Journal of the American Association for Laboratory Animal Science
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Vol 45, No 6
November 2006
Pages 73-79

Comparison of Three Anesthetic Protocols for Intraduodenal Drug Administration Using Endoscopy in Rhesus Monkeys (*Macaca mulatta*)

Simon Authier,[1,2,*] Fernando Chaurand,[1] Margarita Legaspi,[1,2] Catherine Breault,[2] and Eric Troncy[2]

The purpose of this study was to evaluate 3 anesthetic protocols for intraduodenal drug administration by endoscopy in rhesus monkeys (*Macaca mulatta*). Anesthesia was induced using intramuscular ketamine and midazolam, isoflurane (inhalant gas), or intravenous propofol in male and female rhesus monkeys. A noninvasive dosing line was placed in the duodenum by use of endoscopy, and 50% dextrose (3 ml/kg) was administered. Blood pressure, heart rate, body temperature, and reflexes (corneal, palpebral, pharyngeal) and myorelaxation (mandibular reflex and reaction to limb manipulation) were evaluated every 5 min. To estimate intestinal absorption, glycemia was evaluated prior to dextrose administration and at 2, 5, 10, 15, 20, 30, 45, and 60 min after dosing. All 3 protocols resulted in successful induction of anesthesia. Recovery from isoflurane and propofol was significantly faster than from ketamine–midazolam. Duration of the recovery period after isoflurane was less variable than with propofol, but isoflurane produced greater hypothermia. Isoflurane and propofol resulted in predictable glucose absorption after intraduodenal dextrose administration, whereas ketamine–midazolam led to an inconsistent increase in glycemia.

Nonhuman primates typically are considered an acceptable model for preclinical bioavailability studies.[7] Preclinical pharmacokinetic and metabolism evaluations of drugs intended for oral administration in humans are often affected by gastric secretions, which may affect oral drug absorption and bioavailability.[17] The gastric pH of fasted cynomolgus monkeys was similar to that in fasted humans, whereas the pH profiles of these species differed after a solid meal.[9] Measurement of gastric acid secretions in fasted rhesus monkeys reveals that gastric pH in this species also is similar to that of humans.[9,16] Because development of an enteric coating for preclinical screening of new drugs is lengthy and expensive, endoscopic administration directly into the duodenum can be used to bypass the effects of gastric secretions. When solid formulations are evaluated, the size of the tablet or capsule modifies average transit time in the stomach,[5,7] thus complicating synchronization of blood collection for pharmacokinetic analysis with absorption of the test substance in the duodenum. In the absence of an enteric coating and to ensure an optimal pharmacokinetic blood collection schedule, administering solid formulations directly into the duodenum may provide an acceptable alternative. In addition, scientific data describing anesthetic recovery in rhesus monkeys are rare. The aim of this study was to compare recovery from anesthesia and intestinal absorption of a test substance after the use of 3 anesthetic protocols for intraduodenal drug administration using endoscopy.

Materials and Methods

Study subjects. All nonhuman primates used during this study were maintained in accordance with the *Guide for Care and Use of Laboratory Animals*[14] at LAB Research Inc (Laval, Quebec, Canada), which is accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care, International-accredited facility. All procedures were reviewed and approved by LAB Research's Institutional Animal Care and Use Committee before study initiation. The study population comprised 3- to 6-y-old male and female rhesus monkeys (*Macaca mulatta*; Covance Research Products, Alice, TX). Body weights ranged from 3.4 to 4.6 kg for female monkeys and from 3.1 to 3.4 kg for males. Health status evaluation before study initiation confirmed that the monkeys were negative for *Salmonella* spp., *Shigella* spp., *Yersinia* spp., *Cercopithecine herpesvirus 1* (B virus), and tuberculosis. Animals were pair-housed in stainless-steel squeeze-back cages (floor space, 1320 in^2, height, 34 in.), and had been housed in a laboratory environment for 5 mo before initiation of the study. Monkeys received 7 cookies of a standard certified commercial primate chow (Teklad Certified Global 25% Primate Diet 2055C, Harlan Teklad Animal Diet and Bedding, Madison, WI) twice daily and received enrichment including foraging opportunities, television, music, and organic fruits daily. Animals were fasted overnight (food only) prior to anesthesia for endoscopic administration. Municipal tap water purified by reverse osmosis was provided to the animals ad libitum. The environmental conditions in the animal room were controlled (100% fresh conditioned air; temperature, 21 ± 3 °C; humidity, 30% to 70%; 10 to 15 air changes hourly, 12:12-h light:dark cycle).

