

Anesthetic and Postanesthetic Effects of Alfaxalone–Butorphanol Compared with Dexmedetomidine–Ketamine in Chinchillas (*Chinchilla lanigera*)

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Effective and safe anesthetic protocols are required for a variety of surgical and diagnostic procedures in chinchillas. Alfaxalone, a new anesthetic agent in the United States, can be administered intramuscularly and subcutaneously and is therefore potentially useful as an anesthetic induction agent in chinchillas. This study compared the anesthetic efficacy and postanesthetic effects on food intake and fecal output of a combination of intramuscular alfaxalone (5 mg/kg) and butorphanol (0.5 mg/kg; AB anesthesia) with a combination of dexmedetomidine (0.015 mg/kg) and ketamine (4 mg/kg; DK anesthesia) in a blinded, randomized, complete crossover design in chinchillas ($n = 12$). The AB combination resulted in a rapid induction of short-term anesthesia, which was inconsistent in depth and length. In contrast, the DK protocol resulted in rapid induction of a consistent level surgical anesthesia and rapid recovery after administration of atipamezole (0.15 mg/kg IM). Food intake and fecal output were significantly more decreased in the AB group (food, $-65.9\% \pm 17.7\%$; feces, $-72.2\% \pm 18.7\%$) than in the DK group (food: $-37.7\% \pm 8.2\%$, feces: $-16.5\% \pm 15.8\%$) during the first 24 h after anesthesia. Food intake and fecal output remained significantly reduced compared with preanesthetic levels for 4 to 5 d after anesthesia with both protocols. Compared with the AB protocol, the DK protocol provided superior anesthetic efficacy and had fewer postanesthetic side effects in chinchillas and is therefore a more suitable injectable anesthetic combination for this species.

Abbreviations: AB, alfaxalone–butorphanol regimen; DK, dexmedetomidine–ketamine treatment.

Chinchillas (*Chinchilla lanigera*) are a popular animal model, particularly for otologic research, and are increasingly maintained as companion animals.^{19,24} The available scientific literature contain little information regarding the systematic evaluation of anesthetic protocols in chinchillas.^{6,8} A recent study compared the effects of isoflurane to the combination of dexmedetomidine–ketamine (DK) in chinchillas.⁶ The anesthetic and physiologic effects were similar between protocols, except for hypoxemia in the DK group due to the lack of supplemental oxygen provided.⁶ Because intravascular access is challenging to obtain in chinchillas, parenteral nonvascular protocols provide the most accommodating route of anesthesia induction and maintenance. Alfaxalone, which was recently reintroduced into the United States, is a neurosteroidal anesthetic with rapid metabolism and a short half-life.¹¹ Alfaxalone has been gaining popularity in veterinary practice and has been investigated in various species and administration routes, including subcutaneous and intramuscular injection.^{16,22,24} Alfaxalone has the potential for being a suitable anesthetic drug in chinchillas, because it can be administered without requiring intravascular access, has limited cardiovascular effects, and is rapidly metabolized and excreted, potentially resulting in rapid recovery.¹¹

Although recovery from anesthesia may be rapid, the postanesthetic effects of anesthetic protocols on food intake and fecal output should be considered, in particular in hindgut-fer-

menting small rodent species, such as chinchillas. In a previous study, the postanesthetic effects of DK anesthesia resulted in a pronounced decrease in food intake and fecal output after anesthesia, whereas anesthesia with isoflurane had no significant effect on either parameter.⁶ However, a limitation of the cited study was that the DK protocol did not provide supplemental oxygen, whereas isoflurane was delivered in oxygen. Therefore the observed difference in postanesthetic food intake and fecal output could have been related to the pronounced perianesthetic hypoxia in the DK-anesthetized animals rather than to primary drug effects.⁶

The objective of the current study was to determine a suitable dose of alfaxalone alone or in combination with butorphanol administered by intramuscular or subcutaneous injection for the induction of light to surgical anesthesia in chinchillas and to compare the determined protocol with a combination of dexmedetomidine and ketamine. We hypothesized that both protocols would induce reliable anesthesia and have similar postanesthetic effects on food intake and fecal output.

Materials and Methods

This study was approved by the University of Wisconsin–Madison’s IACUC. The study population comprised 12 chinchillas (7 male, 5 female; age, 1 to 3 y; body weight, 0.64 kg \pm 0.13 kg [mean \pm 1 SD]) obtained from a commercial breeder (R and R Chinchillas, Jenera, OH). Animals were housed in a climate-controlled room with a 12:12-h photcycle (lights on, 0700 to 1900), room temperature of 21 to 23 °C, and relative humidity of 40% to 55%. The chinchillas were maintained in

Received: 07 Jul 2016. Revision requested: 22 Aug 2016. Accepted: 12 Dec 2016.
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individual cages (6-cage Rabbit Housing Unit, Allentown Caging, Allentown, NJ) measuring 0.69 m × 0.69 m × 0.46 m with perforated plastic excreta pans. Each cage contained a plastic hide box, and each chinchilla was provided a dust bath at least once each week. The chinchillas were offered tap water from a rabbit ball-tipped water bottle and a commercial pelleted rabbit diet (MannaPro Rabbit pellets, MannaPro Products, Chesterfield, MO). All chinchillas were acclimated to the housing conditions for at least 4 wk prior to starting the experiments and were deemed healthy on the basis of repeated physical examinations and monitoring of food intake, fecal output, and body weight.

