Comparison of 3 Total Intravenous Anesthetic Infusion Combinations in Adult Horses

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ABSTRACT

The objective of this study was to compare 3 total intravenous anesthetic infusion combinations in adult horses for cardiopulmonary changes, muscle relaxation, duration of recumbency, and quality of recovery. This was a prospective, randomized, crossover, experimental study. Six healthy, adult, mixed-breed horses weighing 460 ± 30 kg were used. The 3 total intravenous anesthetic combinations used were: guaifenesin-ketamine-xylazine (1 L of 5%-500 mg-1000 mg) (GKX), diazepam-ketamine-xylazine (50 mg-1000 mg-500 mg) (DKX) in 1 L physiologic saline, and ketamine-xylazine (1000 mg-500 mg) (KX) in 1 L physiologic saline. Each horse was premedicated with 500 mg of xylazine IV and induced with 1000 mg of ketamine IV. The anesthesia was maintained with 1 L of each combination at 2.2 mL/kg/hr IV with a minimum of 1 week between treatments. A 50-mL bolus was administered if the horse showed voluntary movement or movement in response to stimuli. If multiple boluses failed to stop the movement or the movement became dangerous to the horse or personnel, the anesthesia was discontinued. Heart rate, respiratory rate, and temperature were measured prior to and at 5-minute intervals during anesthesia. Direct blood pressures and estimated arterial oxygen saturation via pulse oximetry (SpO_2) were also recorded every 5 minutes during anesthesia. Oxygen at 15 L/min was provided by nasal insufflation if the horse failed to maintain a SpO_2 above 85%. Arterial blood samples were drawn for blood gas analysis at 20 minute intervals. Infusion time, time to sternal, and time to standing were recorded and a subjective evaluation of analgesia, muscle relaxation, and recovery were made. GKX provided excellent anesthesia for all 6 horses for 52 ± 7 minutes with only mild decreases in arterial blood pressures compared with the 2 other infusions. DKX provided adequate anesthesia in 5 out of the 6 horses. However, length of anesthesia was shorter at 45 ± 12 minutes and muscle relaxation and analgesia were less than with GKX. With KX, anesthesia for 3 of 6 horses was aborted due to movement. Anesthesia time for KX was 33 ± 10 minutes. Arterial blood pressure was higher in the DKX and KX groups than in the GKX group. DKX would be adequate for mildly stimulating procedures at this rate, but is not an equivalent substitute for GKX. KX is not adequate anesthesia at this rate.

INTRODUCTION

Although guaifenesin-ketamine-xylazine (GKX) is a well-documented infusion for total intravenous anesthesia that has shown

good analgesia and muscle-relaxant properties,[1,2] guaifenesin is unavailable in some countries. Therefore, choices for total intravenous anesthesia that do not contain guaifenesin are also limited. The purpose of this study was to compare a commonly used total intravenous combination, GKX, with 2 combinations that do not include guaifenesin. The first comparative infusion choice was a ketamine-xylazine (KX) combination (a combination that is often given as an induction protocol and then redosed multiple times to prolong the anesthetic effects) at a rate similar to that used for induction and redosing.[3] Because diazepam is considered a centrally acting muscle relaxant and sedative like guaifenesin, diazepam-ketamine-xylazine (DKX) was selected as the second comparative combination.[4] Diazepam was also chosen over other muscle relaxants due to its low cost and widespread availability. Although there are multiple studies considering DKX as an induction protocol, few have examined this novel combination for long-term infusions.[5] The main purpose of this study was to find a comparable alternative (eg, KX, DKX) to GKX for constant rate infusions in locations where guaifenesin was not an option.

MATERIALS AND METHODS

Animals

The study was performed in 6 adult, mixed-breed horses (2 male, 4 female) 8 ± 5 years old weighing 454 ± 34 kg (age and weight each mean ± SD). The horses were tame and halter broken. A physical examination, auscultation, complete blood count, chemistry profile, and an electrocardiogram (ECG) were completed on each horse prior to anesthesia, confirming the horses were healthy without any significant cardiopulmonary or metabolic abnormalities. The horses were housed in large outside pens and fed grain and coastal hay. Feed was not withheld prior to anesthesia to more closely approximate a field anesthesia scenario. All procedures were approved by the Texas A&M University Laboratory Animal Care Committee.