Study design. We randomly assigned each of 6 rhesus monkeys (3 male and 3 female) to 2 of the 3 anesthetic protocols, giving a sample size of 4 for each protocol. Randomization of male and female monkeys was done separately to maintain an equal-gender ratio. Premedication or drug antagonists were not included in the 3 protocols evaluated to minimize the potential for drug interactions in eventual pharmacokinetic

Received: 4 Jan 2006. Revision requested: 13 Apr 2006. Accepted: 15 May 2006.
[1]LAB Research Inc., Laval, Quebec, Canada; [2]Faculty of Veterinary Medicine, University of Montreal, St-Hyacinthe, Quebec, Canada.
[*]Corresponding author. Email: authiers@preclin.com

studies. Animals reacclimated for 48 h between the 2 protocols. Because of the nature of the procedure (endoscopy) to be performed, deep surgical anesthesia was not required, and the presence of neurologic reflexes (usually absent under surgical anesthesia) was considered acceptable. Anesthetic dosages were selected in light of experience with endoscopic administration in monkeys (a common procedure at our research facility), the results of pilot experiments (which also were used to estimate the smallest sample size needed to show significant difference), and supervision by a veterinary anesthetist (ET).

For blood glucose evaluation, an indwelling catheter was placed in the cephalic vein of each animal before induction of anesthesia. Another indwelling catheter was placed in the cephalic vein of the opposite arm for intravenous propofol administration, when applicable. Monkeys were placed on restraining apparatus similar to a hammock (Mobile restraint unit, Lomir Biomedical, Notre-Dame-de-l'Île-Perrot, Quebec, Canada) for most of the experiment. On each of at least 3 d prior to the study, animals had been acclimated to the restraining apparatus, which was used for isoflurane induction, intramuscular and intravenous injections, and blood collection.

The following protocols were used to induce light anesthesia for endoscopy. One protocol comprised midazolam (0.2 mg/kg) and ketamine (8 mg/kg) given intramuscularly in the thigh. In the second of the protocols, isoflurane at 3.0% to 4.0% with 2.0 l/min oxygen was administered through a Bain coaxial system (Moduflex, Dispomed, Joliette, Quebec, Canada) connected to a mask for induction, followed by orotracheal intubation and maintenance with 2% isoflurane with 1.0 l/min oxygen until dextrose administration. The anesthetic system was connected to an exhaust system (Dispomed) to avoid personnel exposure to isoflurane. Monkeys were exposed to isoflurane through a mask for 5 to 13 min before insertion of endotracheal tubes (rubber, cuffed Magill-type; internal diameter, 4 mm [male monkeys] or 3 mm [female monkeys]; Centre de Distribution Médecine Vétérinaire, St-Hyacinthe, Quebec, Canada). Isoflurane was stopped immediately after endoscopy, and animals were extubated as soon as the animal was able to swallow. For the third protocol, propofol (6 mg/kg) was given intravenously by slow (30 s) bolus. Half of the dose was given initially, with the remainder titrated to effect, and the level of anesthesia was evaluated visually and through neurologic reflexes. Throughout propofol administration, animals were closely monitored to ensure that spontaneous breathing was preserved.

Intraduodenal endoscopic administration. Monkeys were fasted overnight (approximately 16 h) prior to induction of anesthesia. Immediately after induction, a sterile eye lubricant was applied to prevent ocular desiccation. Monkeys were placed on a heating pad immediately after induction or intubation and remained there until their ambulatory status returned to normal. A protective mouth gag was used to keep the mouth open for endoscopy.

