Anesthesia induced by administration of xylazine hydrochloride alone or in combination with ketamine hydrochloride and reversal by administration of yohimbine hydrochloride in captive Axis deer (Axis axis)

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**Objective**—To determine the anesthetic dose and cardiopulmonary effects of xylazine hydrochloride when used alone or in combination with ketamine hydrochloride and evaluate the efficacy of yohimbine hydrochloride to reverse anesthetic effects in captive Axis deer.

**Animals**—35 adult (10 males and 25 females) Axis deer (Axis axis).

**Procedures**—All deer were anesthetized by IM administration of xylazine (3.5 mg/kg; experiment 1), a combination of ketamine and xylazine (1.25 and 1.5 mg/kg, respectively; experiment 2), or another combination of ketamine and xylazine (2.5 and 0.5 mg/kg, respectively; experiment 3). In addition, female deer were also anesthetized by IM administration of a third combination of ketamine and xylazine (1.5 and 1 mg/kg, respectively; experiment 4). Ten to 40 minutes after induction, anesthesia was reversed by IV administration of yohimbine (5, 8, or 10 mg).

**Results**—In male deer, experiment 3 yielded the most rapid induction of anesthesia. In females, experiment 4 yielded the best induction of anesthesia without adverse effects. All doses of yohimbine reversed anesthesia. Duration of anesthesia before administration of yohimbine had no effect on recovery time.

**Conclusions and Clinical Relevance**—A combination of ketamine and xylazine can be used to induce anesthesia in Axis deer. Furthermore, anesthetic effects can be reversed by administration of yohimbine. (Am J Vet Res 2007;68:20–24).

Axis deer (Axis axis) are abundantly distributed throughout India. Thus, they have been chosen for use in developing standardized assisted-reproductive techniques, such as semen collection by electroejaculation and subsequent transcervical artificial insemination, which can subsequently be used in other threatened species of deer. Because they are highly temperamental animals, Axis deer need to be anesthetized for these procedures. Several drugs, such as ketamine hydrochloride, xylazine hydrochloride, tiletamine, zolazepam, and medetomidine, have been routinely used to immobilize a number of wild animals. Of these, ketamine and xylazine are the most commonly used drugs.

Ketamine is a short-acting dissociative anesthetic that provides good sedation and moderate analgesic properties. However, when used as a sole anesthetic, ketamine yields poor muscle relaxation and violent recovery from anesthesia.1 Xylazine, an $\alpha_2$-adrenergic receptor agonist, is a potent sedative and muscle relaxant but has been associated with prolonged and unreliable induction of anesthesia, ruminal stasis, and bradycardia when used alone in some species of deer.2,3 However, a combination of ketamine and xylazine in an appropriate ratio reduces the dosage needed for induction but also provides faster and smoother induction, good muscle relaxation, and smoother recovery from anesthesia. A combination of ketamine-xylazine has been effectively used in cervids, such as the desert mule deer,4 white-tailed deer,5 and fallow deer.6 To our knowledge, no detailed study has been performed in Axis deer, although a few studies5,7,8 have reported the use of xylazine alone or a combination of medetomidine and ketamine for immobilizing Axis deer.

The study reported here was conducted to determine the effect of anesthesia induced in Axis deer by use of xylazine alone or xylazine in combination with ketamine and to study the effects on physiologic variables, such as respiration, heart rate, and rectal temperature. Furthermore, the effectiveness of various doses of yohimbine, an $\alpha_2$-adrenergic receptor antagonist, to reverse anesthetic effects in Axis deer was evaluated.

**Materials and Methods**

**Animals**—Thirty-five captive Axis deer (10 males and 25 females) were used in the study. Mean ± SEM body weight of the males was 53.5 ± 1.1 kg, and mean body weight of the females was 35.2 ± 1.1 kg.
0.7 kg. The deer were part of the collection at the Nehru Zoological Park, Hyderabad, India (78.3° east longitude and 17.2° north latitude), and were also used in an ongoing research program on assisted reproduction in wild animals in India; thus, they were subjected to electroejaculation for semen collection, artificial insemination, or other routine veterinary procedures during anesthesia.

