recorded prior to drug administration, every five minutes post-injection for 90 minutes, and then every 30 minutes up to 180 minutes.

Following data collection, two animals were euthanized following isoflurane administration and decapitation and submitted for gross pathology and histology of the injection site and cranial lung tissue. Of these two animals, one animal had received the 50 mg kg⁻¹ dosage seven days prior to evaluation and the 25 mg kg⁻¹ dosage the day of euthanasia. The other turtle received the doses in reverse order.

Part 2: HD evaluation

Based on data obtained in Part 1, a dosage of 50 mg kg⁻¹ administered in the intracoelomic cavity was chosen to be studied in greater detail in eight separate turtles. Similar to Part 1, baseline measurements were obtained and recorded prior to drug administration including a visually obtained respiratory rate, cloacal temperature, immobility and muscle tone score in both the fore and hind limbs (immobility: 1–4; muscle tone: 1–3; Table 1), and time to intubation/extubation. Tracheal intubation was attempted when the mouth could be opened and the tongue grasped easily; a 16 gauge intravenous catheter (Angiocath™, BD, Franklin Lakes, NJ 07417, USA) was subsequently placed into the glottis.

Fospropofol was administered in the left cranial coelomic cavity using a 27g, ½ inch needle. Following aspiration free of blood, air, or lymph, the drug was injected. Following drug administration, immobility and muscle tone scores and tracheal intubation attempts were evaluated every two minutes. When three identical consecutive measurements of immobility and muscle tone scores in fore and hind limbs were made, measurement intervals were then extended to every five minutes. Respiratory rate was recorded every ten minutes and cloacal temperature every 30 minutes. Heart rate was recorded periodically using a transcutaneous Doppler probe (Parks Medical, Model 801-B, Las Vegas, NV 89119, USA) but was not included in data analysis. Parameters were recorded as described until a complete recovery, defined by the return of immobility scores to baseline values, was achieved.

Statistical analyses

In Part 1, respiratory rate, immobility and muscle tone scores were analyzed via a two-way repeated measures ANOVA with a Student-Newman-Keuls post-hoc test using time point and dose as factors (SigmaPlot 12.0, Systat Software, Inc, San Jose, CA 95110, USA). Data from Part 2 are reported as descriptive statistics. Time until and duration of a movement score of 4 and muscle tone score of 3 in both fore and hind limbs, time until intubation/extubation, and time to return of immobility and muscle tone to baseline values (score of 1) are reported as mean±standard error of the mean. Differences between hind and forelimb scores were analyzed with a one-way ANOVA (SigmaPlot 12.0, Systat Software, Inc, San Jose, CA 95110, USA).

RESULTS

Part 1: efficacy study

Intracoelomic injections were made rapidly with no overt evidence of pain or irritation. Histopathology revealed slight hemorrhage at the injection site but no evidence of pronounced tissue inflammation or necrosis in the underlying musculature or cranial lung

tissue, suggestive of an intracoelomic injection with minimal tissue response. However, inadvertent intramuscular administration cannot be completely ruled out.

There were no significant differences in respiratory rate between the LD and HD groups over time (no dose or dose-time interaction, $P>0.05$; Figure 1A). However there was a statistically significant time effect as respiratory rate was significantly decreased from overall baseline values (baseline respiratory rates for LD: 26.5 ± 5.8 breaths min^{-1} , and HD: 30.0 ± 4.4 breaths min^{-1}) 10–120 min post-injection (all $P<0.05$; Figure 1A). At 180 minutes, the overall respiratory rate was not significantly different from baseline values ($P>0.05$; Figure 1A).

In contrast, immobility scores evaluating all four limbs simultaneously were significantly different between treatment groups with the HD group having significantly higher scores versus the LD group when all time points were combined (dose effect: $P<0.05$; Figure 1B). Immobility scores were significantly higher versus baseline (score=1) following injection from 20–120 min (time effect: all $P<0.05$; Figure 1B). At 180 minutes, locomotion had returned to nearly normal and overall values did not differ from baseline ($P>0.05$). However, there were no interactions between dose and time ($P>0.05$).

Similarly, muscle relaxation scores were significantly higher in the HD versus LD group when all time points were combined (dose effect: $P<0.05$; Figure 1C). Relaxation scores also increased from baseline values (score = 1) from 15–180 minutes post-injection (time effect: all $P<0.05$; Figure 1C). At 180 minutes, the relaxation scores still differed from baseline, mainly due to the effect of the HD group ($P<0.05$; Figure 1C). There were no significant dose-time interactions ($P>0.05$).