An endoscope (Olympus CV-100 processor, Olympus CLV-U20 light source, and Olympus GIF-100 gastroscope, Carsen Group, Markham, Ontario, Canada) with an insertion tube of 9.5 mm was used; sterile lubricant was used to facilitate introduction of the endoscope into the esophagus. The endoscopic procedure was started immediately after sufficient anesthesia was achieved, to minimize the duration of anesthesia and to ensure comparability of recovery periods. Once the lower esophageal sphincter was passed, the stomach was slightly inflated to allow visualization of the antrum. The tip of the endoscope was slid along the greater curvature and advanced into the antrum until it was immediately in front of the pylorus. The pylorus was kept in the center of the field of vision (Figure 1 A). A dosing line (polyvinyl chloride; dead volume, 0.4 ml) was introduced into the duodenum (Figure 1 B), and the endoscope was inserted into the proximal part of the duodenum (Figure 1 C). A bolus of 50% dextrose (3 ml/kg) was administered, followed by a saline flush of 0.8 ml (that is, twice the dead volume of the dosing line). The dosing line was visualized throughout the dosing procedure to ensure that it was properly placed and that no duodenal reflux occurred. Once the dosing was completed, the dosing line was removed and the stomach was gently deflated using a suction pump (Schuco-Vac model 5711-130, Centre de Distribution Médecine Vétérinaire) connected to the endoscope.

Glycemia. Glycemia was measured by use of a drop of blood collected through an indwelling catheter placed in a cephalic vein. Blood samples were taken after induction or intubation (before endoscopy) and at 2, 5, 10, 15, 20, 30, 45, and 60 min after dextrose administration. Blood samples were processed immediately for glucose concentration analysis (Accusoft Advantage glucometer, Roche Diagnostics Canada, Laval, QC, Canada).

Anesthesia monitoring. The following parameters were evaluated every 5 min after induction to quantify recovery associated with the various anesthesia protocols. Monitoring was started immediately at the onset of induction for all protocols. Systemic arterial pressures and heart rate were measured noninvasively by use of an oscillometric sphygmomanometer (Minipack 911, Pacetech, Tampa Bay, FL). A neonatal cuff (size 3) was placed over the proximal part of the arm between the shoulder and the elbow. Monkeys were placed in mobile restraint units throughout anesthetic recovery to minimize movements during blood pressure monitoring. Rectal temperature was monitored until it reached 38 °C. Palpebral reflex (medial and lateral), pharyngeal reflex, corneal reflex, masseter tone, and activity level were evaluated sequentially. The corneal reflex was evaluated with a drop of sterile saline to minimize the impact of repeated evaluation on the cornea. We also evaluated the reaction of the monkey to manipulation of a hindlimb or forelimb; we preferred this method of evaluating reaction to limb manipulation to others in an attempt to minimize stress for the monkeys. To assess this parameter, the evaluator lifted one of the monkey's limbs with one hand and let the limb fall into his/her other hand. The reaction of the monkey was given a score from 0 (no reaction) to 3 (monkey withdrew the limb promptly when manipulated). The same animal health technologist, who was blinded regarding anesthetic protocol, evaluated reaction to limb manipulations for all monkeys. The activity level was classified as normal, slightly decreased (monkey was able to stand but had slow reactions), moderately decreased (monkey was able to sit but unable to stand), or severely decreased (unconscious or recumbent).

Statistical analysis. The motivation for anesthetizing each animal with 2 different protocols was to reduce interindividual variability and facilitate comparisons of the results obtained for each protocol. Differences between anesthetic protocols were analyzed by use of 2-way analysis of variance for repeated measures. Time was treated as a within-subject factor and anesthetic protocol as a between-subjects factor. For cardiovascular parameters and rectal temperature, we obtained the baseline (control) value at the end of follow-up, because these parameters could not be followed during the pretreatment period. A posteriori comparisons were done with Dunnett tests. For categorical parameters (for example, presence or absence of neurologic reflexes or masseter tone), Fisher exact tests were used to compare rate of occurrence in each group at induction of anesthesia (time 0) and 10 min thereafter. The threshold for statistical significance was set at 0.05; results are presented as mean.