Pilot studies were conducted with various dosages and administration routes for the alfaxalone–butorphanol (AB) protocol, using 2 chinchillas for each dosage and route. Dosages that did not result in the desired light to surgical plane of anesthesia were: 5 mg/kg alfaxalone alone (subcutaneous and intramuscular routes), 3 mg/kg alfaxalone combined with 0.5 mg/kg butorphanol intramuscularly, 5 mg/kg alfaxalone combined with 0.5 mg/kg butorphanol subcutaneously, 10 mg/kg alfaxalone alone subcutaneously, and 10 mg/kg alfaxalone combined with 0.5 mg/kg butorphanol subcutaneously. Only the combination of 5 mg/kg alfaxalone combined with 0.5 mg/kg butorphanol administered intramuscularly resulted in induction of short-term light to surgical anesthesia and was therefore evaluated further.

To evaluate the determined AB dosage and compare it with a DK combination, each chinchilla underwent anesthesia twice in a randomized, complete crossover design, with a washout time between anesthetic episodes of at least 7 d. Baseline heart rates, respiratory rates, body weights, and rectal temperatures were obtained prior to anesthesia. Dexmedetomidine and ketamine doses were based upon a previous study.⁶ Dexmedetomidine (0.015 mg/kg; Dexdomitor, Pfizer Animal Health, New York, NY) and ketamine (4 mg/kg; Ketamine Hydrochloride Injection, Hospira, Lake Forest, IL) or alfaxalone (5 mg/kg; Alfaxan, Jurox, Kansas City, MO) and butorphanol (0.5 mg/kg; Torbugesic-SA, Zoetis, Florham Park, NJ) were administered intramuscularly in the epaxial musculature as a single injection using an insulin syringe with an attached 28 gauge hypodermic needle. Forty-five minutes after DK administration, atipamezole (0.15 mg/kg; Antisedan, Pfizer Animal Health) was administered intramuscularly to reverse the effects of dexmedetomidine. Animals were given flow-by oxygen (100% oxygen, 1 L/min) by facemask for 5 min after injection of the anesthetic drugs and were placed in sternal recumbency at that time. Flow-by oxygen was discontinued when the animal recovered its righting reflex. A water-based eye lubricant was instilled in the eyes of all chinchillas after the induction of anesthesia.

Measured reflexes included righting, palpebral, forelimb withdrawal, hindlimb withdrawal, and ear flick reflexes. Reflexes were scored 0 to 2, with 0 indicating a present reflex, 1 indicating a reduced reflex, and 2 indicating an absent reflex. All reflexes were tested prior to drug administration (0 min), at each minute from 1 to 10 min after drug administration, and then every 5 min thereafter for a total of 45 min or until all reflexes had returned to 0, with the exception of the ear flick reflex, which was tested every 5 min. Anesthesia induction time was defined as loss of the righting reflex, which was assessed by placing the chinchillas in dorsal recumbency and observing whether they could return to a normal quadrupedal position. Withdrawal reflexes were assessed by pinching a digit with hemostats and observing a reflex response. The ear flick reflex was tested by touching the inner aspect of the pinna and distal ear canal with a cotton-tipped applicator and monitoring for a

reflex response. Surgical anesthesia was defined as a complete loss in all measured reflexes, including the ear flick reflex (that is, score of 2 for all reflexes). During the 45-min anesthetic period, heart rate, respiratory rate, SpO₂ determined by pulse oximetry of a hindlimb digital pad (model 8500, Nonin Medical, Minneapolis, MN), and rectal temperature were measured at 5-min intervals. Heart rate and respiratory rate were monitored manually by auscultation. After reversal with atipamezole or a spontaneous return to walking, the chinchillas were monitored until recovery from anesthesia was complete, measured as the return of all reflexes. Each chinchilla then was monitored for ataxia every 5 min by allowing the animal to walk 2 to 3 feet to determine whether normal coordination had returned. Thirty minutes after atipamezole had been administered or the animal had regained the ability to walk, each chinchilla was offered 5 carrot treats (Just Tomatoes Etc, Westley, CA) by placing them within their enclosure. The number of carrots consumed within 15 min of them being offered was recorded.

Food intake and fecal output were measured daily starting 48 h prior to anesthesia and for 7 d afterward, at the same time each day, by collecting, sorting, and measuring leftover food and feces found in each cage. The preanesthetic measurements were averaged and used as baseline values. Body weight was measured on each day of an anesthetic event.