For use in the study, deer were captured from the large fenced enclosures of the zoo by allowing the animals to enter small cages containing feed. Deer were then manually restrained and weighed before being moved to their pens. Throughout the study, adult males were housed separately in indoor pens (2.53 × 2.38 × 2.13 m) during the night and were allowed into an adjoining open exercise area (13.72 × 12.19 m) during the day. Female deer were housed together in 2 indoor pens during the night and allowed into 2 open exercise areas (each of which was 13.72 × 12.19 m) during the day.

All deer were exposed to natural photoperiod and were fed once daily (in the morning) with a commercial feed formulated for cattle that was supplemented with a mineral mixture. In addition, fresh green fodder was provided twice daily. The deer had unlimited access to clean drinking water throughout the day. Approval for research on the Axis deer was obtained from the Central Zoo Authority, Ministry of Environment and Forests, Government of India. All experiments were conducted in accordance with the guidelines of the Institutional Ethics Committee for Animal Experimentation.

Experimental design—The study consisted of several experiments and was conducted between March 2001 and December 2004. The 10 males and 25 females were used to determine the effective dose of xylazine or a combination of xylazine and ketamine and to evaluate cardiopulmonary effects, to determine the effective dose of yohimbine for reversal of anesthesia, and to evaluate the effects of duration of anesthesia on the ability of yohimbine to successfully reverse anesthesia and yield a smooth recovery.

Effective dose of anesthetics—Food was withheld overnight from deer preceding each anesthetic episode, but animals were allowed unlimited access to drinking water. Experiments were conducted between 8 and 11 AM. In the study, various anesthetic regimens were evaluated to determine the effective anesthetic dose or combination that would enable electroejaculation procedures for semen collection, artificial insemination, and other routine veterinary procedures in captive Axis deer. Deer in the collection were randomly selected for use in the anesthetic study.

Anesthetic regimens and the number of deer used in each experiment were determined. In experiment 1, the anesthetic used was determined on the basis of a study conducted in Axis deer, and the ketamine-xylazine combination for experiment 2 is commonly used to immobilize wild ungulates in India. The dosages and combinations were modified for experiments 3 and 4. Experiment 1 involved 5 male and 6 female deer. Each deer was anesthetized by administration of xylazine (3.5 mg/kg, IM). Experiment 2 involved 7 male and 8 female deer anesthetized by IM administration of a combination of xylazine (1.5 mg/kg) and ketamine (1.25 mg/kg). Experiment 3 involved 7 male and 6 female deer anesthetized by IM administration of a combination of xylazine (0.5 mg/kg) and ketamine (2.5 mg/kg). Experiment 4 involved only 8 female deer anesthetized by IM administration of a combination of xylazine (1.0 mg/kg) and ketamine (1.5 mg/kg).

For each administration, xylazine or a xylazine-ketamine combination was loaded into a 2-mL projectile dart and injected IM in the thigh muscle of each deer by use of a blowpipe. The 4 experiments were conducted consecutively. There was an interval of at least 15 days between subsequent immobilizations.

After each deer was injected, it was monitored for onset of anesthesia (ataxia or incoordination, progressive drooping of the head), and sternal and lateral recumbency, and the induction time (interval between injection and depth of anesthesia at which the deer did not respond to auditory or tactile stimuli) was determined. Once a deer attained a deep plane of anesthesia, it was placed on a stretcher, and its eyes were covered with a piece of cloth to prevent direct exposure to sunlight. An ophthalmic ointment was applied to the eyes to prevent corneal desiccation and infection. Physiologic variables, such as rectal temperature, heart rate, and respiration rate, were recorded once immediately after induction of anesthesia.

