Comparison of the effects of racemic ketamine and S-ketamine for anesthesia in Rheem gazelles (*Gazella subgutturosa marica*) and Subgutturosa gazelles (*Gazella subgutturosa subgutturosa*)

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Objective—To evaluate effects of racemic ketamine and S-ketamine in gazelles.

Animals—21 male gazelles (10 Rheem gazelles [*Gazella subgutturosa marica*] and 11 Subgutturosa gazelles [*Gazella subgutturosa subgutturosa*]), 6 to 67 months old and weighing (mean ± SD) 19 ± 3 kg.

Procedures—In a randomized, blinded crossover study, a combination of medetomidine (80 µg/kg) with racemic ketamine (5 mg/kg) or S-ketamine (3 mg/kg) was administered IM. Heart rate, blood pressure, respiratory rate, rectal temperature, and oxygen saturation (determined by means of pulse oximetry) were measured. An evaluator timed and scored induction of, maintenance of, and recovery from anesthesia. Medetomidine was reversed with atipamezole. The alternate combination was used after a 4-day interval. Comparisons between groups were performed with Wilcoxon signed rank and paired *t* tests.

Results—Anesthesia induction was poor in 2 gazelles receiving S-ketamine, but other phases of anesthesia were uneventful. A dominant male required an additional dose of S-ketamine (0.75 mg/kg, IM). After administration of atipamezole, gazelles were uncoordinated for a significantly shorter period with S-ketamine than with racemic ketamine. Recovery quality was poor in 3 gazelles with racemic ketamine. No significant differences between treatments were found for any other variables. Time from drug administration to antagonism was similar between racemic ketamine (44.5 to 53.0 minutes) and S-ketamine (44.0 to 50.0 minutes).

Conclusions and Clinical Relevance—Administration of S-ketamine at a dose 60% that of racemic ketamine resulted in poorer induction of anesthesia, an analogous degree of sedation, and better recovery from anesthesia in gazelles with unremarkable alterations in physiologic variables, compared with racemic ketamine. (*Am J Vet Res* 2011;72:1164–1170)

Currently, commercially available ketamine hydrochloride for veterinary use is a racemic mixture of 2 optical isomers, the R(–) enantiomer and the S(+) enantiomer. Racemic ketamine is a popular anesthetic for use in small ruminants.[1–4] Nevertheless, this racemic mixture can induce undesired reactions during the anesthetic recovery period; these reactions are characterized by muscular tremors and rigidity, mydriasis, oculogyric movements, sweating, excitation, ataxia, and schizophrenia-like behavior.[5]

Abbreviations

DAP	Diastolic arterial blood pressure
HR	Heart rate
RR	Respiratory rate
SAP	Systolic arterial blood pressure
Spo_2	Oxygen saturation as measured by pulse oximetry

All of these clinical properties of ketamine are attributable to its interaction with the *N*-methyl-D-aspartate receptor. Ketamine binds to the phencyclidine receptor in the *N*-methyl-D-aspartate channel and thus inhibits glutamate activation in a noncompetitive manner.[6] In rats and mice, the S(+) enantiomer has a 3- to 4-fold greater affinity for the receptor, 1.5- to 3-fold greater hypnotic and analgesic potency, 2- to 3-fold lower cerebral concentration of the first metabolite (norketamine) and thus results in less spontaneous movement, and 2.5-fold greater therapeutic index than

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does the R(–) enantiomer.[7,8] In ponies, the elimination half-life of S-ketamine is 26 ± 22 minutes and that of racemic ketamine is 24 ± 8 minutes.[9] In calves, the elimination half-life of racemic ketamine is 30 ± 4 minutes.[10]

Clinical studies to assess the effects of S-ketamine have been performed in several species. In humans, the incidence of psychomimetic phenomena such as agitation, disorientation, and anxiety appears to be lower with S-ketamine than with racemic ketamine.[8] Faster recoveries[11] have been described and a similar degree of analgesia has been observed in cats that received a combination of medetomidine and S-ketamine (6 mg/kg), compared with effects after administration of a combination of medetomidine and racemic ketamine (10 mgkg).[a] In ponies, the use of S-ketamine (1.1 mg/kg), compared with the use of racemic ketamine (2.2 mg/kg), results in a more rapid recovery of psychomotor function after isoflurane-induced anesthesia.[9]