Statistical analysis. Commercial software (SigmaPlot 12.5, Systat Software, San Jose, CA) was used to perform the data analysis. The data were evaluated for normal distribution by using the Shapiro–Wilk test and for equal distribution by using the Brown–Forsythe test. Physiologic data (heart rate, respiratory rate, temperature, SpO₂), food intake, and fecal output were evaluated by using repeated-measures ANOVA. Simple transformation procedures or ranking of the data were performed, prior to further analysis, when necessary. The Holm–Sidak or Dunn method (for ranked data) were used for posthoc pairwise comparison procedures, when significant differences were found between groups. Physiologic parameters were compared between the 2 anesthetic protocols for only the first 15 min after drug administration, because most animals started to recover from AB-induced anesthesia after this point. Wilcoxon signed rank tests were used to compare induction parameters between the 2 anesthetic protocols. Paired *t* tests were used to compare initial body weights on the day of anesthesia with body weight 7 d later and carrot consumption postanesthesia between both groups. Normally distributed data were reported as mean ± SEM and nonnormally distributed data as median and range, unless stated otherwise. A *P* value less than 0.05 was considered statistically significant.

Results

Anesthetic induction parameters are summarized in Table 1. Compared with the AB protocol, the DK protocol resulted in a significantly (*P* < 0.05) faster loss of palpebral and forelimb and hindlimb withdrawal reflexes. By 5 min after administration, all animals in the DK group had lost all measured reflexes and had achieved surgical anesthesia, which was maintained for 45 min in all cases, until atipamezole was administered. The AB protocol achieved surgical anesthesia in only 7 of the 12 chinchillas, and the duration of surgical anesthesia was short (median, 10 min; range, 5 to 20 min). By 15 min after AB administration, 7 of the 12 animals in were anesthetized, and by 20 min 9 of 12 animals were no longer anesthetized. In the AB group, the median time to return of reflexes was: righting, 21 min (range, 14 to 35 min); palpebral, 24 min (range, 14 to 35 min); forelimb withdrawal, 22 min (range, 10 to 35 min); and

Table 1. Anesthetic induction parameters (min) in chinchillas ($n = 12$) anesthetized with either dexmedetomidine–ketamine or alfaxalone–butorphanol in a crossover study

| | Dexmedetomidine–ketamine | | | Alfaxalone–butorphanol | | | <i>P</i> |
|-----------------------------------|--------------------------|---------|---------|------------------------|---------|---------|----------|
| | Median | IQR | Range | Median | IQR | Range | |
| Righting reflex absent | 2.0 | 1.3-2.0 | 1.0-3.0 | 2.0 | 2.0-3.0 | 1.0-4.0 | 0.063 |
| Palpebral reflex absent | 2.0 ^a | 2.0-3.0 | 2.0-4.0 | 5.0 ^a | 4.5-9.5 | 4.0-15 | 0.0039 |
| Forelimb withdrawal reflex absent | 2.0 ^a | 1.3-2.8 | 1.0-3.0 | 3.5 ^a | 2.0-5.3 | 1.0-8.0 | 0.0078 |
| Hindlimb withdrawal reflex absent | 2.0 ^a | 2.0-3.0 | 1.0-3.0 | 3.0 ^a | 2.5-4.5 | 1.0-6.0 | 0.031 |
| Ear flick reflex absent | 5.0 | 5.0-5.0 | 5.0-5.0 | 5.0 | 5.0-11 | 5.0-15 | 0.13 |

IQR, interquartile range

For induction, data are recorded in minutes after induction via injection.

^aSignificant ($P < 0.05$) difference between anesthetic protocols.

hindlimb withdrawal, 24 min (range, 14 to 35 min). Ataxia had resolved by a median of 41 min (range, 29 to 55 min) after AB administration. Subjectively, anesthesia induction was far less smooth in the AB group compared with the DK group; tremors, twitching, and rolling were observed in the majority of the chinchillas anesthetized with the AB protocol.

After atipamezole administration in the DK group, the righting reflex had recovered by a median of 7 min (range, 3 to 15 min), and ataxia has resolved after a median of 15 min (range, 10 to 30 min). The palpebral, forelimb, and hindlimb withdrawal reflexes all returned by a median of 6 min (range, 3 to 15 min).

Heart rate decreased significantly ($P < 0.05$) over time with both protocols and was higher in the AB group than the DK group during the first 15 min after administration (Figure 1). Respiratory rates were higher in the AB group during the first 15 min after the induction of anesthesia (Figure 2), due to a significant ($P < 0.05$) increase in respiratory rate compared with the preanesthetic rate. In the DK group, the respiratory rate did not change over time and was comparable to the preanesthetic rate. No significant differences were discerned between groups or between time points within each group in regard to SpO₂ levels (median, 100%; range, 95% to 100%). Rectal temperature did not differ significantly between the DK and AB groups and decreased over time. Compared with baseline values, the rectal temperature was significantly lower by 15 min in the AB group and between 30 to 45 min in the DK group (Figure 3). The measured rectal temperatures remained within the reported reference range for rectal temperatures in chinchillas (34.9 to 37.9 °C),¹⁵ except for one animal in the DK group, which became hypothermic at 45 min (34.7 °C).

