Capnography-guided Endotracheal Intubation as an Alternative to Existing Intubation Methods in Rabbits

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Rabbits provide a unique challenge for routine endotracheal intubation in clinical practice because of various distinctive anatomic and physiologic features. Many previously proposed methods for endotracheal intubation in rabbits are limited by several factors, including the needs for expensive equipment and high levels of technical expertise. We evaluated capnography for its effectiveness in assisting endotracheal intubation in rabbits. New Zealand white rabbits were divided into 3 groups of 5 animals. In the first 2 groups, mainstream (nondiverting) or sidestream (diverting) capnography (MC and SC groups, respectively) was used; in the third group (LS group), a laryngoscope with a size 00 Miller blade was used to guide endotracheal tube placement. Anesthesia was induced through intramuscular administration of ketamine (10 mg/kg), medetomidine (0.1 mg/kg), and midazolam (1 mg/kg) mixed in the same syringe prior to administration. Intubation time was defined from the point of opening the jaws to the completion of the first capnogram after intubation. Intubation was accomplished successfully in all animals in both capnography groups, but 2 rabbits in the laryngoscopy group could not be intubated. Intubation time was compared among groups by using one-way ANOVA, and posthoc Bonferroni testing was applied to isolate significant differences between groups. The intubation time (mean $\pm$ 1 SD) was 46.4 ± 12.6 s in the MC group, 147.2 ± 44.2 s in the SC group, and 385.0 ± 114.1 s in the LS group, with intubation time significantly differing among all groups. In conclusion, both mainstream and sidestream capnography-guided endotracheal intubation techniques were more effective and efficient than conventional laryngoscope-guided endotracheal intubation in rabbits. Furthermore, mainstream capnography was preferred over sidestream capnography because mainstream capnography resulted in significantly shorter intubation times.

Abbreviations: EtCO₂, end-tidal carbon dioxide; LS, laryngoscopy; MC, mainstream capnography; SC, sidestream capnography

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General anesthesia is performed in both pet and laboratory rabbits for various medical and surgical procedures including dentistry, castration, ovariectomy, and experimental model surgery. Various CNS depressants, including injectable anesthetics, inhalant anesthetics, neuroleptics, and narcotic analgesics can be administered alone or in combination to induce or maintain general anesthesia. However, inhalant anesthetics have gained popularity as the mainstay for extended procedures in rabbits because they allow for a speedy recovery due to these drugs' exclusive pulmonary metabolism. During inhalation anesthesia, placing an endotracheal tube provides several useful safety features over using a face mask. Endotracheal intubation allows for more efficient ventilatory support, easier control of anesthetic depth, and improved scavenging of waste gases. In addition, endotracheal intubation provides complete protection against accidental inhalation of foreign materials, when general anesthesia obtunds or abolishes the swallowing reflex. However, several distinctive anatomic and physiologic features in rabbits can make intubation a challenging and arduous task. These features include a relatively small oropharyngeal cavity, a narrow laryngeal glottis, long incisors, and a thick fleshy tongue.

In addition, because rabbits are semiobligatory nasal breathers, the epiglottis is positioned dorsally over the soft palate, thus potentially further complicating endotracheal intubation.²² Furthermore, laryngospasm is frequently encountered during the endotracheal intubation of rabbits.

Previously evaluated methods to facilitate endotracheal intubation in rabbits include endoscopy-guided intubation,^{9,21,23} videoendoscopy-guided intubation,¹² blind intubation,^{1,6,13} retrograde intubation,³ direct laryngoscopy,^{15,16,18} capnography-guided intubation,¹⁰ nasotracheal intubation,¹⁹ and miniaturized light stylet-guided intubation.²⁰ Several workers also reported the use of a laryngeal mask airway as an alternate method for establishing a patent airway in rabbits.⁸ However, several limitations remain with the laryngeal mask method, including an incomplete airtight seal for waste-gas removal and restricted oral space for dental work, which is required frequently in rabbits.^{2,8,17} A modified laryngeal mask airway tube was reported to be superior in preventing air leakage and allowing for easier control of anesthetic depth,⁴ but the device is rather large, consequently precluding ideal conditions for dentistry. Successful use of fiber-optic or videoendoscopy to guide endotracheal intubation in rabbits has been described in the literature.^{9,12,21} However, many laboratories and veterinary practices do not have routine access to the necessary endoscopic equipment to make this intubation technique widely applicable.