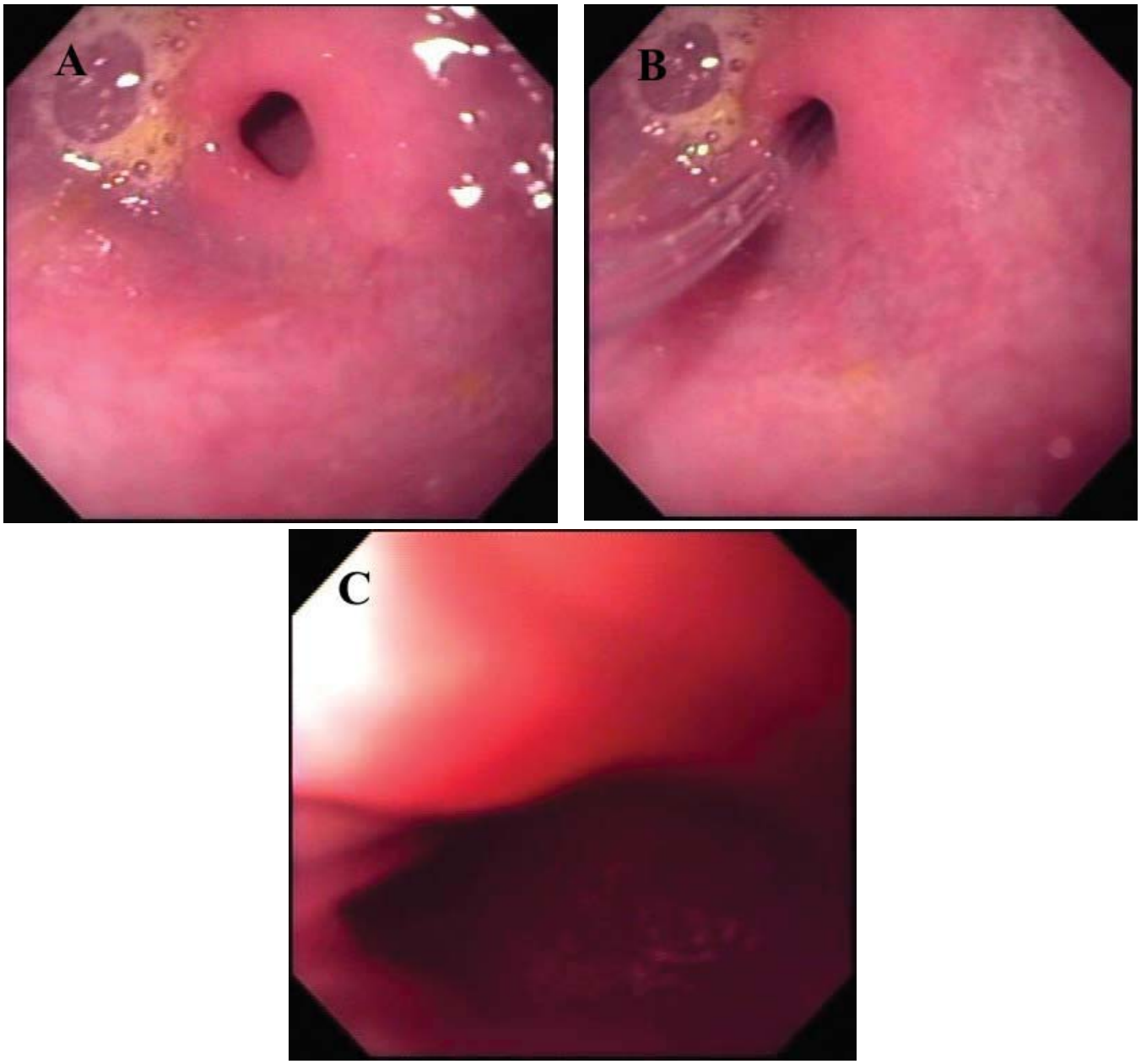

Figure 1. (A) View of the pylorus from the antrum. (B) Dosing line inserted in the pylorus. (C) Proximal duodenal mucosa with characteristic granular surface.

Results

Induction of anesthesia. The induction mask, when used, was well tolerated by all monkeys. All protocols resulted in uneventful and successful induction of anesthesia. No dysphoria or hyperactivity was noted during induction with the 3 protocols evaluated. Spontaneous respiration was maintained throughout the procedure for all monkeys. All monkeys required the complete dose of propofol to achieve an appropriate anesthetic level before initiation of the endoscopic administration. No additional dose of propofol was required to complete the endoscopic administration of dextrose for any animal in this group.

Endoscopy procedure. All 3 protocols allowed intraduodenal administration of 50% dextrose without complication. The average duration of the complete endoscopic dosing procedure (from first insertion into the mouth to complete withdrawal) was 5 min for isoflurane, 4 min for propofol, and 5 min for ketamine–midazolam.