Xylazine in combination with S-ketamine (2 mg/kg) causes less respiratory depression in horses than does the combination of xylazine and racemic ketamine (3 mg/kg).[b] Similarly, better recovery outcome and stronger analgesic effects have been observed when S-ketamine is used at the same dose as racemic ketamine (2 mg/kg) in combination with diazepam in horses.[12] In pregnant sheep, S-ketamine causes less respiratory depression in the dam and fetus than does the racemic mixture of ketamine.[13]

Several anesthetic protocols that include racemic ketamine and α_2-adrenoreceptor agonists have been developed for use in anesthetizing gazelles.[14–18,c] However, there can be undesired ataxia and excitation when racemic ketamine is used.[14] The objective of the study reported here was to evaluate the effects of S-ketamine and racemic ketamine on induction of, maintenance of, and recovery from anesthesia in gazelles.

Materials and Methods

Animals—Twenty-one male gazelles (10 Rheem gazelles [*Gazella subgutturosa marica*] and 11 Subgutturosa gazelles [*Gazella subgutturosa subgutturosa*]) that ranged from 6 to 67 months of age and had a mean ± SD body weight of 19 ± 3 kg were used in the study. The study was approved by the Animal Care and Use Committee of the University of Zurich and conducted in compliance with Swiss cantonal guidelines governing animal care and housing.

Procedures—A randomized, prospective, blinded, crossover study was conducted at the Veterinary Hospital of the Al Wabra Wildlife Preservation, Doha, Qatar. The study was performed in November (mean ± SD ambient temperature, 25.3 ± 1.3°C; mean relative humidity, 60.6 ± 13.2%; barometric pressure, 30 mm Hg). One week before the experiments began, the selected gazelles were moved from a communal pen (16,000 m^2) of males to 4 smaller enclosures (1,000 m^2); each smaller enclosure had direct access to a restraint area. Every morning for 7 consecutive days, the gazelles were moved to the restraint area by a group of qualified keepers who used a system of sliding doors to place the animals in individual wooden transport crates (92 × 39 × 72 cm). The crated gazelles were transferred 1 km to the hospital. Identification of each gazelle was confirmed, and exact body weight of each gazelle was obtained.

Each gazelle was anesthetized 2 times for health evaluation; the washout period between anesthetic episodes was 4 days. Food and water were withheld for at least 3 hours before induction of anesthesia and until each gazelle had completely recovered from anesthesia.

Prior to induction of anesthesia, the apparent stress (calm or nervous) of each gazelle was evaluated and recorded. Induction of anesthesia was performed with each gazelle in its individual crate. A blindfold was placed on each gazelle to reduce possible associated stress. A combination of medetomidine[d] (80 µg/kg) and racemic ketamine[e] (5 mg/kg) or S-ketamine[f] (3 mg/kg) was administered IM in the gluteal muscles. For the second anesthetic episode, the alternate combination of medetomidine and ketamine was administered.

Within 1 minute after injection of the anesthetic agents, the blindfold was removed and the gazelle was allowed to leave the transport crate and enter an empty room (2.25 × 3.30 m^2) for monitoring of anesthetic induction. An evaluator, who was not aware of the anesthetic treatment administered to each gazelle, observed each gazelle and graded induction as good, acceptable, poor, or inadequate **(Appendix)**. First signs of effect (eg, lowering of the head and ataxia), time from injection until first signs of effect, time from injection until lateral recumbency, and total induction time (defined as time from injection until the gazelle could be safely approached) were recorded by the same evaluator. It was considered safe to approach the gazelle if it did not react or move its ears in response to hand clapping. If the gazelle could not be safely approached by 30 minutes after administration of the anesthetic drugs, additional ketamine was administered IM (1.25 mg of racemic ketamine/kg or 0.75 mg of S-ketamine/kg). The time at which each gazelle could be safely approached was designated as the onset of anesthesia (time 0).