Food consumption immediately after recovery from anesthesia was similar for both groups, in which 8 of 12 chinchillas ate all offered carrots treats within 15 min. However, for 5 d after anesthesia, food intake was significantly ($P < 0.05$) decreased in both groups when compared with baseline. Reduction in food intake was greater after AB anesthesia than DK anesthesia for the first 2 d (Figure 4). In both groups, the largest decrease in food consumption occurred within the first 24 h after anesthesia (AB group, $-65.9\% \pm 17.7\%$ [range, -98.1% to -42.0%]; DK group, $-37.7\% \pm 8.2\%$ [range, -50.6% to -27.2%]). In addition, fecal output was significantly ($P < 0.05$) reduced in both groups after anesthesia (Figure 5), and chinchillas that had received AB had a greater reduction in fecal output ($-72.2\% \pm 18.7\%$; range, -100% to -34.4%) over the first 24 h after anesthesia than chinchillas given DK ($-16.5\% \pm 15.8\%$; range, -40.3% to 13.1%). Fecal output returned to baseline levels by 4 d (DK group) to 5 d (AB group) after anesthesia. Body weight did not differ between anesthetic protocols or within groups over time.

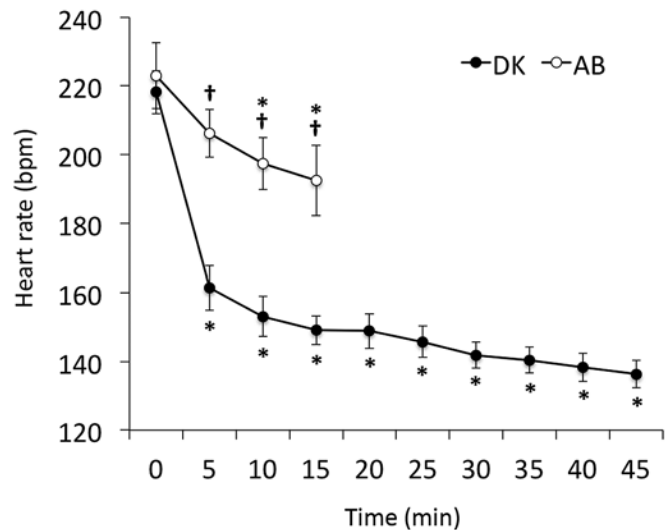


Figure 1. Heart rate (mean \pm SEM) of chinchillas ($n = 12$) anesthetized with dexmedetomidine–ketamine (DK) or alfaxalone–butorphanol (AB) in a complete crossover design. *, Value differed significantly ($P < 0.05$) from preanesthetic baseline value within the same protocol; †, values differed significantly ($P < 0.05$) between anesthetic protocols at the same time point. For the AB group at 15 min, the data of 11 of 12 animals were included.

Discussion

The DK and AB protocols evaluated resulted in different levels and durations of anesthesia. Induction times were rapid with both protocols, but compared with DK anesthesia, the AB protocol resulted in shorter, shallower, and less consistent anesthesia. In addition, the induction with the AB protocol was much less smooth compared with the DK protocol. These results contrast with the smooth induction of deep sedation after the intramuscular administration of alfaxalone (4 to 8 mg/kg) in rabbits.¹⁰ In swine, the intramuscular administration of alfaxalone (5 mg/kg) resulted in an induction that was rated as poor to fair, whereas the addition of diazepam (0.5 mg/kg) improved the quality of induction.¹⁸ However, in our current study, the combination of alfaxalone with butorphanol still resulted in poor-quality induction in chinchillas.

The intramuscular route for administration of alfaxalone has been evaluated in a variety of species, including turtles, tortoises, pigs, dogs, cats, and rabbits,^{7,10,12,17,18,21} and the subcutaneous route has been evaluated in mice and cats.^{9,16} Only sparse information is available regarding the effects of alfaxalone in rodents, particularly for the nonvascular administration routes (that is, subcutaneous, intramuscular, intraperitoneal).^{9,13} Intraperitoneal administration of alfaxalone at 20 mg/kg resulted