Experimental Design

Each horse received each treatment. The order of drug combination administered was randomized and the horses were anesthetized with a minimum of 1 week between exposures. A 14G 5¼-inch catheter (BD Angiocath, Becton Dickinson, Infusion Therapy Systems, Sandy, Utah, USA) was placed percutaneously in an external jugular vein prior to anesthesia. All horses were premedicated with xylazine (1.1 mg/kg IV) (Tranquived, Vedco Inc., St. Joseph, Missouri, USA) and induced 3-5 minutes later with ketamine (2.2 mg/kg IV) (Ketaved, Vedco, Inc., St. Joseph, Missouri, USA). All drugs were given through the catheter. After induction, the horses were placed in right lateral recumbency in a padded recovery stall. Horses were not intubated. Oxygen insufflation was given if the oxygen saturation via pulse oximetry (SpO_2) decreased below 85%.

Drug Combinations

After induction, 3 different continuous intravenous infusions were used: 1) KX: xylazine (0.5 mg/mL) combined with ketamine (1 mg/mL) in 1 L of 0.9% sodium chloride (Hospira Inc., Lake Forest, IL USA); 2) DKX: xylazine (0.5 mg/mL) combined with ketamine (1 mg/mL) and diazepam (0.05 mg/mL) (Diazepam, Abbot Laboratories, North Chicago, IL, USA) in 1 L of 0.9% sodium chloride; and 3) GKX: xylazine (0.5 mg/mL) combined with ketamine (1 mg/mL) in 1 L of 5% (50 mg/mL) guaifenesin (Guaifenesin, Injection, Vedco, Inc., St. Joseph, Missouri, USA).

Infusions (2.2 mL/kg/hr IV) were administered until 1 L was used or the horse no longer maintained lateral recumbency. A horse that moved in response to stimuli or voluntarily moved received 50-mL boluses of infusion. If multiple boluses failed to decrease movement or the movement became dangerous to the horse or personnel, the infusion was stopped.

Data Collection

A baseline heart rate, respiratory rate, and rectal temperature were obtained from each

horse prior to anesthesia. Once anesthetized, an ECG was displayed with leads placed in base-apex position. A 20G 1.16-inch arterial catheter (BD Insyte, Becton Dickinson, Infusion Therapy Systems, Sandy, Utah, USA) was placed in the facial artery and connected to a transducer zeroed at the level of the base of the heart. A commercial hemodynamic monitor was used to measure direct arterial blood pressure and display ECG (ProPaq 106EL, Protocol Systems, Inc., Beaverton, Oregon, USA). A pulse-oximeter probe (Nellcor VetSat, Puritan Bennett, Inc., Pleasanton, Calif, USA) was placed on the tongue to monitor SpO_2. A temperature probe was placed rectally. Heart rate, respiratory rate, systolic arterial blood pressure (SAP), diastolic arterial blood pressure (DAP), mean arterial blood pressure (MAP), rectal temperature, and SpO_2 were recorded at 5-minute intervals after the horse became recumbent. Arterial blood samples were obtained from the arterial catheter at 20-minute intervals for acid-base and blood gas analysis. Arterial blood samples were analyzed immediately (IRMA Blood Analysis System, Diametrics Medial Inc., St. Paul, Minn, USA). A peripheral nerve stimulator (Microstim Neurotechnology, Houston, TX, USA) was attached to the lateral aspect of the neck with one electrode a hand's breadth caudal to the ramus of the mandible and the other electrode cranial to the scapula to differentiate between those animals still anesthetized and those who were awake, but lying quietly. The horses were stimulated at 15-minute intervals with 4 pulses of 70 mA at a frequency of 2 Hz and the response recorded unless the horse was clearly awake (Table 1). A muscle relaxation score was recorded at 5, 30, and 60 minutes. Muscle relaxation and quality of recovery were rated subjectively by 2 unblinded personnel (Table 1).

Time of anesthesia was recorded as the time infusion was began until 1000 mL was infused or infusion was stopped. Time from stopping the infusion until animal rolled into and remained sternal was recorded as time to sternal. Time from stopping the infusion until horse was able to stand and remain standing was recorded as time to standing.

Statistical Analysis

A mixed model was used for analysis of the physiological measurements and lab data taken during anesthesia (repeated measures by animal with a compound symmetry covariance matrix) (SAS, Version 8.0, SAS Institute, Cary, NC, USA). At each time point, specific physiological value (eg, heart rate) was used as the dependent variable, and the specific anesthetic regimen was used as the independent variable. Differences were reported as least square means. A *P*-value of <0.05 was considered significant. No statistical evaluation of the subjective data (ie, analgesia, muscle relaxation, recovery) was preformed. Data are recorded as mean ± standard deviation for continuous variables.