Each gazelle was then blindfolded and moved to an examination table for the procedures. The degree of sedation (light anesthesia, deep sedation, light sedation, and no effect) was evaluated every 5 minutes (Appendix). Heart rate was directly measured by use of a stethoscope,[g] and RR was measured by means of direct observation of thorax excursions. Systolic arterial blood pressure and DAP were measured noninvasively by use of a wrist cuff[h] designed for human patients, which was fitted around the left humerus. Rectal temperature was measured intermittently with a thermister.[i] The Spo_2 measurements were obtained by use of an infrared probe[j] placed on the rostral third of the tongue (ie, the pigmented area).

At 10 minutes after onset of anesthesia, 10 mL of venous blood was collected from a jugular vein for use in hematologic and biochemical analyses. An arterial blood sample (0.5 mL) was obtained from the auricular artery at 20 minutes after onset of anesthesia for use in determining the respiratory and acid-base status of the gazelle. The arterial blood sample was immediately analyzed for pH, Pco_2, Po_2, and lactate concentration by use of a point-of-care portable

clinical analyzer.[k] The results were not corrected for temperature.

At 30 minutes after the onset of anesthesia, each gazelle was moved from the table to an individual padded recovery pen (310 × 97 cm^2). Atipamezole[l] (0.4 mg/kg, IM) was administered to antagonize the medetomidine, and the blindfold was removed. Recovery from anesthesia was continuously monitored for 30 minutes and graded at 5-minute intervals as good, acceptable, poor, or inadequate (Appendix). The first signs of recovery (eg, swallowing or tongue movement), time from administration of the antagonist until first signs of recovery, and time from administration of the antagonist until sternal recumbency were recorded. Eating, urinating, and defecating were also recorded during the first 30 minutes after administration of the antagonist. The gazelles remained in the individual pens for 24 hours; food and water were provided. Recovery from anesthesia was graded 1, 6, and 12 to 24 hours after administration of the antagonist.

Quality of induction, maintenance of anesthesia, and recovery from anesthesia were assessed subjectively by use of a visual analogue scale.[19] The scale comprised a 10-cm line, with the left end (0 cm) considered the worst quality possible and the right end (10 cm) considered the best quality possible. An evaluator (OMJ) placed a mark on the line that corresponded to the assessment of quality; the distance from the left end to the mark was recorded as the subjective quality of each anesthetic phase.

Statistical analysis—Data were evaluated for a normal distribution by use of the Kolgomorov-Smirnov test. Time intervals and physiologic variables (HR, RR, rectal temperature, SAP, DAP, and Spo_2) were expressed as median and interquartile range (25th to 75th percentiles), whereas other results were expressed as mean ± SD. Comparison of arterial blood gas values between treatments was performed via a paired *t* test. Nonparametric data were compared by use of a Wilcoxon signed rank test. Scores were analyzed with a Fischer exact test. Physiologic variables and the score for the visual analogue scale for each treatment were analyzed over time by use of a Friedman test and 2-way repeated-measures ANOVA, respectively. When differences were obtained in the aforementioned tests, a pairwise multiple comparison procedure was performed by use of the Holm-Sidak method. Values of $P < 0.05$ were considered significant. Analysis was performed by use of a statistical analysis package.[m]

Results

Induction of anesthesia was safely performed, and maintenance of and recovery from anesthesia were uneventful in all gazelles. All gazelles were considered to be healthy on the basis of clinical examination and results of hematologic, biochemical, and parasitological analysis.

One adult gazelle was not laterally recumbent by 30 minutes after initial drug administration during the first anesthetic episode. After administration of an additional dose of S-ketamine (0.75 mg/kg IM), the gazelle became laterally recumbent within 3 minutes. On the basis of behavioral patterns, enlargement of the preorbital glands, and odiferous secretions from these glands, this gazelle was judged to be the dominant male of the group. Because of potential additional factors influencing the effect of the administered drugs, data for this gazelle were excluded from the statistical analysis for both treatments.