All animals from Part 1 recovered fully from both the LD and HD fentanyl dosages. Although immobility scores significantly increased over time, they were higher in the HD group and 6/6 turtles attained a immobility score of 4 at some point in the study whereas only 1 turtle reached a immobility score of 4 in the LD group. Similarly, 4/6 HD turtles attained a muscle relaxation score of 4 whereas only 2/6 turtles reached a relaxation score of 4 in the LD group. Thus, the 50 mg kg^{-1} drug dosage (HD) provided less variable effects and was chosen to further evaluate for efficacy and duration of effect in Part 2.

Part 2: anesthetic depth and motor function scoring

Mean turtle baseline temperatures were 19.7 ± 0.2 °C and were well maintained throughout the study period, with a mean temperature of 21.4 ± 1.4 °C at the end of the study periods. Results of Part 2 are summarized in Table 2. Similar to Part 1, HD propofol significantly reduced respiratory rates from 21.5 ± 2.9 breaths min^{-1} to a minimum of 0.1 ± 0.1 breaths min^{-1} (data not shown; $P<0.05$) before returning to near baseline values by 180 min ($P>0.05$). The average time to complete loss of locomotion (immobility score=4) was 39.0 ± 4.1 min post-injection while locomotion returned to baseline values at 174.2 ± 11.4 min (Table 2). Time to complete loss of muscle tone in fore and hind limbs (score=3) was 30.8 ± 3.6 and 24.0 ± 3.6 min, respectively and the time to return of muscle tone in fore and hind limbs (score=1) occurred at 179.2 ± 12.7 and 179.2 ± 12.1 min, respectively; values were not significantly different between the fore and hind limbs (all $P>0.05$; Table 2). Seven out

of eight turtles were successfully intubated at an average time of 45.7 ± 5.4 min post-injection and extubation occurred 147.0 ± 23.2 min following injection. However, 2/8 turtles exhibited prolonged effects with an immobility score of 4 and muscle relaxation score of 3 for greater than 360 min when resuscitative intervention was elected. While intubated, these animals received positive pressure ventilation with room air at 3 breaths min^{-1} , atropine (0.4 mg kg^{-1} IV, 0.4 mg ml^{-1} , Phoenix Pharmaceuticals, Inc, Burlingame, CA 94010, USA) to antagonize vagal-induced bradycardia, and doxapram (4.5 mg kg^{-1} IV, 20 mg ml^{-1} , Laboratories, Bedford, OH 44146, USA) as a centrally-mediated respiratory stimulant. Due to the presence of frothy fluid in the endotracheal tube of one of these animals, furosemide (2 mg kg^{-1} IM, 10 mg ml^{-1} , Phoenix Pharmaceuticals, Inc, Burlingame, CA 94010, USA) was also administered. Approximately 30 minutes following resuscitative efforts, both animals were moving and ventilating spontaneously. These turtles were removed from the duration/recovery statistical analysis in regards to duration of immobility score 4 and muscle tone score 3, return to baseline locomotion and muscle tone, and time to extubation (Table 2).

DISCUSSION

The results of this study indicate that intracoelomically-administered fospropofol can result in a clinical level of anesthesia consistent with that of intravenously administered propofol. Injections of the drug into the animals were quick, simple, and did not result in evidence of tissue irritation or necrosis. However, individual turtle responses, even at the higher of the two chosen doses (HD), were somewhat variable with one turtle exhibiting minimal locomotor depression and muscle relaxation while two others demonstrating such profound and prolonged levels of anesthesia that resuscitative measures were necessary for recovery at 360 minutes.

In Part 1, the HD group had significantly greater immobility and muscle relaxation scores when compared to the LD group guiding us to choose the HD even though there was no statistical significance between groups for respiratory rate. However, in Part 2, the HD dosage only resulted in clinically-acceptable anesthesia in 5/8 turtles with two having no purposeful movement by the end of the study period and one never achieving sufficient muscle relaxation for tracheal intubation.

High variability in clinical response to an anesthetic agent by reptiles is well documented in the literature.^{5,6,8,14,15,25,34} This is especially true when anesthetic agents are administered via extravascular routes. For example, intramuscular administration of a combination of medetomidine and ketamine in adult alligators resulted in highly variable onset of sedation which ranged from 10 to 65 minutes.¹⁴ In another example, the intraosseous administration of propofol to red-eared sliders resulted in inadequate anesthetic effects in four out of twelve animals administered identical dosages.⁸ A limitation of this study is that we cannot confirm that fospropofol was delivered intracoelomically (versus intramuscular). This could account for additional variability in our results; future tracer studies would be warranted to discern the precise location of drug disposition via our injection technique. Temperature effects in this latter study were hypothesized to be one reason for the inconsistency of animal responses. While cloacal temperature was not monitored in Part 1, it was measured in Part 2

of the study and found to remain relatively consistent over time. Animals were held under identical and consistent ambient temperature and no attempts were made to warm animals upon recovery. While temperature can have profound effects on drug pharmacokinetics and anesthetic recovery in animals, the constancy of temperature in the present subjects does not explain the variable clinical responses. Another possible cause of the large variability observed in this study is cardiac shunting observed in reptilian species. The turtle heart is divided into two atrial chambers, but only a single ventricle.¹⁶ The variable shunting pattern of blood in the reptilian cardiovascular system has been described elsewhere and it is known that shunting can result in a bypass of pulmonary circulation under certain conditions.¹⁶ It is possible that variability in cardiovascular shunting among individual animals could result in variability in propofol uptake, clearance and eventual extent of total hepatic metabolism, leading to inconsistent sedation and recovery (He et al. 2000).