Capnography-guided intubation in rabbits has been reported as an effective alternative to existing intubation methods.¹⁰

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Capnography is a noninvasive monitoring technique using an infrared absorption measurement system to record the change in the partial pressure of CO₂ within the breathing gases. This technology provides the graphic display of a waveform as a function to express the change in CO₂ pressure over time.^{5,11} Capnography is useful in determining the correct placement of an endotracheal tube by detecting CO₂ in exhaled gases. Because the presence of CO₂ is a simple criterion for confirming successful endotracheal intubation, capnography was shown to be an effective tool for accomplishing endotracheal intubation in rabbits.¹⁰ Despite its demonstrated effectiveness, however, capnography-guided endotracheal intubation in rabbits was not widely adopted within clinical or laboratory veterinary medicine previously because capnography was not routinely available in most laboratory and clinical settings. In contrast, many veterinarians and veterinary practices now routinely use capnography to monitor their anesthetized patients' ventilatory function. The adoption of capnography has increased as equipment prices have fallen and technologic advances have allowed capnography ventilatory monitoring to be incorporated into multiparameter patient monitors. Therefore, many practices now can perform capnography-guided intubation in rabbits without having to purchase a dedicated piece of monitoring equipment. Therefore, we felt that a renewed examination of capnography-guided endotracheal intubation in rabbits was clinically relevant.

Capnography is divided into 2 main types: sidestream (or diverting) and mainstream (or nondiverting).^{5,11} Sidestream capnography uses a suction pump and a long gas-sampling tube to pull a small amount of gas from the patient's airway at a sampling rate of 30 to 250 mL/min; the collected gas sample is analyzed within the equipment. A delay of several seconds between when a gas sample is initially collected and when it is analyzed exists because of the transit time necessary between the point of sampling and the sensor. Mainstream capnography uses a miniaturized sensor housed in the adaptor that is placed between the endotracheal tube and breathing circuits; consequently, no delay exists between the sampling and reading of the CO₂. Although an earlier study showed that sidestream capnography was a useful intubation method in rabbits, the use of mainstream capnography has not been evaluated in the intubation of domestic or laboratory species.¹⁰ In the current study, we hypothesized that mainstream capnography—because of its ability to sample, analyze, and display CO₂ concentrations in real time—would be advantageous over sidestream capnography in reducing intubation times in rabbits. In addition, we wanted to further investigate the utility of capnography-guided intubation in rabbits as compared with the conventional technique of laryngoscopy-guided endotracheal intubation in rabbits.

Materials and Methods

All experiments were performed according to requirements of the Seoul National University Institutional Laboratory Animal Research Committee regarding the use of animals for experimentation, with prior approval (110622-5) of the study design and experimental protocols.

Animals. Healthy New Zealand White rabbits (*Oryctolagus cuniculus*; $n = 15$; weight: mean, 3.8 kg; range, 2.6 to 5.1 kg; age: mean, 6.6 mo; range, 5 to 8 mo) were housed individually in the environmentally controlled and secured animal facility (temperature, 18 to 21 °C; humidity, 45% to 65%; 15 air changes hourly; ammonia concentration, less than 10 ppm; 12:12-h light:dark cycle; and noise level, less than 60 dB). All rabbits were reported to be SPF by the vendor (Orient Bio, Seongnam, Korea) and were known to be free of the following recognized pathogens:

