Median effective dose of propofol required for induction of anesthesia in goats

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Objective—To determine the median effective dose (ED₅₀) of propofol required for induction of anesthesia in goats and the frequency of myoclonic activity and apnea associated with propofol administration.

Design—Clinical trial.

Animals—28 healthy mature goats.

Procedure—ED₅₀ was determined by use of the up-and-down method. The first goat was given 4 mg of propofol/kg (1.8 mg/lb) of body weight, IV. Dose was increased by 25% for the next goat if endotracheal intubation was not possible and decreased by 20% if it was. For each subsequent goat, dose was determined on the basis of response of the previous goat. The ED₅₀ was calculated by use of probit analysis. Induction time, frequency and duration of apnea, frequency of myoclonus, and other adverse effects were recorded.

Results—ED₅₀ was determined to be 5.1 mg/kg (2.3 mg/lb). Mean (± SD) induction time was 23.2 ± 4.7 seconds. Apnea was observed in 27 of 28 goats; mean (± SD) duration of apnea was 72.9 ± 38.3 seconds. Dose did not correlate with duration of apnea.

Myoclonic activity was observed in 16 of 28 goats; frequency of myoclonus was not associated with dose. Cyanosis, regurgitation, and signs of pain during injection were not observed.

Clinical Implications—Administration of propofol at 5.1 mg/kg (2.3 mg/lb), IV, should permit endotracheal intubation in half of unpremedicated, healthy, mature goats. Myoclonus and apnea were associated with propofol administration. (J Am Vet Med Assoc 1997;211:86-88)

Propofol has been used as an anesthetic agent in various domestic species. It is a nonbarbiturate agent characterized by rapid onset of effects and short duration of action. Total body clearance of propofol is rapid, even exceeding hepatic blood flow, which makes propofol a suitable agent for anesthetic maintenance.

Use of propofol as an induction agent in goats has been reported, but that study was mainly concerned with the pharmacokinetics of propofol, and only a limited number of goats and a single dose of propofol (4 mg/kg [1.8 mg/lb] of body weight) were used. The median effective dose (ED₅₀) of propofol required to induce anesthesia in goats has not been determined.

The primary objective of the study reported here was to determine the ED₅₀ of propofol required to induce anesthesia in unpremedicated goats. In addition, we wanted to determine induction time, frequency and duration of apnea, frequency of myoclonic activity, and other adverse effects.

Materials and Methods

Goats—The study was approved by the University of Florida's Institutional Animal Care and Use Committee. Twenty-eight mature mixed-breed female goats with mean body weight (± SD) of 32.5 ± 6.0 kg (71.5 ± 13.2 lb) were used in the study. Goats were preconditioned and kept in the animal facility for 1 week prior to the study. They were determined to be healthy on the basis of results of physical examination and CBC. Food was withheld for 24 hours and water was withheld for 12 hours before the study. Goats were weighed immediately before the study.

Goats did not receive any preanesthetic medication. The dorsal surface of the forelimb was clipped and scrubbed, and a 20-gauge, 2-in, over-the-needle catheter* was placed percutaneously into the cephalic vein. An infusion cap was attached to the catheter hub. The catheter was taped in place and flushed with heparinized saline (0.9% NaCl) solution. Goats were left undisturbed for 15 minutes prior to administration of propofol.

Propofol administration—An emulsion of 1% propofol® was administered as an intravenous bolus at a rate of 1 ml/sec, and 3 ml of heparinized saline solution was administered immediately afterward. Goats were minimally restrained during propofol administration. Endotracheal intubation was attempted 30 seconds after injection. Intubation was performed with goats in sternal recumbency and with an assistant opening the mouth and pulling the tongue rostrally. If the goat swallowed, tried to retract its tongue, closed its mouth, or moved its head and endotracheal intubation could be performed, response to that particular dose was considered negative. If the goat did not swallow, try to retract its tongue, close its mouth, or move its head and endotracheal intubation could be performed, response to that particular dose was considered positive. To determine the ED₅₀ of propofol, the up-and-down method was used. The first goat was given propofol at a dose of 4 mg/kg (1.8 mg/lb). The dose for the next goat was increased by 25% if there was a negative response or decreased by 20% if there was a positive response. The calculated doses were, thus, evenly distributed on a logarithmic scale. The dose for each goat was selected on the basis of response of the previous goat.