Glycemia. Blood glucose reached maximum at an average of 37.5 min after dextrose administration for isoflurane compared with 37.7 min for propofol. Of the 4 monkeys anesthetized with ketamine–midazolam, 2 had no distinct increase in glycemia after dextrose administration, and the average increase in glucose concentration in these animals was not statistically significant. In the 2 monkeys showing an increase in blood glucose, maximum glycemia was reached at 10 and 15 min after dextrose administration. An average increase of 103% compared with the baseline (control) level was noted for isoflurane and of 134% for propofol (Table 1).

Cardiovascular parameters. Monitoring was initiated immediately after induction of anesthesia. Values recorded at the end of the monitoring period were considered to represent baseline because animals had recovered from anesthesia. Compared with the control value measured at 60 min postinduction, heart rate after induction with propofol was globally decreased ($P = 0.0004$), and a posteriori contrast was positive at 0 and 5 min after induction. Heart rate rapidly (approximately 20 min)

Table 1. Glycemia of rhesus monkeys

	Glucose (mmol/l)					
	Ketamine–midazolam		Isoflurane		Propofol	
	Baseline	Maximum	Baseline	Maximum	Baseline	Maximum
Male 1	5.4	5.1	na	na	4.1	7.4
Male 2	4.3	4.8	3.4	7.6	na	na
Male 3	na	na	3.0	5.4	3.0	5.6
Female 1	5.8	4.6	na	na	1.9	8.1
Female 2	5.4	7.6	3.5	4.6	na	na
Female 3	na	na	4.1	10.1	3.5	11.7
Average	5.2	5.5	3.2	6.5	3.0	7.0

na, not applicable.
Monkeys were randomized to 2 of the 3 protocols, thus yielding 4 animals in each group.

Table 2. Systemic arterial pressures

Time (min)	Average systemic arterial pressure (mm Hg)					
	Isoflurane		Propofol		Ketamine–midazolam	
	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
0	90.25	44.75	98.50	75.25	98.25	61.75
5	90.75	45.00	107.50	60.50	140.75	80.25
10	107.50	69.25	123.25	57.00	116.00	77.75
15	100.00	65.00	112.25	80.00	110.00	65.50
20	106.75	72.75	118.75	76.00	102.50	74.75
25	107.25	70.00	131.00	94.50	128.00	74.00
30	115.00	69.25	122.50	85.50	111.25	78.50
35	97.25	67.75	108.25	69.00	128.75	98.25
40	113.50	78.50	115.00	73.50	127.75	93.25
45	118.50	71.00	118.75	71.50	110.00	69.25
50	104.25	61.50	109.25	58.75	119.75	82.50
55	99.71	46.63	119.96	86.63	102.87	66.35
60	126.50	76.00	129.50	81.75	114.75	83.00

At all time points, the diastolic pressure with isoflurane was significantly lower than that for the two other protocols ($P < 0.05$ for all comparisons).

returned to baseline levels and was stable thereafter. Because of increased variability the apparent initial decrease in heart rate was not statistically significant in the 2 other anesthesia groups. There was no statistical difference in heart rate among the 3 groups. A statistically significant ($P = 0.02$) decrease in diastolic pressure was noted for isoflurane compared with ketamine–midazolam and propofol (Table 2).

Rectal temperature. For monkeys receiving isoflurane, rectal temperature could be recorded only after intubation, which explains the lower body temperature values recorded initially. Isoflurane created most prolonged decrease in body temperature, returning to an average of 38 °C at 70 min after isoflurane was stopped compared with 15 min after induction with propofol and 55 min with ketamine–diazepam (Figure 2). The observed difference in the delay before going back to a normal temperature was statistically significant ($P = 0.02$) between the propofol and isoflurane protocols. Among the 3 protocols, propofol created the least decrease in body temperature with a minimum of 37.95 °C at 40 min after induction (Figure 3) and was significantly different ($P < 0.04$ for all comparisons) from the 2 other protocols at 15 and 30 min after induction.

Neurologic reflexes. Palpebral, corneal, and pharyngeal reflexes were preserved at all times for monkeys receiving ketamine–midazolam. Palpebral and corneal reflexes were lost just prior to intubation until 10 min after isoflurane was stopped for the 4 monkeys in this group. For all monkeys anesthetized with isoflurane, pharyngeal reflex was absent from intubation until 15 min after isoflurane was stopped. Monkeys receiving propofol lost palpebral and corneal reflexes for variable periods (0 to 10 min); 1 monkey receiving propofol never lost the pharyngeal reflex. The other 3 monkeys in this group lost the pharyngeal reflex for 5 (1 monkey) and 10 min (2 monkeys) after induction. The loss of neurologic reflexes just after induction and at 10 min later was statistically significantly different ($P = 0.01$ for all comparisons) between the ketamine–midazolam and isoflurane groups; the propofol group did not differ from the 2 other groups. No difference in medial and lateral palpebral reflexes could be identified in any group.