Pasteurella multocida, *Pasteurella aeruginosa*, *Bordetella bronchiseptica*, *Salmonella* spp., *Treponema cuniculi*, cilia-associated respiratory bacillus, *Clostridium piliforme*, *Encephalitozoon cuniculi*, *Psoroptes cuniculi*, *Cheyletiella parasitivorax*, *Listrophorus gibbus*, *Passalurus ambiguus*, *Eimeria* spp., rotavirus, poxvirus, and calicivirus. All rabbits were fed a standard nutritionally complete diet formulated for rabbits (Purina laboratory rabbit diet, Cargill Agri Purina, Seongnam, Korea) with free access to water and, to avoid stress and behavioral changes, were acclimated to the laboratory setting for 1 wk prior to initiation of experimental work. Rabbits were divided into 3 groups ($n = 5$ per group): sidestream capnography (SC), mainstream capnography (MC), or laryngoscopy (LS). Each group was comprised 2 male and 3 female rabbits; average weight did not differ between groups. Clinical examination prior to anesthetic induction included heart rate, respiratory rate, rectal temperature, gut motility, mucous membrane color, capillary refill time, and palpation of external lymph nodes. In addition, a small volume of blood was obtained from a central auricular vein in nonsedated animals that had been placed in a rabbit restrainer. Blood samples were used to measure PCV, total protein, BUN, and blood glucose prior to anesthesia induction.

Anesthetic protocol. The rabbits were food-fasted for 1 to 2 h prior to anesthesia induction, but water was always available. Immediately after preanesthetic physical examination, anesthesia was induced through intramuscular injection of a combination of ketamine (10 mg/kg; Ketalar, Yuhan, Seoul, Korea), medetomidine (0.1 mg/kg; Dormitor, Zoetis Korea, Seoul, Korea), and midazolam (1 mg/kg; Midazolam 5, Bukwang Pharma, Seoul, Korea) mixed in a single syringe immediately prior to administration. The rabbits were then allowed to reach an anesthetic depth suitable for intubation as judged by moderately relaxed jaw tone, lack of voluntary movement in response to interdigital web pinch in a hindlimb, and absence of an ear tickle reflex in response to gentle digital stimulation of the auricular canal.

The animals were then intubated by using 1 of the 3 following techniques. Rabbits successfully intubated were allowed to spontaneously breathe 100% oxygen for an additional 5 min, during which time vital signs including heart rate, respiratory rate, temperature, end-tidal carbon dioxide (EtCO₂), oxygen saturation, and anesthetic depth were monitored. At 5 min after successful endotracheal intubation, atipamezole (0.5 mg/kg; Antisedan, Zoetis Korea Ltd., Seoul, Korea) was administered through intramuscular injection to expedite recovery. Extubation occurred when rabbits had regained the swallowing reflex and demonstrated signs of awareness, including head lifting and limb movement. At the time of extubation, the last set of physiologic parameters were collected (extubation variables), and the endotracheal tube or facemask was removed. Rabbits were then placed in a transportable rabbit carrier furnished with a warm blanket bed and an oral water drip bottle. After anesthesia, temperature (portable digital rectal thermometer), oxygen saturation and heart rate (transcutaneous pulse oximeter), and respiratory rate (visual observation) were monitored until the rabbits resumed normal activities. All animals returned to their hutches within 2 h after extubation, and routine husbandry was resumed.

Supplemental administration of sevoflurane through face masks and a vaporizer setting of 2% to 5% in 100% oxygen was initiated when a subject's anesthetic depth became inadequate for intubation according to the criteria listed earlier. Once the rabbits again achieved an adequate anesthetic depth, intubation was attempted again. However, the trial was aborted in cases requiring more than 9 min to intubate; anesthesia in these

animals was reversed by using atipamezole, and 100% oxygen was supplemented through a facemask. Postanesthetic recovery of these rabbits was managed in the same manner as described for those intubated successfully.