RESULTS

Results of all preanesthetic complete blood count and chemistry profiles were within normal values. All preanesthetic ECGs were within normal limits.

GKX

GKX produced good anesthesia in all 6 horses. Scores for muscle relaxation and analgesia are given in Table 1. Three of the horses required 50-mL GKX boluses due to voluntary movement or movement in response to stimulation. One horse received 1 bolus, while the remaining 2 horses received 3 boluses each. There was no response to stimulus in 4 of the horses although 1 horse did react to replacement of the temperature probe. The remaining 2 horses showed only very minimal response (nystagmus, deep breathing). Muscle relaxation was excellent in 4 horses and adequate in the remaining 2 with only mild stiffness of the limbs. The objective data obtained are provided in Table 2. The mean heart rate was significantly higher compared with the DKX and KX heart rates at 20 minutes. The mean SAP, DAP, and MAP at 20 and 40 minutes were significantly lower than the DKX and KX groups. Three of the horses were given supplemental oxygen by nasal insufflation at

15 L/min due to SpO_2 levels below 85% at induction. Once insufflation began, the SpO_2 increased. Despite oxygen supplementation, the horses remained hypoxemic and slightly hypercapnic. Recovery scores are given in Table 1. Five of the horses had excellent recoveries with only 1 horse taking 2 attempts to rise and showing moderate ataxia once standing. Times for anesthesia, sternal, and standing are given in Table 3. The 1-L infusion was completed in all 6 horses at an average rate of 0.042 ± 0.006 mL/kg/min over an average of 52 ± 7 minutes.

Table 1. Number of Horses Under Each Subjective Score for 3 Total Intravenous Anesthesia Combinations.

	Minutes From Induction					
	5 min			30 min*		
Muscle Relax Score (0-2)	0	1	2	0	1	2
GKX	0	2	4	1	0	5
DKX	1	1	4	0	1	4
KX	0	3	3	4	0	0
	Minutes From Induction					
	15 min			**30 min***		
Analgesia Score (0-2)	0	1	2	0	1	2
GKX	0	2	4	0	0	6
DKX	1	1	4	2	1	2
KX	3	2	1	4	0	0
Recovery Score (1-4)	1	2	3	4		
GKX	5	1	0	0		
DKX	3	3	0	0		
KX	5	1	0	0		

GKX = guaifenesin–ketamine-xylazine; DKX = diazepam-ketamine-xylazine; KX = ketamine-xylazine.

Values are number of horses in each category.

Muscle relaxation score: 0 = rigidity of head, neck, and limb muscles; 1 = partial relaxation of head, neck, or limb muscles; 2 = complete relaxation.

Analgesia score: 0 = much response (eg, voluntary movement); 1 = minimal response (eg, nystagmus); 2 = no response.

Recovery score: 1 = horse stands smoothly on first attempt with very little ataxia; 2 = horse stands fairly smoothly with 1-2 attempts and obvious ataxia; 3 = horse stands fairly with 3 or more attempts, ataxia, and some difficulty; 4 = horse requires assistance to stand.

*At 30 minutes, n ≤ 6 since some horses could not be maintained for 30 minutes; n = 6 for 5 minutes, 15 minutes, and recovery.

DKX

DKX produced good anesthesia in 5 of the 6 horses. Scores for muscle relaxation and analgesia are given in Table 1. Two horses received 50-mL DKX boluses due to voluntary movement or movement due to stimulation. The horses received 1 and 2 boluses each, respectively. There was no response to stimulus in 2 of the horses and only very minimal response in 1 horse (nystagmus, deep breathing). Muscle relaxation was excellent in 4 horses and adequate in one with only mild stiffness of the limbs. The remaining horse was hyperreactive to noise, attempted to roll sternal when stimulated, and never showed any muscle relaxation in recumbency. This horse was given three 50-mL DKX boluses in an attempt to maintain lateral recumbency at 16, 19, and 21 minutes. The horse continued to attempt to roll sternal so the infusion was stopped in this horse at 25 minutes with only 550 mL administered. The objective data obtained are provided in Table 2. The mean heart rate was significantly lower than the GKX heart rate at 20 minutes. The mean SAP, DAP, and MAP were significantly higher than the GKX group at 20 and 40 minutes. The arterial CO_2 concentration was significantly lower than the KX group at 20 and 40 minutes but oxygen levels were still considered hypoxic and slightly hypercapnic. Recovery scores are given in Table 1. Five of the horses had excellent recoveries. The horse in which anesthesia was ineffective took 2 attempts to rise and showed moderate ataxia once standing. The infusion of 1 L was complete in 5 of the 6 horses and discontinued at 550 mL in the sixth horse. The average rate of infusion for the 6 horses was 0.046 ± 0.007 mL/kg/min over a range of 25 to 60 minutes (Table 3).