Effective dose of reversal agent—In preliminary experiments, reversal of anesthesia was monitored in randomly selected deer administered 3 doses of yohimbine (5, 8, or 10 mg). For the study reported here, the 7 males in experiment 3 and 8 females in experiment 4 were each anesthetized 3 times (once for each dose of yohimbine), with at least a 15-day interval between subsequent anesthetic episodes. Thirty minutes after induction of anesthesia, a dose of yohimbine was administered IV into a jugular vein by direct venipuncture. Recovery time was recorded as the interval that elapsed between yohimbine administration and when the deer was able to stand on its own and to walk when disturbed. Deer were monitored intermittently for 3 to 6 hours after recovery from anesthesia to detect signs of resedation.

Effect of duration of anesthesia on recovery—To determine the effect of the duration of anesthesia on recovery after administration of yohimbine, a separate experiment was conducted. A dose of 10 mg of yohimbine (equivalent to a dosage of 0.2 to 0.3 mg/kg) was used for this experiment on the basis of results of the aforementioned reversal experiment. All 10 males and some of the 25 females were used in the experiments. Randomly selected male and female deer were anesthetized with a combination of xylazine and ketamine (0.5 and 2.5 mg/kg, respectively; or 1.0 and 1.5 mg/kg, respectively). Anesthesia was reversed by IV injection of 10 mg of yohimbine at each of 3 time periods (10 to 20, 21 to 30, or 31 to 40 minutes) after induction of anesthesia, and recovery time was recorded. There was an interval of at least 15 days between subsequent anesthetic episodes.

Statistical analysis—Data were reported as mean ± SEM. An unpaired Student’s t-test was used to detect significant differences among anesthetic regimens and...
physiologic variables in males. The Mann-Whitney U test was used to detect significant differences among anesthetic regimens and physiologic variables in females. The Mann-Whitney U test was also used to determine the variation in recovery time for various doses of yohimbine administered to males and females. A nonparametric 1-way ANOVA (Kruskal-Wallis test) was used to detect significant differences in male and female deer after injection of xylazine administered at various time points during the anesthetic period.

**Results**

**Effective dose of anesthetics**—A total of 169 anesthetic episodes were induced in the 35 adult Axis deer by administration of xylazine alone or in combination with ketamine. No deaths were recorded for any of the anesthetic episodes.

Administration of xylazine alone to male and female deer did not result in anesthesia (Tables 1 and 2). In contrast, male and female deer were effectively anesthetized by administration of a combination of 1.5 mg of xylazine/kg and 1.25 mg of ketamine/kg. However, this combination was not suitable for Axis deer because the males did not yield ejaculates during electroejaculation and females had irregularities in respiration rate and heart rate.

Administration of a combination of 0.5 mg of xylazine/kg and 2.5 mg of ketamine/kg provided effective anesthesia (mean ± SEM induction time, 7.7 ± 0.7 minutes) for males, all of which responded to the electroejaculation procedure and yielded ejaculates that did not contain urine contamination. None of the males had signs of sudden recovery from anesthesia or other adverse effects during the electroejaculation procedure. In females, administration of a combination of 0.5 mg of xylazine/kg and 2.5 mg of ketamine/kg safely and effectively induced anesthesia, but effects such as excessive salivation, a short duration of immobilization (<20 minutes), and poor muscle relaxation were evident (Table 2).

Administration of a combination of 1.0 mg of xylazine/kg and 1.5 mg of ketamine/kg resulted in effective anesthesia in female deer. Mean ± SEM induction time was 6.8 ± 0.6 minutes, which was significantly less than the mean induction time for the combinations of xylazine and ketamine used in experiments 2 (P = 0.005; Mann-Whitney U test) and 3 (P = 0.002; Mann-Whitney U test). All females administered this combination of xylazine and ketamine (1.0 and 1.5 mg/kg, respectively) remained in a deep plane of anesthesia for up to 40 minutes.

Induction time of males and females receiving the same anesthetic regimen differed significantly (P = 0.01) in experiments 2 and 3. In addition, mean physiologic values in male deer immediately after induction of anesthesia were significantly higher for respiration rate (P = 0.05), heart rate (P = 0.01), and rectal temperature (P = 0.01) when anesthetized by administration of 0.5 mg of xylazine/kg and 2.5 mg of ketamine/kg, compared with values when anesthetized by administration of 1.5 mg of xylazine/kg and 1.25 mg of ketamine/kg (Table 1). Respiration rate and heart rate in females differed significantly (P = 0.01; Mann-Whitney U test) among the anesthetic regimens (Table 2). Rectal temperature in females did not differ significantly among the anesthetic regimens.