The induction of anesthesia was considered good when the overall grade was always good or acceptable. Quality of anesthesia induction was good or acceptable in all gazelles, except for 2 gazelles receiving the S-ketamine treatment, for which it was poor (**Table 1**). The body weight (mean ± SD,12 ± 0.3 kg) and age (6 and 8 months) of those 2 gazelles were noticeably lower than values for the remainder of the group (mean body weight, 19 ± 2.6 kg; mean age, 30 ± 13 months).

In 30 of the 40 anesthetic episodes, the gazelles were calm during the preinduction period. Preinduction stress of the gazelles did not appear to be more prevalent prior to the second anesthetic episode, compared with that observed prior to the first anesthetic episode. No specific excitation behaviors were consistently evident before both anesthetic inductions. For the 2 gazelles with poor or inadequate quality of anesthetic induction, preinduction stress status was assessed as calm in 1 gazelle and nervous in the other. Mean ± SD assessment of the quality of induction by means of the visual analogue scale was similar for both treatments (racemic ketamine, 9.6 ± 0.3; S-ketamine, 9.2 ± 0.5).

The first signs of drug effect observed for both treatments were ataxia and lowering of the head. These signs were detected in the racemic ketamine and S-ketamine treatments after a mean of 2.7 minutes (range, 2.0 to 4.0 minutes) and 2.0 minutes (range, 2.0 to 2.7 minutes), respectively. These results differed significantly ($P = 0.038$). No significant differences were detected between treatments for any

Table 1—Induction quality, degree of sedation during maintenance of anesthesia, and quality of recovery from anesthesia* in 20 gazelles (10 Rheem gazelles [*Gazella subgutturosa marica*] and 10 Subgutturosa gazelles [*Gazella subgutturosa subgutturosa*]) anesthetized by IM administration of a combination of medetomidine (80 µg/kg) and racemic ketamine (5 mg/kg) or S-ketamine (3 mg/kg).

	Induction quality				Degree of sedation				Recovery quality			
Treatment	Good	Acceptable	Poor	Inadequate	Light anesthesia	Deep sedation	Light sedation	No effect	Good	Acceptable	Poor	Inadequate
MRK	18	2	0	0	9	8	3	0	13	4	3	0
MSK	18	0	2	0	10	6	4	0	17	3	0	0

A combination of medetomidine and 1 form of ketamine was administered IM to each gazelle; after a washout period of 4 days, each gazelle received the other anesthetic treatment.

*Represents the first 30 minutes after administration of atipamezole (0.4 mg/kg, IM).

MRK = Medetomidine and racemic ketamine. MSK = Medetomidine and S-ketamine.

of the times recorded during induction (ie, time from injection until first signs of effect, time from injection until lateral recumbency, and total induction time), maintenance of anesthesia (time from administration of anesthetic agents until administration of the antagonist), or recovery (time from administration of the antagonist until first signs of recovery and time from administration of the antagonist until sternal recumbency; **Table 2**).

The degree of sedation achieved was similarly distributed for both treatments (Table 1). Most of the gazelles were in a plane of light anesthesia or deep sedation. The degree of sedation as assessed by means of the visual analogue scale was similar for both treatments and did not change significantly over time.

Results for cardiorespiratory variables as well as blood pressures, rectal temperature, and Spo_2 did not differ significantly between treatments (**Table 3**). Respiratory rate progressively decreased over time, and at 25 minutes and thereafter, it was significantly lower than at the beginning of maintenance of anesthesia for both treatments. Rectal temperature significantly decreased over time for both treatments. The Spo_2 improved significantly 15 minutes after administration of the anesthetic agents.

Results for pH and arterial blood gases were not significantly different between treatments (**Table 4**). None of the gazelles were hypoxemic (Pao_2 < 60 mm Hg) or had evidence of acid-base alterations.