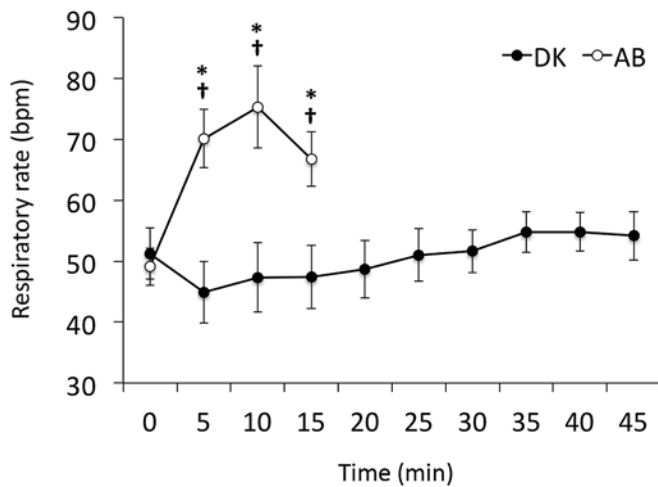


Figure 2. Respiratory rate (mean \pm SEM) of chinchillas ($n = 12$) anesthetized with dexmedetomidine–ketamine (DK) or alfaxalone–butorphanol (AB) in a complete crossover design. *, Value differed significantly ($P < 0.05$) from preanesthetic baseline value within the same protocol; †, values differed significantly ($P < 0.05$) between anesthetic protocols at the same time point. For AB group at 15 min, data of 11 of 12 animals were included.

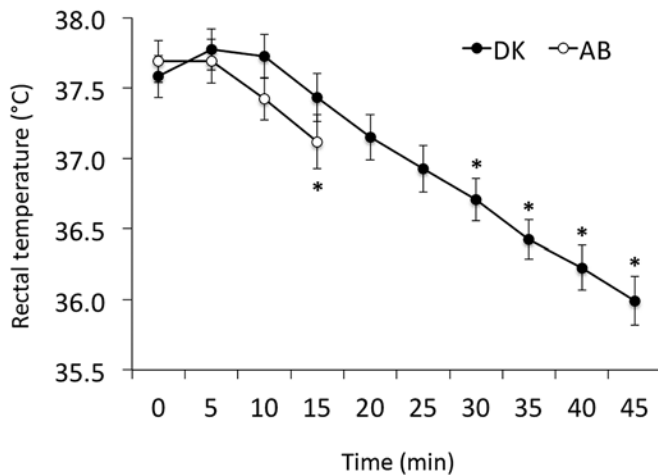


Figure 3. Rectal temperature (mean \pm SEM) of chinchillas ($n = 12$) anesthetized with dexmedetomidine–ketamine (DK) or alfaxalone–butorphanol (AB) in a complete crossover design. *, Value differed significantly ($P < 0.05$) from preanesthetic baseline value within the same protocol; †, values differed significantly ($P < 0.05$) between anesthetic protocols at the same time point. For AB group at 15 min data of 11/12 animals were included.

in the induction of anesthesia in 7 of 10 rats within 3 to 6 min (duration of effect, 29.6 ± 21.4 min).¹³ In mice, alfaxalone at 100 mg/kg SC resulted in low anesthetic scores and did not induce surgical anesthesia.⁹ In contrast, the combination of alfaxalone (20 mg/kg) with medetomidine (0.3 mg/kg) and butorphanol (5 mg/kg) and administered subcutaneously induced surgical anesthesia in mice.⁹

Induction times in chinchillas receiving AB were comparable to those of rabbits given alfaxalone only (4 to 8 mg/kg IM), all of which lost the righting reflex for 37 to 58 min.¹⁰ Similar results were reported for cats after intramuscular administration of alfaxalone.²¹ In contrast, chinchillas that receiving alfaxalone alone at either 3 or 5 mg/kg IM did not lose the righting reflex or become sedated. Higher doses of intramuscular alfaxalone

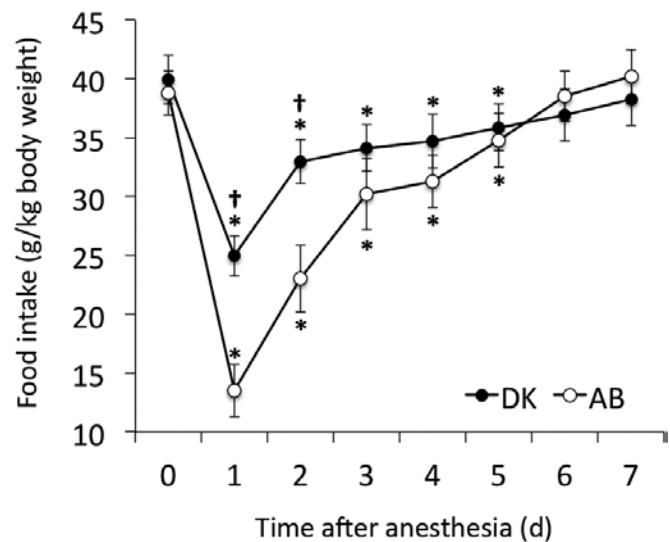


Figure 4. Food intake (mean \pm SEM) of chinchillas ($n = 12$) before and after anesthesia with dexmedetomidine–ketamine (DK) or alfaxalone–butorphanol (AB) in a complete crossover design. *, Value differed significantly ($P < 0.05$) from preanesthetic baseline value within the same protocol; †, values differed significantly ($P < 0.05$) between anesthetic protocols at the same time point.