**Effective dose of reversal agent**—The shortest mean ± SEM recovery time in males (0.7 ± 0.1 minutes) and females (0.5 ± 0.1 minutes) was observed when 10 mg of yohimbine was administered. Recovery time in males after administration of 10 mg of yohimbine was significantly shorter, compared with that after administration of 5 mg (2.5 ± 0.1 minutes; P = 0.002) or 8 mg (2.0 ± 0.1 minutes; P = 0.001). In females, recovery time after administration of 10 mg of yohimbine was significantly (P = 0.002) shorter, compared with that after administration of 5 mg (2.7 ± 0.1 minutes) or 8 mg (1.8 ± 0.1 minutes). Overall, no difference in recovery time was observed between males and females when administered the same dose of yohimbine.

Table 1—Mean ± SEM values for anesthetic and physiologic variables in male Axis deer (Axis axis) after IM administration of xylazine alone or in combination with ketamine.

<table>
<thead>
<tr>
<th>Xylazine (mg/kg)</th>
<th>Ketamine (mg/kg)</th>
<th>No. of deer</th>
<th>Onset of anesthesia (min)</th>
<th>Induction time (min)</th>
<th>Respiration rate (breaths/min)</th>
<th>Heart rate (beats/min)</th>
<th>Rectal temperature (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5</td>
<td>0</td>
<td>5</td>
<td>4.3 ± 0.2</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>1.5</td>
<td>1.25</td>
<td>7</td>
<td>5.8 ± 0.7</td>
<td>11.8 ± 0.4</td>
<td>21.7 ± 1.1</td>
<td>31.0 ± 1.1</td>
<td>39.2 ± 0.2</td>
</tr>
<tr>
<td>0.5</td>
<td>2.5</td>
<td>NR</td>
<td>4.4 ± 0.3</td>
<td>7.7 ± 0.7*</td>
<td>26.3 ± 0.5</td>
<td>46.4 ± 2.2*</td>
<td>NR</td>
</tr>
</tbody>
</table>

*Within a column, value differs significantly (*P = 0.01; †P < 0.05; Student t test) from the value for the other xylazine-ketamine combination.
NR = Not recorded because the deer remained alert and unapproachable.

Table 2—Mean ± SEM values for anesthetic and physiologic variables in female Axis deer after IM administration of xylazine alone or in combination with ketamine.

<table>
<thead>
<tr>
<th>Xylazine (mg/kg)</th>
<th>Ketamine (mg/kg)</th>
<th>No. of deer</th>
<th>Onset of anesthesia (min)</th>
<th>Induction time (min)</th>
<th>Respiration rate (breaths/min)</th>
<th>Heart rate (beats/min)</th>
<th>Rectal temperature (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5</td>
<td>0</td>
<td>6</td>
<td>4.6 ± 0.3</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>1.5</td>
<td>1.25</td>
<td>6</td>
<td>4.9 ± 0.4</td>
<td>8.1 ± 0.4*</td>
<td>21.9 ± 0.9*</td>
<td>32.3 ± 1.1</td>
<td>38.0 ± 0.2</td>
</tr>
<tr>
<td>0.5</td>
<td>2.5</td>
<td>NR</td>
<td>5.1 ± 0.3</td>
<td>10.5 ± 0.4*</td>
<td>51.7 ± 1.2*</td>
<td>54.3 ± 5.5</td>
<td>38.7 ± 0.2</td>
</tr>
<tr>
<td>1.0</td>
<td>1.5</td>
<td>8</td>
<td>4.3 ± 0.4</td>
<td>6.8 ± 0.6*</td>
<td>33.5 ± 2.5*</td>
<td>47.6 ± 2.2*</td>
<td>39.2 ± 0.3</td>
</tr>
</tbody>
</table>

*Within a column, values with different superscript letters differ significantly (P < 0.05; Mann-Whitney U test).
See Table 1 for remainder of key.
Effect of duration of anesthesia on recovery—No significant differences in recovery time were observed in males ($X^2 = 0.223; P = 0.895$; Kruskal-Wallis test) or females ($X^2 = 1.1; P = 0.777$; Kruskal-Wallis test) administered yohimbine at various time points after induction of anesthesia (Table 3). Furthermore, no signs of resedation were detected for 3 to 6 hours after recovery, except for a slight amount of salivation in a few deer of both sexes.