The first sign of recovery from anesthesia after administration of the antagonist in all gazelles for both treatments was swallowing. Recovery from anesthesia was considered adequate when the overall grade always was good or acceptable. Recovery from anesthesia was good or acceptable in all gazelles receiving both treatments, except for 3 gazelles given the racemic ketamine treatment, for which a grade of poor was assigned during their first anesthetic episode. The body weight of those 3 gazelles (mean ± SD, 22 ± 1.3 kg) was higher than that for the remainder of the group (mean, 18 ± 1.5 kg), and they were between 31 and 43 months of age. Values for the visual analogue scale increased significantly at 20, 25, and 30 minutes after recovery from anesthesia for the racemic ketamine treatment (scores of 8.0, 8.0, and 7.9 cm, respectively), compared with values for the S-ketamine treatment (scores of 9.4, 9.8, and 9.8 cm, respectively).

Recovery was also evaluated at 1, 6, and 12 to 24 hours after administration of the antagonist; there were no significant differences between treatments at those time points. All gazelles had a recovery grade of good at 1, 6, and 12 to 24 hours, except for 1 gazelle (a 20-month-old gazelle that weighed 18.4 kg) receiving the racemic ketamine treatment (first anesthetic episode) that had a grade of poor at 6 hours.

No differences between subspecies of gazelles were detected for any of the variables evaluated.

Eating, urinating, and defecating were detected during the first 30 minutes of recovery from anesthesia

Table 2—Median (interquartile range [25th to 75th percentiles]) time after IM administration of anesthetic agents (induction) and atipamezole* (recovery) until various endpoints in 20 gazelles anesthetized by administration of a combination of medetomidine and racemic ketamine or S-ketamine.

	Induction			Recovery		
Treatment	**Induct-first (min)**	**Lateral (min)**	**Induct-total (min)**	**Maintenance (min)**	**Recover-first (min)**	**Recover-sternal (min)**
MRK	2.7 (2.0–4.0)[a]	5.7(5.0–8.0)	8.5 (6.5–11.5)	47.0 (44.5–53.0)	2.5 (2.2–5.7)	6.7 (4.5–9.0)
MSK	2.0 (2.0–2.7)[b]	5.5 (4.0–7.7)	8.0 (6.5–9.5)	46.0 (44.0–50.0)	3.5 (2.5–4.5)	6.0 (4.5–8.0)

*Administered IM at a dosage of 0.4 mg/kg.
[a,b]Values with different superscript letters differ significantly ($P = 0.038$).
Induct-first = Time from anesthetic administration until first signs of anesthesia. Induct-total = Total induction time. Lateral = Time from anesthetic administration until lateral recumbency. Maintenance = Time from anesthetic administration until administration of the antagonist. Recover-first = Time from administration of the antagonist until first signs of recovery from anesthesia. Recover-sternal = Time from administration of the antagonist until sternal recumbency.
See Table 1 for remainder of key.

Table 3—Median (interquartile range [25th to 75th percentile) HR, RR, rectal temperature, SAP, DAP, and Spo_2 for 20 gazelles anesthetized by IM administration of a combination of medetomidine and racemic ketamine or S-ketamine.