Masseter tone. Masseter tone was lost for a period of 10 min in 1 of the 4 monkeys receiving ketamine–midazolam. All 4 monkeys in this group had decreased masseter tone for 5 to 30 min after injection. Masseter tone was absent throughout the anesthesia maintained with isoflurane and was absent or severely decreased for 10 (1 monkey) to 15 min (3 monkeys) after isoflurane was stopped. The masseter tone was absent or decreased from 5 (1 monkey) to 10 min (3 monkeys) after propofol induction. The loss of masseter tone just after induction and at 10 min later was statistically significantly different ($P = 0.045$ for all comparisons) between the ketamine–midazolam and isoflurane groups. The propofol group did not differ from the 2 other groups.

Reaction to limb manipulation, recovery, and ambulatory status. Reaction to limb manipulation was decreased or absent for 15 to 45 min after injection of ketamine–midazolam. Only 2

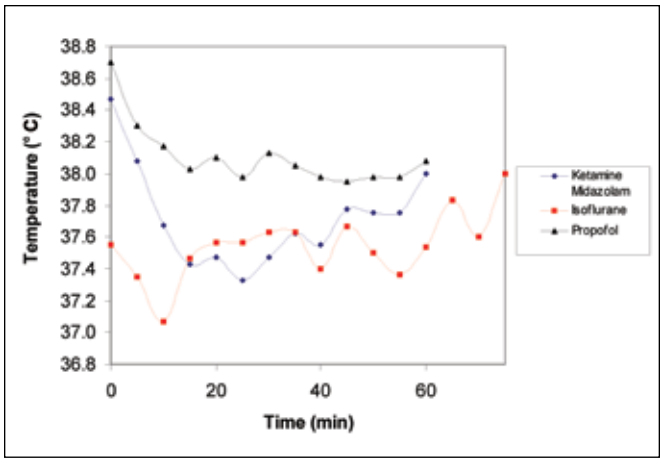

Figure 2. Average rectal temperature (° C) in rhesus monkeys during recovery from anesthesia induced with ketamine–midazolam, isoflurane and propofol. Among the 3 protocols, propofol caused the smallest decrease in body temperature; this protocol differed significantly from the other 2 protocols at 15 and 30 min after induction ($P < 0.04$ for all comparisons).

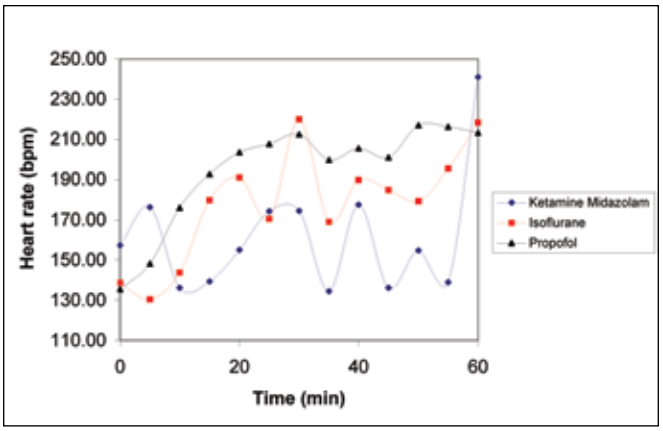

Figure 3. Average heart rate (bpm, beats/min) in rhesus monkeys during recovery from anesthesia induced with ketamine–midazolam, isoflurane, and propofol. Heart rate was decreased globally when anesthesia was induced with propofol ($P = 0.0004$).