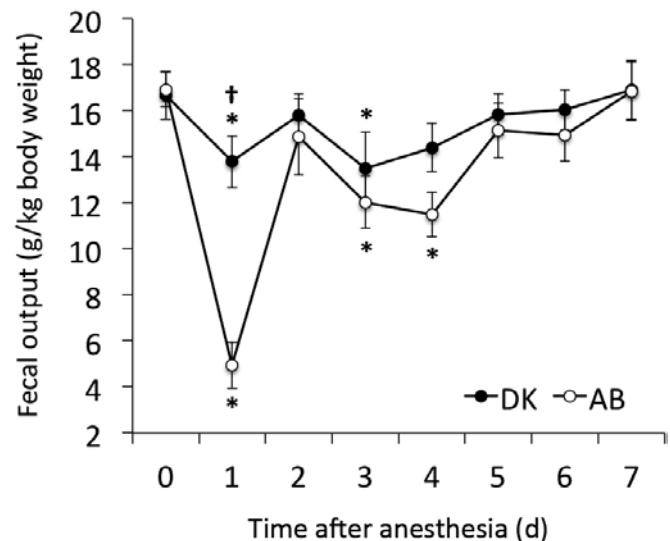


Figure 5. Fecal output (g/kg body weight; mean \pm SEM) of chinchillas ($n = 12$) before and after anesthesia with dexmedetomidine–ketamine (DK) or alfaxalone–butorphanol (AB) in a complete crossover design. *, Value differed significantly ($P < 0.05$) from preanesthetic baseline value within the same protocol; †, values differed significantly ($P < 0.05$) between anesthetic protocols.

were not considered clinically feasible in chinchillas, due to the large volume to be administered; even at the 5-mg/kg dose, the volumes administered ranged from 0.25 to 0.47 mL. In addition, most of the chinchillas exhibited a pain response during the end of the intramuscular injection of alfaxalone alone or in combination with butorphanol, which we assumed to be due to the large amount of drug administered in the lumbar musculature. Pain responses during intramuscular injection of large volumes of alfaxalone have been reported in rabbits and cats as well.^{10,21}

The subcutaneous route might be less painful when large volumes of alfaxalone have to be administered and was effective in cats given alfaxalone (3 mg/kg) combined with butorphanol

(0.2 mg/kg) and in mice.^{9,16} However, in the chinchillas in our pilot studies, subcutaneous administration of alfaxalone (10 mg/kg) alone or combined with butorphanol (0.5 mg/kg) did not induce either sedation or anesthesia; instead, animals became temporarily ataxic before recovering completely. Therefore we do not recommend subcutaneous administration of alfaxalone, either alone or in combination with other drugs, in chinchillas.

Several sedative drugs, including butorphanol, midazolam, diazepam, medetomidine, or dexmedetomidine, have been evaluated in combination with alfaxalone in various species.^{1,7,9,16,18,21} The dose combination we used in the current study was a compromise between an injection volume that we deemed clinical and ethically acceptable and the desired level of chemical restraint. We did not evaluate higher doses of butorphanol or different sedative drugs, such as midazolam, in combination with alfaxalone in chinchillas, which might have resulted in a deeper or prolonged plane of anesthesia. However, considering the significant postanesthetic effects of the evaluated AB combination, higher doses of butorphanol were not considered. Additional research is required to evaluate the effects of butorphanol on postanesthetic food intake and fecal output in chinchillas.

α_2 -adrenergic receptor agonists, such as medetomidine and dexmedetomidine, have been investigated in chinchillas.^{5,6,8} Heart rates in chinchillas anesthetized with DK were significantly lower than those with the AB protocol. The heart rates in our DK group are comparable to those in a previous study that compared the same DK protocol with isoflurane anesthesia.⁶ In addition, echocardiographic parameters were affected similarly in chinchillas anesthetized with DK or isoflurane.^{5,14}

Respiratory rates differed significantly between protocols in the current study, due to a significant increase in respiratory rate in the AB group. In contrast, rabbits anesthetized with alfaxalone (4 to 8 mg/kg IM), which became bradypneic (30 breaths per minute or less). One of the rabbits became apneic and died after receiving alfaxalone at 8 mg/kg IM. The respiratory depression was dose-dependent and greatest at the 6- and 8-mg/kg doses.¹⁰ Hyperthyroid cats given AB subcutaneously (3 mg/kg and 0.2 mg/kg) and euthyroid cats provided alfaxalone intramuscularly (2.5 to 10 mg/kg) also became bradypneic.^{16,21} Given our findings, alfaxalone does not appear to induce bradypnea in chinchillas when administered at 5 mg/kg IM combined with butorphanol at 0.5 mg/kg. In the DK group, the respiratory rate did not change over time and was comparable to the preanesthetic rate. This finding is consistent with previous studies that evaluated the same protocol (without supplemental oxygen) in chinchillas.⁶

Body temperature decreased with both protocol over time and remained within the reported reference range for chinchillas¹⁵ except for one animal in the DK group, which became mildly hypothermic at 45 min. This decrease in rectal temperature is consistent with a previous study that compared the DK protocol with isoflurane anesthesia in chinchillas.⁶ Hypothermia can result in delayed drug metabolism and excretion of anesthetic and analgesic drugs, hypotension, and delayed recovery.⁴ Therefore the provision of supplemental heat may be helpful in counteracting the anesthesia-associated decrease in body temperature in chinchillas.