KX

KX provided poor anesthesia at the dosage used. Scores for muscle relaxation and analgesia are given in Table 1. Four of the horses received multiple boluses in an attempt to maintain them in lateral recumbancy. In 3 of the horses, anesthesia was

Table 2. Mean (± SD) Values for Physiological and Laboratory Data for 3 Total Intravenous Anesthesia Combinations in Horses.

		Time Following Induction			
	Baseline	**20 minutes**	**n**	**40 minutes**	**n**
GKX					
HR	51 ± 6	42 ± 5*†	6	45 ± 6	6
RR	21 ± 7	15 ± 7	6	15 ± 7	6
TEMP	100.9 ± 1.1	100.5 ± 1.4	6	100.3 ± 1.4	6
SAP		110 ± 21*†	5	107 ± 29*†	6
MAP		83 ± 23*†	5	84 ± 24*†	6
DAP		70 ± 25*†	5	73 ± 22*†	6
SpO_2		88 ± 3	6	87 ± 2	6
pH		7.36 ± 0.02	5	7.38 ± 0.03	6
pCO_2		49 ± 2	5	48 ± 2†	6
pO_2		58 ± 13	5	47 ± 16	6
DKX					
HR	54 ± 11	38 ± 4‡	6	39 ± 5	5
RR	19 ± 4	17 ± 2	6	18 ± 8	5
TEMP	100.6 ± 0.8	101.0 ± 1.2	6	101.0 ± 1.1	5
SAP		150 ± 19‡	5	147 ± 13‡	5
MAP		123 ± 15‡	5	121 ± 12‡	5
DAP		105 ± 13‡	5	103 ± 10‡	5
SpO_2		88 ± 3	6	88 ± 6	5
pH		7.39 ± 0.04	5	7.40 ± 0.03	5
pCO_2		47 ± 4†	5	47 ± 2†	5
pO_2		60 ± 10	5	61 ± 14	5
KX					
HR	49 ± 9	39 ± 4‡	6	45 ± 17	4
RR	17 ± 2	15 ± 4	6	18 ± 4	4
TEMP	100.2 ± 0.5	100.3 ± 0.4	6	99.6 ± 0.1	4
SAP		158 ± 28‡	6	164 ± 27‡	4
MAP		129 ± 25‡	6	139 ± 23‡	4
DAP		112 ± 23‡	6	125 ± 19‡	4
SpO_2		87 ± 8	6	87 ± 4	4
pH		7.39 ± 0.03	4	7.40 ± 0.02	4
pCO_2		51 ± 3*	4	51 ± 2*‡	4
pO_2		56 ± 7	4	57 ± 7	4

*Significantly different from DKX.

†Significantly different from KX.

‡Significantly different from GKX.

HR = heart rate (bpm); RR = respiratory rate (bpm); TEMP = rectal temperature (degrees Fahrenheit); SAP = systolic blood pressure (mmHg); MAP = mean blood pressure (mmHg); DAP = diastolic blood pressure (mmHg); SpO_2 = percentage of hemoglobin saturation with oxygen; pH = arterial blood pH; pCO_2 = carbon dioxide concentration in arterial blood (mmHg); pO_2 = oxygen concentration in arterial blood (mmHg).

ineffective; the horses moved and attempted to roll sternal. The remaining 3 horses showed reaction to the stimulus (vocalizing, movement) and poor muscle relaxation. The objective data obtained are provided in Table 2. The mean heart rate was significantly lower than the GKX group at 20 minutes. The mean SAP, DAP, and MAP were significantly higher than the GKX group at 20 and 40 minutes. The arterial CO_2 concentration was significantly higher than the DKX group at 20 and 40 minutes. The horses were considered hypoxic and hypercapnic. Recovery scores are given in Table 1. Five of the horses had excellent recoveries. One horse in which the infusion was stopped at 22 minutes required 2 attempts to stand and showed moderate ataxia upon standing. Times for anesthesia, sternal, and standing are given in Table 3. Three horses remained recumbent for the infusion of the full 1 L, whereas in 3 horses anesthesia was discontinued at 925, 800, and 500 mL and 40, 22, and 19 minutes, respectively. The average rate of infusion for the 6 horses was 0.059 ± 0.009 mL/kg/min for an average of 34 minutes (Table 3).