Another explanation for pharmacologic variability in anesthetic response could be physiologic and hematologic differences and, potentially, abnormalities among study animals. Turtles were deemed healthy on the basis of physical examination, but no attempt was made to measure baseline hematologic and biochemical variables. Anesthetic death of red-eared sliders following propofol administration has been attributed to severe hypoproteinemia due to intestinal parasitism.³⁸ Variability in plasma protein among subjects could lead to differences in protein binding of the drug and, therefore, variable clinical effects. However, baseline hematologic screening was not performed in the present study and the possibility of hypoproteinemia cannot be ruled out as necropsy findings in two turtles did reveal trematodes or trematode granulomas (Spirorchid) in the lungs, intestines, and stomach (data not shown).

Extensive cardiovascular and acid-base monitoring at baseline and during the observation period was not performed although heart rate was periodically. Although heart rate data would have been valuable to determine the safety of this agent in turtles, the primary intent of this preliminary investigation was to evaluate the sedative and/or anesthetic effects of fospropofol. Although the study of cardiovascular parameters was not the primary goal of these studies, heart rate was periodically measured to ensure the life of the turtle, especially with the prolonged apneas seen with fospropofol. The two animals that exhibited profound clinical effects had heart rates ranging from 18–42 beats min⁻¹ whereas the other 6 turtles had heart rates ranging from 20–42 beats min⁻¹ (data not shown nor analyzed due to small sample size). The heart rate of this species at 22°C has been published as roughly 20 beats per minute.⁹ Without baseline measurements and statistical analyses in the study subjects, no conclusion can be drawn on the cardiovascular effects of this drug or the effects of the cardiovascular system on the drug. Further study is required to elucidate these details. Similarly, no attempts at monitoring respiratory gases or arterial blood gases were made. Severe individual alterations in any of these parameters could have explained some of the individual animal variability in clinical anesthetic effect.

In red-eared sliders, immobility scores and muscle tone did not return to baseline levels (scores=1) until approximately 174–179 min post-fospropofol injection, a relatively long duration of action. This is considerably longer than the recovery time for intravenous propofol, reported to be approximately 60 to 90 minutes in this species, depending on

dosage.³⁸ All animals demonstrated remarkably low respiratory rates during the entire observation period. Although arterial blood gases were not evaluated in the current study, this may have been associated with profound hypoventilation, leading to elevated partial pressure of arterial carbon dioxide and a respiratory acidosis. While reptiles are highly tolerant of apnea and breath-hold for long periods of time, it is possible that a respiratory acidosis was indeed induced, decreasing plasma protein binding and resulting in a more profound anesthetic effect with a longer duration of action.³³ When assisted ventilation was performed in the two animals that required intervention (in addition to receiving doxapram and atropine), the animals recovered quickly afterwards. However, the confounding effects of doxapram and atropine make evaluation of this hypothesis difficult. While respiratory depression could have affected recovery, it is possible that simple mechanical ventilation would have resulted in a shorter duration of effect.

The general anesthesia of many reptiles has been described as occurring in the cranial to caudal direction, with relaxation of the head and forelimbs occurring before that of the tail and hind limbs with recovery occurring in the opposite direction.^{3,38} The data of this study did not support this finding as there were no significant differences in loss or return of muscle tone in the fore versus hind limbs.

The substitution of a noncharged hydroxyl group for the charged phosphate group on the propofol molecule makes fospropofol water-soluble. However, this substitution makes the molecule non-lipophilic, limiting its access to the central nervous system. In vivo enzymatic cleavage of the methyl phosphate group liberates the 2,6 diisopropylphenol molecule, and the newly liberated propofol can exert sedative effects on the central nervous system.^{11,37} This conversion is not immediate and, therefore, the liberated propofol exerts a less profound effect on the central nervous system than traditional formulations of the drug. The resulting clinical effect as described in human subjects is that of a delayed onset of sedation rather than a quick onset of anesthesia as seen with propofol. Although the effects of bolus dosing of fospropofol in veterinary species remains poorly characterized, long-term fospropofol infusions in rabbits (6–8 hrs) result in increased anesthetic recovery times when compared to propofol infusions.¹⁸ In addition, one of the 16 rabbits studied died upon anesthetic recovery, presumably due to the large fospropofol dose required for a satisfactory anesthetic plane and thus, fospropofol was found to be inadequate for safe, long-term anesthesia in rabbits.¹⁸