		Time during maintenance of anesthesia (min)*						
Variable	**Treatment**	**0**	**5**	**10**	**15**	**20**	**25**	**30**
HR (beats/min)	MRK	44 (40–48)	46 (40–52)	46 (40–48)	48 (40–52)	48 (42–52)	48 (41–49)	44 (40–48)
	MSK	44 (40–50)	46 (40–50)	47 (44–52)	46 (44–48)	48 (44–48)	48 (44–48)	48 (44–50)
RR (breaths/min)	MRK	20 (16–26)[a]	18 (16–26)[a,b]	20 (14–28)[a,b]	20 (12–24)[a,b]	20 (14–24)[a,b]	18 (16–22)[b]	17 (16–24)[b]
	MSK	24 (16–30)[a]	20 (14–30)[a,b]	20 (12–30)[a,b]	18 (14–26)[a,b]	18 (14–24)[a,b]	14 (12–24)[b]	16 (12–24)[b]
Rectal temperature (°C)	MRK	38.7 (38.4–39.3)[a]	38.7 (38.4–39.3)[a]	38.5 (38.2–39.0)[b]	38.3 (37.9–38.8)[c]	38.1 (37.9–38.6)[d]	38.0 (37.9–38.7)[d,e]	38.1 (37.7–38.5)[e]
	MSK	39.1 (38.7–39.4)[a]	38.6 (38.3–39.2)[b]	38.7 (38.3–38.9)[c]	38.5 (38.1–38.8)[d]	38.1 (37.7–38.6)[e]	38.0 (37.7–38.5)[e]	37.8 (37.5–38.4)[f]
Spo_2 (%)	MRK	87 (84–91)[a]	86 (85–87)[a]	86 (85–88)[a]	88 (85–89)[a,b]	88 (87–89)[a,b]	89 (87–91)[b]	89 (89–91)[b]
	MSK	87 (82–90)[a]	87 (85–89)[a]	88 (86–90)[a]	90 (87–93)[a,b]	89 (89–92)[a,b]	91 (89–92)[b]	91 (90–92)[b]
SAP (mm Hg)	MRK	115 (107–119)	102 (85–117)	112 (102–118)	105 (81–115)	100 (83–116)	104 (90–116)	103 (88–108)
	MSK	100 (94–104)	101 (100–104)	101 (83–104)	88 (78–109)	101 (86–112)	97 (88–100)	96 (83–100)
DAP (mm Hg)	MRK	56 (53–59)	59 (56–67)	57 (51–67)	60 (54–64)	53 (48–56)	52 (50–56)	52 (49–57)
	MSK	53 (47–67)	52 (44–55)	51 (43–57)	54 (43–59)	54 (50–57)	51 (42–58)	54 (47–56)

Values did not differ significantly ($P \geq 0.05$) between treatments at any time point.
*The time at which each gazelle could be safely approached was designated as the onset of anesthesia (time 0).
[a–f]Within a row, values with different superscript letters differ significantly ($P < 0.05$).
See Table 1 for remainder of key.

Table 4—Mean ± SD results of arterial blood gas analysis of samples obtained from gazelles anesthetized by IM administration of a combination of medetomidine and racemic ketamine or S-ketamine.

Treatment	pH	Pco_2 (mm Hg)	Po_2 (mm Hg)	Total CO_2 (mmol/L)	HCO_3^- (mmol/L)	Base excess (mmol/L)	Spo_2 (%)	Lactate (mmol/L)
MRK	7.39 ± 0.02	50.7 ± 2.4	64 ± 4	32 ± 2	30.8 ± 2.1	5 ± 2	91 ± 2	0.41 ± 0.12
MSK	7.39 ± 0.03	49.6 ± 2.8	64 ± 3	32 ± 2	30.6 ± 2.1	6 ± 2	91 ± 3	0.36 ± 0.07

See Table 1 for remainder of key.

in 6, 9, and 5 gazelles, respectively, for both treatments. Within 1 hour after administration of the antagonist, eating, urinating, and defecating had been detected in all gazelles.

Discussion

Analysis of the results of the study reported here revealed that administration of a combination of medetomidine and S-ketamine at 60% of the dose of racemic ketamine can achieve a degree of anesthesia similar to that for the combination of medetomidine and racemic ketamine. No gazelles had a poor or inadequate recovery from anesthesia after administration of S-ketamine, whereas 3 gazelles had a poor recovery after administration of racemic ketamine. On the other hand, quality of anesthesia induction with S-ketamine was poor in 2 gazelles, and 1 required administration of an additional dose of S-ketamine before it could be safely approached.

The dominant male of the group required administration of additional S-ketamine during the first anesthetic episode. After the gazelles were redistributed into smaller groups, the hierarchy disappeared; this male was anesthetized with only a single dose of racemic ketamine in the second anesthetic episode. Differences in pharmacokinetics and pharmacodynamics of administered drugs attributable to the hormonal milieu in animals have been recognized in gazelles. This hormonal milieu plays an important role in the environmental and interactive behavior of the animals in a colony. The influence of these interactions in controlled experiments needs to be further evaluated before conclusions can be made.[20] The authors cannot clarify whether the necessity of administering additional S-ketamine was attributable to hormonal influences or to the drug combination.