of the 4 monkeys receiving ketamine–midazolam completely lost reaction to limb manipulation. Monkeys were recumbent for 15 (2 monkeys), 20 (1 monkey), and 30 min (1 monkey) after injection of ketamine–midazolam. Monkeys in this group had normal ambulatory status at 25 (1 monkey), 40 (1 monkey), and 50 min (2 monkeys) after induction. No reaction to limb manipulation was noted from intubation to termination of isoflurane anesthesia; monkeys had normal reaction to limb manipulation and ambulatory status at 15 (1 monkey) and 20 min (3 monkeys) after isoflurane was stopped. Monkeys were recumbent from 10 (2 monkeys) to 15 min (2 monkeys) after induction with propofol and regained normal ambulatory status at 15, 20, 25, and 30 min, respectively, after induction. The comparative analysis showed that duration of recumbency was marginally different ($P = 0.05$) between the ketamine–midazolam (20 ± 3.53 min) and propofol (12.5 ± 1.44 min) groups. The delay for ambulatory recovery was significantly different ($P = 0.01$ for both comparisons) between the ketamine–midazolam (41.25 ± 5.9 min) and both propofol (22.5 ± 3.23 min) and isoflurane (18.75 ± 1.25 min), with no difference between the last 2 groups. Consciousness returned faster with propofol, but full recovery appears to be faster after isoflurane. Only 1 monkey vomited during the recovery period; this animal had received ketamine–midazolam.

Discussion

Comparison of different anesthetic protocols in rhesus monkeys is useful not only for selection of an appropriate procedure for endoscopy but for a wide variety of noninvasive procedures. Anesthetic protocols that were evaluated in the current study are similar to protocols used with other species, including humans; therefore the findings may also be applicable to other species. All 3 anesthetic protocols evaluated were considered acceptable for induction of anesthesia of short duration. Administration routes selected for the different anesthetic protocols included 3 widely used routes of induction (inhalant gas, intravenous, and intramuscular).

Intramuscular administration of ketamine and midazolam resulted in safe but relatively long-lasting sedation that lasts longer than the recovery time after most general anesthesia protocol. As expected with its mechanism of action, ketamine did not abolish any neurologic reflex. Ketamine has no cardiovascular depressant effect, and in combination with midazolam resulted in relatively stable arterial pressure with variable and slightly reduced heart rate. These variations in heart rate could be attributable to the imperfect loss of consciousness as well as to the retained reaction to limb manipulation that we found in 2 of the 4 monkeys. The hypothermic effect noted with this protocol was compatible with the peripheral vasoconstriction that occurs in humans after induction with ketamine.[6] The relatively high baseline glycemia values seen with this protocol could potentially result from increased plasmatic catecholamine. Interestingly, a combination of ketamine and midazolam increased plasmatic epinephrine and norepinephrine 10 min after intravenous bolus injection in healthy human volunteers.[13] Due to the prolonged sedation it induced, we do not consider this protocol appropriate for intraduodenal endoscopic administration in rhesus monkeys. Nevertheless, this practical intramuscular induction protocol in combination with premedication, including an antiemetic agent, may be useful for other minimally invasive procedures. As complementary information, the preferred anesthetic protocol for minimally invasive procedures in our laboratory is intramuscular injection of ketamine and acepromazine without premedication. A cocktail of 1 ml acepromazine (10 mg/ml) mixed with 10 ml ketamine (100 mg/ml) is given at 0.05 ml/kg for manipulation and detailed physical examinations of aggressive monkeys; at 0.1 ml/kg for intradermal tuberculin injection, dental prophylaxis, and tattoo identification; and at 0.15 ml/kg for minor surgeries (for example, biopsies) and when intubation is needed. Midazolam was preferred to acepromazine in the current study to minimize the risk of increased pyloric tone, which interferes with duodenoscopy.[12]

The pharmacokinetics of propofol involves a 3-compartment linear model with rapid tissue redistribution, thus explaining its short duration of action.[10] Relatively wide interindividual pharmacokinetic and pharmacodynamic variability is reported to occur in humans.[2,11] The inconsistent retention of reflexes we noted in the current study suggests that a similar variability could be present in rhesus monkeys, but evaluation of a greater number of subjects and assessment of propofol pharmacokinetics in rhesus monkeys would be needed to confirm this hypothesis. Induction with propofol resulted in moderate and transient cardiovascular depression that mostly affected heart rate. Reported cardiovascular effects of propofol in other species include bradycardia, hypotension, and negative inotropism.[15] The presence of minimal cardiovascular effects is likely to be associated with stable renal function. These 2 factors are important to ensure validity of pharmacokinetic stud-

ies. Very short duration with minimal effects on body temperature and complete loss of consciousness (as reflected by the loss of neurological reflexes for 10 to 15 min and the absence of reaction to limb manipulation) are also favorable features of the use of this protocol for endoscopic administration. Propofol is metabolized by the liver via glucoronide conjugation mediated by cytochrome P450.[2] Drug interactions between propofol and test substances that are metabolized by this important metabolic pathway can be expected, increasing elimination time for both drugs. This interaction is a possible limitation to the use of this protocol for endoscopic administration of test substances.