Fospropofol has a delayed onset of sedation in humans, and is consequently used as a sedative for medical procedures such as bronchoscopy and colonoscopy rather than an agent to be used for anesthetic induction.^{10,11} As such, one would predict that this drug would similarly behave as a sedative in reptiles, allowing for examination and performing non-painful procedures in reptiles where intravenous access can be difficult. The findings of this study are consistent with this hypothesis since intracoelomic administration results in sedative/anesthetic effects 20–50 min post-injection. However, the effects are somewhat variable between turtles and must be used with caution at the doses and route studied.

CONCLUSIONS

Reptiles present a great anesthetic challenge in regards to intravenous access sites, physiologic adaptations that may cause unexpected shunting of the cardiac output, and the ability to tolerate long periods of apnea.¹⁶ Reptiles can demonstrate quite variable responses to current anesthetic techniques and no perfect agent exists to perform sedation or anesthesia of brief to moderate duration, especially without intravenous access. This study demonstrated that intracoelomic fentanyl at 50 mg kg⁻¹ results in an anesthetic level sufficient for tracheal intubation in the majority of turtles studied. However, it should be administered with caution due to varied anesthetic effects in three out of eight turtles. Further studies on alternative routes and species should be performed to further assess its safety and utility in veterinary medicine.

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Figure 1.

Respiratory rate, immobility, and muscle relaxation scores in 6 red-eared slider turtles following 25 mg kg^{-1} (LD) and 50 mg/kg^{-1} (HD) intracoelemic fospropofol. **(1A)** Respiratory rate significantly decreased from 10–120 min post-injection. However, there was no difference between LD and HD groups. **(1B)** Over all time points, the HD group had significantly higher immobility scores versus the LD dose. In addition, fospropofol administration significantly increased immobility scores from 20–120 minutes post-injection. There were no time-dose interactions. **(1C)** Similarly, over all time points, the HD

group had significantly higher muscle relaxation scores versus the LD groups. Fospropofol increased the muscle relaxation scores from 15–180 minutes post injection and there was no time-dose interaction. AU: arbitrary units. * $P < 0.05$ time point significantly different from baseline values when both groups are combined. # $P < 0.05$ between LD and HD groups when all time points are combined.

Table 1

Scoring system used for locomotion and muscle relaxation following LD and HD intracoelomic fospropofol injection in turtles.

Immobility Scores (Parts 1 and 2):

- 1: Normal locomotion or retraction into shell
- 2: Slowed or ataxic spontaneous movement
- 3: Movement only in response to stimulus
- 4: Complete absence of movement

Muscle Relaxation Scores (Part 1):

- 1: Normal tone or retraction; difficult to pull limbs out of shell
- 2: Head and/or 1–2 limbs relaxed and out of shell; slight retraction when stimulated
- 3: Head and/or 3–4 limbs relaxed and out of shell; slight retraction when stimulated
- 4: Head and all limbs relaxed and out of shell; no retraction when stimulated

Muscle Relaxation Scores (Part 2):

- 1: Normal tone or retraction; difficult to pull limbs out of shell
 - 2: Head and/or 1–2 limbs relaxed and out of shell; slight retraction when stimulated
 - 3: Head and limbs relaxed and out of shell; no retraction when stimulated:
-

In Part 1, all limbs were assessed simultaneously for tone and thus scored between 1–4; in Part 2, front and hind limbs were assessed individually and relaxation scored between 1–3.

Table 2

Descriptive statistics and number of animals in each group following HD intracoelomic fentanyl administration.

	Time (minutes)	Sample Size
Anesthetic Induction Times		
Immobility score of 4	39.0±4.1	8
Muscle tone score of 3 (front limb)	30.8±3.6	8
Muscle tone score of 3 (hind limb)	24.0±3.6	8
Tracheal intubation	45.7±5.4	7
Anesthetic Duration/Recovery Times		
Duration at immobility score of 4	43.8±9.6	6
Return to baseline locomotion (immobility score of 1)	174.2±11.4	6
Duration at muscle tone of 3 (front limb)	120.2±15.0	6
Return to baseline muscle tone (front limb)	179.2±12.7	6
Duration at muscle tone of 3 (hind limb)	130.5±15.7	6
Return to baseline muscle tone (hind limb)	179.2±12.1	6
Tracheal extubation	147.0±23.2	5

Data are represented as mean±SEM. Of 8 turtles, one did not reach adequate depth to intubate and two had excessive anesthetic depth for greater than 360 minutes which required resuscitative efforts to recover. Thus, these animals were not considered in the intubation and recovery times as shown above