The 2 gazelles that had signs of excitement during anesthetic induction after administration of S-ketamine weighed less and were younger than the remainder of the gazelles in the group. Young animals have a higher body water content that results in a higher volume of distribution of water-soluble drugs such as ketamine.[21] Therefore, plasma concentrations of drugs may be reduced. If the water solubility of S-ketamine is higher than that of the racemic mixture, this may have led to the problems with induction of anesthesia in these 2 gazelles. These could probably be prevented by use of a slightly higher dosage in juveniles.

The doses of medetomidine and racemic ketamine used were selected on the basis of previous satisfactory and successful anesthetic episodes in these species at the Al Wabra Wildlife Preservation. Results of previous studies in rats,[22] mice,[23] cats,[11] dogs,[24] ponies,[9] horses,[12] and humans[7] suggest that the dose of S-ketamine should be reduced to approximately 50% to 70%, in comparison with the dose of racemic ketamine, to achieve the same effect.[25] Therefore, we chose 3 mg of S-ketamine/kg and 5 mg of racemic ketamine/kg for the present study in gazelles. The solution of S-ketamine had a concentration of 60 mg/mL. A solution with a higher concentration, such as that of 100 mg/mL for the racemic ketamine solution, would allow the administration of 40% less volume than when administering racemic ketamine. This would be advantageous when delivering a drug combination via dart (ie, the lower the volume in the dart syringe, the higher the probability of complete delivery of the drugs).[26]

The first signs observed after drug administration, ataxia and head lowering, appeared sooner with S-ketamine. However, time from drug administration to lateral recumbence as well as total time of induction of anesthesia was similar in both groups. Therefore, this difference was not considered clinically relevant. Induction of anesthesia in captive addax gazelles receiving medetomidine (57.4 ± 8.6 μg/kg) and racemic ketamine (1.22 ± 0.3 mg/kg) IM lasted for 2.9 ± 1.1 minutes.[14] However, those addax gazelles required supplemental ketamine (dose not described) to deepen the degree of sedation or to prolong the maintenance period (total maintenance time from drug administration until reversal, 48.6 ± 21.8 minutes). This combination was used at higher doses, which was appropriate for minor procedures such as health evaluation or transfer.

In contrast, the dose rates used in the present study would probably not be sufficient for major procedures. Most gazelles achieved a plane of only light anesthesia or deep sedation. Light sedation, and therefore an increased risk of voluntary muscle control during maintenance of anesthesia, was observed in 3 and 4 of the anesthetic episodes with racemic ketamine and S-ketamine, respectively. The combination of racemic ketamine with an α_2-adrenoreceptor agonist has been reported to be effective and safe and will permit handling and minor manipulations in adult Rheem gazelles (*G subgutturosa marica*) and mountain gazelles (*Gazella gazella*),[27] beira antelopes (*Dorcatragalus megalotis*),[c] addax antelopes (*Addax nasomaculatus*),[14] impalas (*Aepyceros malampus*),[n] and reindeer (*Rangifer tarandus*).[28] However, mild sedation that lasts up to 4 hours after administration of atipamezole for medetomidine reversal has been described in addax antelopes, impalas, and reindeer. Interestingly, we observed safe induction of adequate anesthesia, maintenance of anesthesia, and recovery from anesthesia in the gazelles of the present study without any abnormalities after administration of the antagonist.

Assessment of cardiopulmonary function in wild animals is problematic because of the difficulty in obtaining values in resting animals. With the drug regimens used in the study reported here, cardiopulmonary function was remarkably stable during maintenance of anesthesia, and no differences between the treatments were detected. Only RR significantly decreased over time for both treatments. This may have been attributable to the mild respiratory depression caused by the combination of ketamine and medetomidine.[4,8]

Reference values for pH and arterial blood gases are lacking for *G subgutturosa* animals; thus, values for measured variables were compared with the values described for sheep and goats.[1,29] The results revealed mild hypercapnia in both groups of gazelles, as expected from the administration of ketamine.[8]

Recovery from anesthesia was significantly better after administration of S-ketamine. Three gazelles had a grade of poor for recovery from anesthesia after administration of racemic ketamine. This has also been reported in cats,[9] ponies,[11] and humans.[30] It has been suggested that racemic ketamine is responsible for the psychomimetic effects. Differences in plasma protein binding that lead to differences in renal clearance may be expected for chiral compounds.[9] Therefore, different rates of renal clearance for norketamine enantiomers could explain the residual effects during recovery. In addition, studies[7,30–32] have revealed that the clearance of racemic ketamine is slower, compared with that of S-ketamine. At 24 hours after administration of the antagonist, all gazelles in the present study had completely recovered.