In a previous study, the DK protocol resulted in hypoxemia in chinchillas breathing room air instead of receiving supplemental oxygen.⁶ In the current study, provision of supplemental oxygen prevented the development of hypoxemia. Therefore

we recommend providing supplemental oxygen to chinchillas anesthetized with DK whenever possible.

Atipamezole was administered by intramuscular injection in this current study and resulted in recovery of the righting reflex by a median of 7 min (range: 3 to 15 min). This recovery time is comparable to the results of a previous study in which atipamezole was administered subcutaneously after 45 min of DK anesthesia in chinchillas.⁶ The righting reflex had recovered by a median of 5 min (range, 4 to 15 min) after subcutaneous injection.⁶ Likewise, the recovery of the other evaluated reflexes was comparable between the subcutaneous and intramuscular routes of atipamezole administration.⁶

Both the AB and the DK protocols decreased food intake in chinchillas for 4 to 5 d after recovery from anesthesia. However, the AB protocol led to greater reduction in food intake and fecal output. To our knowledge, no information has been published on the postanesthetic effects of alfaxalone alone or combined with butorphanol in other species. Food intake after the same DK protocol was decreased in chinchillas breathing room air instead of supplemental oxygen.⁶ In both the previous⁶ and current studies, the greatest decrease in food intake occurred in the first 24 h after anesthesia. The reduction in food intake was greater in chinchillas that were hypoxic during the anesthetic period ($-61\% \pm 25\%$)⁶ than in the chinchillas, which did not become hypoxic ($-37.7\% \pm 8.2\%$). Similarly, the decrease in fecal output in the first 24 h after DK anesthesia was substantially less in the DK group in the current study, which received supplemental oxygen ($-16.5\% \pm 15.8\%$), than in the DK-anesthetized chinchillas that breathed room air ($-50\% \pm 30\%$) in the previously published study.⁶ These differences in postanesthetic fecal output and food intake between chinchilla with or without supplemental oxygen during DK anesthesia suggests that oxygen supplementation during DK anesthesia attenuates the postanesthetic negative effects on food intake and fecal output and that hypoxemia is responsible, at least in part, for the documented reduction in food intake and fecal output in the previously published study.⁶ Other possible factors that lead to a postanesthetic reduction in food intake and subsequently fecal output are the direct depressive effects of the evaluated drugs (including the atipamezole administered to the DK group), leading to decreased feeding behavior.^{2,6,20} Isoflurane has no significant effects on postanesthetic food intake or fecal output in chinchillas anesthetized for 45 min or in mice.^{3,6} Therefore we recommend DK anesthesia with oxygen supplementation or isoflurane anesthesia for chinchillas, because fewer postanesthetic effects on food intake and fecal output have been documented with these regimens compared with DK anesthesia without oxygen supplementation or AB anesthesia.

In conclusion, the AB combination administered intramuscularly to chinchillas resulted in a rapid induction of short-term anesthesia, which was inconsistent in both duration and depth. The AB protocol resulted in more severe reductions in postanesthetic food intake and fecal output than those in chinchillas anesthetized with DK. Anesthesia with DK resulted in rapid induction of surgical anesthesia in all animals and was readily reversible with atipamezole. Compared with the AB regimen, the DK protocol provided superior anesthetic efficacy and had fewer postanesthetic side effects in our chinchillas and is therefore a more suitable injectable anesthetic combination for this species.