Induction time (time from injection to time the goat assumed sternal recumbency) and duration of apnea after induction were recorded with a stopwatch. Apnea was defined as a lack of breathing for > 20 seconds after injection of propofol. Signs of pain (eg, vocalization, limb withdrawal, and agitation) during administration of propofol were recorded, as were signs of myoclonic activity, regurgitation, and cyanosis. The tongue and oral mucous membranes were observed for cyanosis. Detection of ruminal material in the oral cavity was considered indicative of regurgitation.

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Analysis of data—The ED₉₀ of propofol was calculated by use of probit analysis of the number of animals that had positive or negative responses at each dose. Pearson's and Spearman's rank correlation coefficients were used to examine relationships among induction time, duration of apnea, and dose of propofol. Logistic regression was used to determine whether development of myoclonus was associated with dose. Calculations were performed by use of a statistical package. For all tests, a value of P < 0.05 was considered significant.

Results
Doses of propofol used in the study were 3.2, 4.0, 5.0, 6.25, and 7.8 mg/kg (1.45, 1.8, 2.27, 2.8, and 3.5 mg/lb), with 2, 7, 10, 7, and 2 goats, respectively, receiving propofol at each dose. There were 2 negative responses at a dose of 3.2 mg/kg, 2 negative and 5 positive responses at a dose of 4.0 mg/kg, 5 positive and 5 negative responses at a dose of 5.0 mg/kg, 5 positive and 2 negative responses at a dose of 6.25 mg/kg, and 2 positive responses at a dose of 7.8 mg/kg. The ED₉₀ was determined to be 5.1 mg/kg (2.3 mg/lb). Mean (± SD) induction time was 23.3 ± 4.7 seconds. We did not detect a significant correlation between dose and induction time. Apnea was observed in 27 of 28 (96%) goats. Mean duration of apnea was 72.9 ± 38.3 seconds. When data from goats that had positive responses (ie, goats in which endotracheal intubation was successful) were analyzed, dose was not correlated with duration of apnea. Myoclonic activity involving the face or limbs was observed in 16 of 28 (57%) goats. Percentages of goats that developed myoclonus at doses of 3.2, 4.0, 5.0, 6.25, and 7.8 mg/kg were 50, 57, 40, 43, and 0%, respectively. Frequency of myoclonus was independent of dose. Signs of pain were not detected at the time of injection. Cyanosis and regurgitation were not observed in any of the goats during or after induction.

Discussion
In this study, ED₉₀ of propofol for induction of anesthesia in goats was 5.1 mg/kg (2.3 mg/lb). This dose was higher than the dose (4 mg/kg [1.8 mg/lb]) previously reported in a study of 5 goats. The difference may be related to rate of administration of propofol; however, rate of administration in the previous study was not specified. The difference may also be related to the criteria used to determine whether the response was satisfactory, as well as to individual differences in assessment of response. Behavior of goats in this study, which was typical of goats that were not used to constant human handling, may have played a role in the difference. Animals with higher sympathetic tone appear to require higher doses of anesthetic agents. The dose reported here should be used with caution if docile or pet goats are anesthetized with propofol.

At the rate of administration in this study (1 ml/sec), mean administration time was 17.0 ± 5.6 seconds and mean induction time was 23.2 ± 4.7 seconds. It appears that rapid control of the airway can be accomplished at this rate of administration. Rapid endotracheal intubation minimizes the danger associated with regurgitation during anesthetic induction in goats, and none of the goats in this study regurgitated during anesthetic induction.