In the present study, S-ketamine, at a dose 60% that of the dose of racemic ketamine, was administered in combination with medetomidine; at the end of anesthesia, the antagonist atipamezole was administered as a medetomidine antagonist. The combination of medetomidine and S-ketamine resulted in inconsistent anesthetic induction, an analogous degree of sedation, and better recovery from anesthesia in gazelles with stable intra-anesthetic cardiopulmonary function.

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e. Ketasol, provided by Dr. E Graub AG, Bern, Switzerland.
f. Keta-S, provided by Dr. E Graub AG, Bern, Switzerland.
g. Littmann Stethoscopes, Saint Paul, Minn.
h. Vital Scan plus BP1600, Braun, Kronberg, Germany.
i. Digital Hiber thermometer, Actherm ACT 2000, Kreuzwertheim, Germany.
j. Nellcor Puritan Bennett Division, Pleasanton, Calif.
k. I-stat PCA, AxonLab, Baden, Switzerland.
l. Antisedan, provided by Dr. E Graub AG, Bern, Switzerland.
m. NCSS 2007, version 7.1.4, NCSS LLC, Kaysville, Utah.
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Appendix

Scoring system used to assess quality of induction of anesthesia, degree of sedation, and quality of recovery from anesthesia for 20 gazelles anesthetized by IM administration of a combination of medetomidine and racemic ketamine or S-ketamine.

Variable	Description
Quality of induction of anesthesia	
Good	1 or 2 smooth attempts to achieve sternal recumbency, quiet in sternal recumbency, and slight lateral ataxia resulting in sternal recumbency or a smooth transition to lateral recumbency
Acceptable	1 or 2 attempts to achieve sternal recumbency, slight ataxia (disorientated, smooth lateral or forward steps), or smooth but not direct achievement of sternal or lateral recumbency
Poor	Excitement during induction, abrupt achievement of sternal or lateral recumbency, or risk of injury to the animal or the handler
Inadequate	Additional administration of anesthetic required to induce recumbency, or fatal injury
Degree of sedation during maintenance of anesthesia	
Light anesthesia	Smooth, complete relaxation; tongue can be easily extracted, absence of anal and palpebral reflexes, and no involuntary tail movements
Deep sedation	Muscular rigidity and absence of anal reflex but slow palpebral reflex or voluntary tail movements
Light sedation	Spontaneous motor activity, struggling during manipulation, or presence of anal or palpebral reflexes
No effect	Additional administration of anesthetic required to induce recumbency, or risk of injury to the animal or to the handler
Quality of recovery from anesthesia during the first 30 minutes after administration of antagonist	
Good	Quiet, chewing, head is lifted to achieve sternal recumbency, slight imbalance in sternal recumbency, standing after 1 or 2 attempts, sufficient strength with slight ataxic movements, or quiet in sternal recumbency
Acceptable	Tense, imbalance in sternal recumbency, standing after several attempts, mild ataxia, and lack of coordination or remaining in sternal recumbency
Poor	Anxious, paddling, violent head movements, rolling, moderate ataxia, or jumping
Inadequate	Sedation required, remaining in lateral recumbency for 30 minutes without reaction, or fatal injury
Quality of recovery from anesthesia at 1, 6, and 12 to 24 hours after administration of antagonist	
Good	Quiet in sternal recumbency or standing with coordinated movements
Acceptable	Tense, sternal recumbency but too weak to stand when approached at < 6 hours
Poor	Anxious, sedated, and sternal recumbency but too weak to stand when approached at ≥ 6 hours
Inadequate	Unable to stand at ≥ 6 hours, sedation required, or fatal injury