References

1. Adami C, Imboden T, Giovannini AE, Spadavecchia C. 2016. Combinations of dexmedetomidine and alfaxalone with butor-

- phanol in cats: application of an innovative stepwise optimisation method to identify optimal clinical doses for intramuscular anaesthesia. *J Feline Med Surg*. 18:846–853.
2. **Berlan M, Galitzky J, Tran MA, Montastruc P.** 1991. Anorectic effect of α 2-antagonists in dogs: effect of acute and chronic treatment. *Pharmacol Biochem Behav* 39:313–320.
 3. **Cesarovic N, Nicholls F, Rettich A, Kronen P, Hassig M, Jirkof P, Arras M.** 2010. Isoflurane and sevoflurane provide equally effective anaesthesia in laboratory mice. *Lab Anim* 44:329–336.
 4. **Clark-Price S.** 2015. Inadvertent perianesthetic hypothermia in small animal patients. *Vet Clin North Am Small Anim Pract* 45:983–994.
 5. **Doss GA, Mans C, Stepien RL.** 2016. Echocardiographic effects of dexmedetomidine–ketamine in chinchillas (*Chinchilla lanigera*). *Lab Anim*. 51:89–92.
 6. **Fox L, Snyder LB, Mans C.** 2016. Comparison of dexmedetomidine–ketamine with isoflurane for anesthesia of chinchillas (*Chinchilla lanigera*). *J Am Assoc Lab Anim Sci* 55:312–316.
 7. **Hansen LL, Bertelsen MF.** 2013. Assessment of the effects of intramuscular administration of alfaxalone with and without medetomidine in Horsfield's tortoises (*Agrionemys horsfieldii*). *Vet Anaesth Analg* 40:e68–e75.
 8. **Henke J, Baumgartner C, Roltgen I, Eberspacher E, Erhardt W.** 2004. Anaesthesia with midazolam–medetomidine–fentanyl in chinchillas (*Chinchilla lanigera*) compared to anaesthesia with xylazine–ketamine and medetomidine–ketamine. *J Vet Med A Physiol Pathol Clin Med* 51:259–264.
 9. **Higuchi S, Yamada R, Hashimoto A, Miyoshi K, Yamashita K, Ohsugi T.** 2016. Evaluation of a combination of alfaxalone with medetomidine and butorphanol for inducing surgical anesthesia in laboratory mice. *Jpn J Vet Res* 64:131–139.
 10. **Huynh M, Poumeyrol S, Pignon C, Le Teuff G, Zilberstein L.** 2014. Intramuscular administration of alfaxalone for sedation in rabbits. *Vet Rec* 176:255.
 11. **Jones KL.** 2012. Therapeutic review: alfaxalone. *Journal of exotic pet medicine* 21:347–353.
 12. **Kischinovskiy M, Duse A, Wang T, Bertelsen MF.** 2013. Intramuscular administration of alfaxalone in red-eared sliders (*Trachemys scripta elegans*)—effects of dose and body temperature. *Vet Anaesth Analg* 40:13–20.
 13. **Lau C, Ranasinghe MG, Shiels I, Keates H, Pasloske K, Bellingham MC.** 2013. Plasma pharmacokinetics of alfaxalone after a single intraperitoneal or intravenous injection of Alfaxan in rats. *J Vet Pharmacol Ther* 36:516–520.
 14. **Linde A, Summerfield NJ, Johnston M, Melgarejo T, Keffer A, Ivey E.** 2004. Echocardiography in the chinchilla. *J Vet Intern Med* 18:772–774.
 15. **Ozawa S, Mans C, Beaufere H.** 2016. Comparison of rectal and tympanic temperatures in chinchillas (*Chinchilla lanigera*). *J Am Vet Med Assoc*. In press.
 16. **Ramoo S, Bradbury L, Anderson G, Abraham L.** 2013. Sedation of hyperthyroid cats with subcutaneous administration of a combination of alfaxalone and butorphanol. *Aust Vet J* 91:131–136.
 17. **Rodrigo-Mocholí D, Belda E, Bosmans T, Laredo FG.** 2016. Clinical efficacy and cardiorespiratory effects of intramuscular administration of alfaxalone alone or in combination with dexmedetomidine in cats. *Vet Anaesth Analg* 43:291–300.
 18. **Santos González M, Bertran de Lis BT, Torrent B, Tendillo Cortijo FJ.** 2013. Effects of intramuscular alfaxalone alone or in combination with diazepam in swine. *Vet Anaesth Analg* 40:399–402.
 19. **Saunders R.** 2009. Veterinary care of chinchillas. In *Practice* 31:282–291.
 20. **Springer DA, Baker KC.** 2007. Effect of ketamine anesthesia on daily food intake in *Macaca mulatta* and *Cercopithecus aethiops*. *Am J Primatol* 69:1080–1092.
 21. **Tamura J, Ishizuka T, Fukui S, Oyama N, Kawase K, Itami T, Miyoshi K, Sano T, Pasloske K, Yamashita K.** 2015. Sedative effects of intramuscular alfaxalone administered to cats. *J Vet Med Sci* 77:897–904.
 22. **Tamura J, Ishizuka T, Fukui S, Oyama N, Kawase K, Miyoshi K, Sano T, Pasloske K, Yamashita K.** 2015. The pharmacological effects of the anesthetic alfaxalone after intramuscular administration to dogs. *J Vet Med Sci* 77:289–296.
 23. **Wang AY, Shen Y, Wang JT, Friedland PL, Atlas MD, Dilley RJ.** 2014. Animal models of chronic tympanic membrane perforation: a 'time-out' to review evidence and standardize design. *Int J Pediatr Otorhinolaryngol* 78:2048–2055.
 24. **Warne LN, Beths T, Whittem T, Carter JE, Bauquier SH.** 2015. A review of the pharmacology and clinical application of alfaxalone in cats. *Vet J* 203:141–148.