DISCUSSION

The dose of xylazine and ketamine in the GKX we used was a well-established and published dose.[1] Data collected indicated GKX had the greatest amount of respiratory and cardiovascular depression as seen by the decreased arterial blood pressure and hypoxia. These finding are consistent with previous studies using GKX in horses.[6]

Table 3. Mean Times (± SD) for 3 Total Intravenous Anesthesia Combinations in Horses.

	Minutes From Induction			Dose Rate	Boluses (# of
	Duration	Stern	Stand	(mL/kg/min)	horses)
GKX	52 ± 7*†	15 ± 6	24 ± 10	0.042 ± 0.006	3
DKX	45 ± 12*†	14 ± 8	20 ± 6	0.046 ± 0.007	3
KX	34 ± 10*‡	10 ± 6	18 ± 10	0.059 ± 0.009*‡	4

*Significantly different from DKX.

†Significantly different from KX.

‡Significantly different from GKX.

Duration = total infusion time; Stern = time from cessation of infusion to sternal; Stand = time from cessation of infusion to standing; Dose Rate = mL of combination/kg body weight/minutes of infusion; Boluses = number of horses receiving boluses during total infusion time.

The DKX combination provided what appeared to be adequate anesthesia. The dose chosen was based on research by Brock and Hildebrand[5] that states that diazepam (0.1 mg/kg) could be substituted for guaifenesin (100 mg/mL) to produce comparable quality anesthesia in horses. Although this study looked mainly at induction doses, we felt it was a good basis for the infusion dosage chosen. With the infusion, the time of anesthesia was shorter and it required a higher rate to maintain anesthesia than with GKX. Guaifenesin is a central-acting skeletal muscle relaxant that selectively depresses or blocks nerve impulse transmission at the internuncial neuron level of the spinal cord, brainstem, and subcortical areas of the brain,[7] whereas diazepam is a central-acting muscle relaxant whose principal effects are at the supraspinal level.[11] The pharmacokinetics are also different for the 2 drugs. Diazepam has a half-life of 2.5 to 21 hours, whereas guaifenesin's half-life is approximately 60 to 84 minutes.[12] So, although they are both central-acting muscle relaxants, their major area of action is different, and the different pharmacokinetics may account for the differences seen. One horse did not respond well to the combination and never attained adequate anesthesia. However, this horse had the least response to the GKX and KX combinations as well and was more excitable and reactive than the other horses. Variable response between breeds or individuals and the resistance of high-strung patients to sedation or anesthesia is well documented.[13] Higher DAP, SAP, and MAP suggest less cardiovascular depression than the GKX group (Table 2). Research by Muir et al[14] demonstrated no significant cardiopulmonary changes in association with intravenous boluses of diazepam as opposed to guaifenesin, which has been shown to decrease MAP and PaO_2.[11,14]

Guaifenesin itself has been shown to cause a drop in MAP and partial pressure of oxygen in arterial blood (PaO_2) when given intravenously in horses.[7] Muir,[8] however, states that maintaining a MAP greater than 70 mmHg at all times is sufficient to maintain organ and tissue perfusion. Since the MAP never fell below 70 mmHg in this study, this is probably clinically insignificant and would likely increase with surgical stimulation. An increased partial pressure of carbon dioxide in arterial blood ($PaCO_2$) and decreased PaO_2 were also noted. Although literature shows that $PaCO_2$ up to 70 mmHg appear to be well tolerated in horses, the PaO_2 and SpO_2 correlate with clinically significant hypoxia and hypoxemia even with oxygen supplementation.[8] This could be due to hypoventilation, which is partially supported by the slightly increased $PaCO_2$. Guaifenesin is known to cause hypoventilation, but the resultant hypoxia is often effectively counteracted by oxygen administration.[9] Ventilation/perfusion mismatch is a more probable cause of these changes. During anesthesia, ventilation is directed preferentially to the uppermost region of the lung while perfusion is concentrated caudodorsally.[10] In other words, the uppermost regions of the lungs containing oxygen do not have perfusion to transport this oxygen to the tissues and the caudodorsal areas of lungs with perfusion do not have an adequate oxygen supply, thus creating hypoxemia.