With complete recovery of neurologic reflexes and ambulatory status within 20 min after isoflurane was stopped for all monkeys, this protocol had the shortest and most reproducible recovery. The decrease in arterial pressure associated with reflex tachycardia represents an important and well-known cardiovascular effect of isoflurane in other species.[4] Decreasing the level of anesthetic might minimize this effect. Depression of body temperature regulation centers combined with heat lost through airways via the Bain coaxial system likely explain the significant temperature decreases that we noted. In light of our results, the prolonged and more pronounced decrease in body temperature associated with isoflurane without premedication does not seem to prolong recovery time compared with that of the other protocols evaluated. A study of recovery after anesthesia with isoflurane that compares constant and variable body temperatures would be useful to assess the effect of hypothermia on recovery duration. Isoflurane is metabolized at 0.2% to 1.0% by the liver, mostly by cytochrome P450 CYP2E1.[3,8] We do not consider this slight metabolism of isoflurane to represent a disqualifying condition to using this protocol for endoscopic administration of test substances.

As mentioned previously, the monkeys used in the current study were acclimated to the laboratory environment for 5 mo and to the restraining apparatus (Mobile restraint unit, Lomir Biomedical) for the 3 d preceding the procedure. The specific design of this sling allowed us to place the monkeys in horizontal position, leading to more quiet and comfortable animals. These monkeys were well conditioned to work with technicians, a characteristic that may have facilitated mask induction. We consider that induction with isoflurane without premedication would be insufficient for monkeys restrained by hand or in a chair; aggressive or excited monkeys would not be good candidates for mask induction.

Potential occupational exposure of staff to halogenated anesthetic gases should be considered when using the isoflurane protocol. Conflicting evidence exists in the scientific literature about the effects of trace levels of anesthetic gases on the health and performance of operating room personnel. Genetic mutations, cancer, complications during pregnancy (for example, spontaneous abortion), hepatic and renal disease, immunologic effects, and psychomotor changes have been linked to exposure to trace gases. In most instances, definitive proof is lacking.[1] Any veterinary or laboratory facility using inhalant anesthetics (that is, halogenated hydrocarbons and nitrous oxide) should institute and maintain a control program for waste anesthetic gases, in light of the possibility that trace gases may adversely affect human health. Briefly, this control program includes establishing standard operating procedures for appropriate checkout of materials and equipment and routine maintenance for volatile anesthesia equipment (particularly regarding filling of vaporizers and verifying scavenging system efficacy), limiting the opening (rate) of flowmeters and vaporizers to their time of use on animals (to the level sufficient for the procedure, such as evaluated in the current study), using cuffed endotracheal tubes, eliminating (in so far as possible) residual gases through the scavenging system before disconnecting the patient, and using mask induction in well-ventilated rooms with nonrecirculating ventilation systems (such as the Bain coaxial system) or under a fume hood.

In conclusion, all 3 anesthesia protocols we tested are appropriate for induction of anesthesia for diagnostic endoscopic examinations. However, in our opinion, intramuscular ketamine–midazolam is contraindicated for endoscopic dosing because of its prolonged recovery time, which subsequently increases the postanesthetic care required by the monkeys. The choice between intravenous propofol and inhalant isoflurane will depend on available technology, the experience of personnel with each method, and potential drug–drug interactions. The quality of the induction, anesthesia, and recovery achieved with these 2 induction agents was comparable. Both agents appear to have a similar effect on duodenal absorption, but isoflurane causes more cardiovascular depression and body temperature alterations despite a trend to provide faster recovery.

Acknowledgments

We thank Guy Beauchamp (Faculty of Veterinary Medicine, University of Montreal) for assistance with statistical analysis; Jessica Hutta (LAB Research Inc) for critical reading of the manuscript; and animal health technologists Isabelle Gilbert, Caroline Charette, and Natacha Lemoine (LAB Research Inc) for providing exceptional care to the nonhuman primates used in this study.

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