### Discussion

To our knowledge, the study reported here is the first detailed study on anesthesia induced by a combination of ketamine and xylazine and antagonism by yohimbine in captive Axis deer. The ketamine-xylazine combinations used in the study were effective in anesthetizing Axis deer of either sex, despite the fact we used lower doses than those reported for other cervids. It provided rapid, safe, and reliable anesthesia for performing electroejaculation and semen collection, artificial insemination, and other short-term (11 to 40 minutes) procedures without evidence of adverse effects. Furthermore, the anesthetic effects were reversed successfully by administration of various doses of yohimbine.

Axis deer are nervous and excitable animals; therefore, chemical immobilization in this species has been associated with a high percentage of complications and fatalities. However, there were no complications or fatalities in the study reported here. Doses were identified that were most effective (0.5 mg of xylazine/kg and 2.5 mg of ketamine/kg in males and 1.0 mg of xylazine/kg and 1.5 mg of ketamine/kg in females). Other doses resulted in inadequate sedation or affected the reproductive procedures performed.

In another study, investigators described the use of xylazine at a dosage of 3.5 mg/kg for moderate to heavy sedation in free-ranging Axis deer. However, in our study, xylazine alone at that dosage was not sufficient to induce anesthesia in males or females, although initial signs of anesthesia and sternal recumbency were attained within 3 to 5 minutes after injection. The deer remained fully aware of their surroundings 10 to 20 minutes after drug administration and were easily excited and responded to the slightest disturbance. Contrast, 1.5 mg of xylazine/kg and 1.25 mg of ketamine/kg proved to be a good anesthetic combination. In fact, this combination is being used effectively in India for immobilizing numerous ungulates, including Axis deer, for blood collection, minor surgical interventions, and relocation of animals. However, in our study, the main reason for anesthetizing the male deer was for collection of semen by electroejaculation.

Although administration of 1.5 mg of xylazine/kg and 1.25 mg of ketamine/kg effectively and smoothly induced anesthesia with no apparent adverse effects on cardiopulmonary function, males anesthetized with this combination failed to ejaculate during electroejaculation procedures. The exact cause for this failure is not known but probably is the result of the high xylazine content, which may have caused complete muscular relaxation and thus affected penile erection. When we modified the combination for experiment 3 such that the dosage of xylazine was reduced to only 0.5 mg/kg and ketamine was increased to 2.5 mg/kg, male deer were anesthetized within 7 to 8 minutes, and these deer consistently responded to the electroejaculation procedure and yielded quality ejaculates. In the study reported here, other combinations of ketamine and xylazine in males were not evaluated because the dosages used for experiment 3 rapidly and smoothly induced anesthesia that enabled successful electroejaculation. A similar combination containing a higher ketamine-to-xylazine ratio had been used in other studies in which investigators successfully induced electroejaculation in various nondomestic ruminants, such as gazelles (Gazella dama mhorr, Gazella dorcas neglecta, and Gazella cuvieri). Elder’s deer (Cervus eldi thimin), and scimitar-horned oryx (Oryx dama mhorr).

In female deer, xylazine alone did not induce anesthesia, which was similar to the result observed in male deer. Administration of 1.5 mg of xylazine/kg and 1.25 mg of ketamine/kg effectively induced anesthesia within 5 to 7 minutes after injection, but effects on cardiopulmonary function were of serious concern, and the respiration and heart rates were irregular. When administered 0.5 mg of xylazine/kg and 2.5 mg of ketamine/kg, female deer had longer inductions, excessive salivation, poor muscle relaxation, and a shorter anesthetic period (< 20 minutes). This shorter anesthetic period was not convenient for handling animals to perform experimental procedures. Thus, analysis of the results of experiments 2 and 3 in females suggested that increased xylazine dosages were associated with decreased induction time and adverse physiologic effects, such as bradycardia and respiratory depression.