Goats were not given a sedative before induction of anesthesia, because induction of, and recovery from, anesthesia is generally smooth in goats, even without premedication. However, in this study, propofol administration resulted in myoclonic activity in 16 of 28 (57%) goats. Myoclonic activity ranged from twitching of the facial muscles to involuntary movement of the legs during the induction process. Frequency of myoclonus was not associated with dosage; however, neither of the 2 goats given propofol at a dosage of 7.8 mg/kg (3.5 mg/lb) developed myoclonic activity. In a previous study, myoclonic activity or some form of excitement was observed most often in animals that did not receive preanesthetic medication, and the authors speculated that myoclonic activity was a manifestation of excitement related to a light plane of anesthesia. It was also suggested that myoclonic activity was related to a light plane of anesthesia in a study involving horses. In that study, paddling limb movements were observed following administration of propofol at doses of 2, 4, and 8 mg/kg (0.9, 1.8, and 3.6 mg/lb). Many horses were in a light plane of anesthesia, even at the highest dose. It appears that a critical blood concentration of propofol may be needed to prevent myoclonic activity, but the explanation for this myoclonic activity after administration of propofol remains unclear. Additional studies in goats are needed to determine whether premedication with a sedative or use of a higher dose of propofol will eliminate or minimize myoclonic activity.

Apnea has been reported as a possible adverse effect of propofol administration and was observed in 27 of 28 (96%) goats. Apnea observed in the present study was likely attributable to the effect of propofol in blunting the ventilatory response to an increase in inspired CO₂ and decreasing the sensitivity of the ventilatory response to CO₂. This high incidence of apnea may be attributed to the rapid rate of drug administration. Propofol depresses ventilation in a dose-dependent manner, and rapid administration of propofol can result in a higher plasma concentration within a short period. Use of a slow rate of administration and titration of the dose of propofol have been advocated to minimize apnea. However, in 1 study, it was found that the rate of administration did not affect the incidence of apnea in human beings. The rapid rate of administration used in this study was selected because we wanted to be able to control the airway immediately. Despite the high incidence of apnea, during the study, clinical signs of cyanosis were not detected in any of the goats. However, this does not eliminate the possibility of hemoglobin desaturation or hypoxemia, and if propofol is administered rapidly in goats, there should be provisions for assisting ventilation and supplying a high inspired oxygen concentration.

Results of this study suggest that propofol can be used to induce anesthesia in unpremedicated, healthy goats. A dose of 5.1 mg/kg (2.3 mg/lb), IV, given at a high rate of administration should permit endotracheal intubation in 50% of goats. Myoclonus and apnea were associated with propofol administration in goats. Thus, we recommend that additional doses of propofol be available so that anesthetic induction can be completed.
in goats that cannot be intubated after the initial dose and that ventilation be supported if apnea persists.

References


From My Armchair: W. W. Armistead

Professional pecking order

The pecking order of disciplines at most universities is illogical but, nonetheless, a fact of life. As a veterinarian, I have always been aware that, in the minds of most academicians, veterinary medicine is at least a notch below human medicine. There are other unwarranted discriminations. For example, agricultural engineers are considered less admirable than other engineers whose specialty designations (eg, electrical, civil, aeronautical) suggest that they are more highly specialized and, therefore, more sophisticated.

Scientific snobbery of this kind usually has its origin in a tendency to gauge the worth of a discipline by the perceived nobility of its subject—the notion that it is somehow more noble to study people than other animals, more commendable to study jet aircraft than farm tractors, or less of a challenge to ventilate a hog barn than a country club. Certainly, bovine physiology is no less complicated than human physiology, and the principles of surgery are the same whether they are applied to princes or poodles.

Every academic discipline merits respect, but respect is achieved only through understanding. Veterinary medicine’s prestige is highest on campuses where the veterinary colleges have abandoned their old castle-and-moot philosophy and sought interaction with other campus scientists and scholars. In academia, familiarity more often breeds respect than contempt.

W. W. Armistead