We had concerns relating to the inactivation of diazepam in physiologic saline, fluid bag or tubing, therefore, the drugs were mixed just prior to use. Studies have shown the stability of diazepam with saline for up to 24 hours; however, PVC fluid bags and tubing can adsorb 20%-90% of the diazepam.[15] Future research should possibly use less adsorptive bags and lines, such as polyethylene, or use a higher concentration of diazepam to account for possible loss. There are few references discussing DKX as an infusion, but those that use DKX as an induction protocol found it comparable to GKX.[5] Our study showed less muscle relaxation and shorter duration of anesthesia when compared with GKX; however, different handling of the solution, a higher dose of diazepam in the infusion, or a loading dose of diazepam may have provided a better anesthetic protocol.

The KX dose we used was extrapolated from a study using repeated KX dosing. McCarty and colleagues[3] found that approximately 13 minutes after an induction dose of 1.1 mg/kg of xylazine and 2.2 mg/kg of ketamine, repeated doses of one third the induction dose could be administered approximately 12 minutes apart to maintain longer periods of adequate anesthesia. We extrapolated this data to produce a KX dose for 1 hour; however, this KX rate provided poor relaxation and poor analgesia. Inadequate anesthesia was produced in 50% of the horses. Even when the infusion was bolused, the horses' plane of anesthesia did not seem to deepen. On the contrary, 4 of the horses seemed to show increased movement after boluses of the KX infusion. Muir[13] described poor analgesia and muscle relaxation when the ratio of ketamine to xylazine became too high and the excitatory effects of the ketamine overcame the sedative effects of the xylazine. Because our ratio of ketamine to xylazine remained the same as the induction dose and previous studies of repeated bolusing, this is unlikely the cause. We can hypothesize that perhaps the rate of administration was simply too slow to provide adequate anesthesia or to deepen the plane of anesthesia. The $PaCO_2$ was higher at both 20 and 40 minutes with the KX group compared with the GKX and DKX groups; however, it was not high enough to be clinically significant as discussed earlier with GKX. All horses stayed recumbent a minimum of 19 minutes, which is likely a result of the induction drugs and not the infusion. Typically, horses will remain recumbent for approximately 18-20 minutes with this dose of xylazine and ketamine.[16] Several references discussed short-term anesthesia of less than 30 minutes for KX but at the time of the research, there were few references discussing long-term infusions using KX.[17] After completion of our research, Mama et al[18] published a paper with 1-hour infusion rates using KX; however, they used much larger doses, 2.5 to 4 times the amounts, of both xylazine and ketamine, and guaifenesin was included in the induction protocol. Guaifenesin's muscle relaxant and sedative effects can last over 60 minutes and may account for some of their results.[12] Although this provided adequate restraint with only mild muscle twitching or movement, it caused prolonged recovery periods of 33 to 69 minutes. Oxygen supplementation was necessary and AV block were a common sequela at the increased doses. Since the objective of our study was to determine if KX was an appropriate field anesthetic where supportive measures and guaifenesin are not readily available, this dosage would not appear to be a viable choice. Further research would be needed to determine if an optional infusion rate can be found.

Statistical analysis was completed on all the KX data even though the 40-minute data only had an $n = 4$. It is questionable whether the statistical analysis is valid with such a small group and should be considered when viewing these results. Subjective data was not statistically analyzed. The system used in this study did not provide ample data for analysis. A more technical scoring system or analyzing the number of boluses given might provide more objective data for statistical analysis. Further research may be able to draw more definitive conclusions if these data are obtained and analyzed.

In conclusion, although GKX is still deemed to provide the most consistent and reliable total intravenous anesthesia of the 3 combinations for field anesthesia, DKX could provide adequate anesthesia for mildly stimulating procedures in countries where guaifenesin is not available. Addition of a muscle relaxant clearly appears to improve the quality of anesthesia as shown by poor results with KX alone. Further research is warranted to see if the addition of an opioid, initial bolus, or increased rate of diazepam administration may further enhance this combination.

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