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**Table 3**—Mean ± SEM recovery time of anesthetized male and female Axis deer after IV administration of 10 mg of yohimbine at various time periods after induction of anesthesia.

<table>
<thead>
<tr>
<th>Duration of anesthesia (min)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of reversal attempts</td>
<td>Recovery time (min)</td>
<td>No. of reversal attempts</td>
</tr>
<tr>
<td>10 to 20</td>
<td>10</td>
<td>0.7 ± 0.1</td>
</tr>
<tr>
<td>21 to 30</td>
<td>18</td>
<td>0.6 ± 0.1</td>
</tr>
<tr>
<td>31 to 40</td>
<td>12</td>
<td>0.6 ± 0.1</td>
</tr>
</tbody>
</table>

*Anesthetized by IM administration of a combination of 0.5 mg of xylazine/kg and 2.5 mg of ketamine/kg. †Anesthetized by IM administration of a combination of 1.0 mg of xylazine/kg and 1.5 mg of ketamine/kg.
Considering the aforementioned results, we modified the combination of anesthetics (1 mg of xylazine/kg and 1.5 mg of ketamine/kg). This combination induced smoother, more rapid inductions, and the anesthetic effects and cardiopulmonary functions were acceptable and comparable to those reported in other cervids.1,16 as well as in Axis deer immobilized by administration of etorphine and acepromazine.10

Yohimbine, an α2-adrenergic receptor antagonist, has been used to reverse the effects of xylazine as well as ketamine-xylazine combinations.17 In most ruminants, the recommended dosage of yohimbine is 0.125 mg/kg, but higher dosages (up to 0.48 mg/kg) have been found to be more effective in reversing anesthesia induced by administration of ketamine-xylazine or xylazine alone in white-tailed deer.17 In the study reported here, yohimbine (0.1 to 0.3 mg/kg) was effective in reversing anesthesia induced by a combination of ketamine and xylazine in both sexes of captive Axis deer, and recovery from anesthesia was dependent on the dose of yohimbine administered. These results confirm observations of other studies.1,17 Recovery from anesthesia was extremely rapid, and a dose of 10 mg of yohimbine was sufficient for complete recovery of both sexes of Axis deer within 0.5 to 1 minute after IV injection. Such a rapid recovery may be necessary and advantageous to free-ranging deer, which must avoid predation in the wild. However, it was also observed that an additional increase in yohimbine dose (to 15 mg) did not improve the recovery (data not shown).

It has been suggested that early administration of an antagonist does not help animals to recover from the residual effects of ketamine, and an anesthesia duration of approximately 30 minutes is necessary to metabolize ketamine residues.18 In contrast to this finding, we observed in the study reported here that the effect of yohimbine was independent of the duration of anesthesia in male and female deer and that anesthesia could be reversed as early as 10 minutes after injection of ketamine.

In the study reported here, administration of a combination of xylazine (0.5 mg/kg) and ketamine (2.5 mg/kg) to male Axis deer induced safe, reliable, and effective anesthesia that enabled electroejaculation for semen collection. Female deer could be handled safely up to 40 minutes after injection of a combination of 1.0 mg of xylazine/kg and 1.5 mg of ketamine/kg. Anesthetic effects were reversed in a dose-dependent manner within 2.5 minutes after IV injection of 5 to 10 mg of yohimbine. Further, duration of anesthesia had no impact on recovery after administration of yohimbine.

References


b. Snam Vijay, Snam Feeds, Hyderabad, India.
c. Agrimin, Glaxo India Ltd, Mumbai, India.
d. Ililum Xylazil, 100 mg/mL, Troy Laboratories, Smithfield, NSW, Australia.
e. Ketamine, 100 mg/mL, Troy Laboratories, Smithfield, NSW, Australia.