Intubation techniques and time measurement. A single person performed the endotracheal intubations throughout the study, to avoid potential bias between intubators. Rabbits were intubated in a random order to minimize bias introduced as the intubator became more technically proficient as the experiment progressed. Randomization was accomplished by using a computer program (Prism, version 7, GraphPad Software, La Jolla, CA). After anesthetic induction, when the anesthetic depth was deemed appropriate for intubation, the animals were positioned in sternal recumbency. An assistant held the jaws open by using a commercial rodent wire mouth gag (catalog no. D1032, Rodent Wire Mouth Gag, iM3, Vancouver, WA); the head was elevated with the neck extended and the tongue gently retracted to facilitate a clear view of the larynx. The intubator sprayed 0.25 mL of 2% lidocaine (Lidocaine HCl 400, Daihan Pharm, Seoul, Korea) into the laryngeal inlet under laryngoscopic guidance. Rabbits were then placed in a relaxed sternal position for 1 min to allow the local anesthetic to take effect. Then, with the rabbit's neck extended and its head supported, a capnograph airway adapter was connected to the machine end of a 3.5-mm internal diameter, cuffed endotracheal tube (Sheridan/HVT, Teleflex Medical, Research Triangle Park, NC); the endotracheal tube was introduced into the mouth and positioned in the caudal oropharynx just proximal to the larynx. Once the tube was positioned, the maximal EtCO₂ value was determined over several respiratory cycles; this value was subsequently used as the preintubation baseline EtCO₂ value in each animal. In MC and SC groups, the endotracheal tube was advanced through the larynx into the trachea; successful endotracheal intubation was confirmed by a characteristic capnogram.¹¹

In the LS group, after the establishment of the preintubation baseline EtCO₂, intubation was performed exclusively by using a laryngoscope with a size 00 Miller blade, a 3.5-mm internal diameter cuffed endotracheal tube, and a 3-French polyurethane urinary catheter as a guide stylet. Once the arytenoids were visualized at the laryngeal inlet, the polyurethane urinary catheter was advanced into the trachea, and the endotracheal tube was threaded over the catheter, and into the trachea. On visual confirmation of endotracheal tube placement in the trachea and detection of audible breath sounds through the endotracheal tube, the stylet catheter was removed promptly.

After successful intubation in all groups, the endotracheal tube was attached to a breathing circuit airway adapter for direct capnography monitoring and connected to a Bain circuit with a fresh gas flow of 100% oxygen at 0.5 to 1.0 L/min. The endotracheal tube was tied snugly around the rabbit's head, and the cuff was gently inflated until no air leakage was noticed at a peak inspiratory pressure of 20 cm H₂O. Time to successful intubation was measured from when the jaws were first opened to when intubation was confirmed by capnography. The EtCO₂ readings taken at this time were defined as the postintubation EtCO₂. Mainstream capnography was used in all intubated animals to monitor EtCO₂ and respiratory rate during the remaining period. The animals were allowed to breathe 100% oxygen until recovery from anesthesia as expedited by atipamezole reversal (intramuscular injection). The EtCO₂ reading taken just prior to the extubation at the time of recovery was defined as the at-extubation EtCO₂.

Physiologic parameter measurement and recovery. Physiologic parameter measurements obtained throughout the experimental

period included heart rate (stethoscope or EKG), respiratory rate (observation or capnogram), and EtCO₂. EtCO₂ measurements were obtained through either mainstream or sidestream capnography. Mainstream capnography was performed by using a multiparameter patient monitor (model V1407, Vetland Medical Sales and Services, Louisville, KY) with built-in mainstream capnograph (Capnostat 5, Philips Respironics, Amsterdam, Netherlands). EtCO₂ by sidestream capnography was monitored by using a respiratory gas monitor (Capnomac Ultima, Datex Ohmeda Division, GE Healthcare Korea, Seoul, Korea). Specifically, the mainstream capnography adapter, which housed an infrared sensor, was attached to the machine end of the endotracheal tube to simultaneously sample and analyze CO₂ and display capnograms on an external monitor (Figure 1 A). The sidestream capnograph sampled CO₂ from a sampling adapter attached to the machine end of the endotracheal tube through a small-bore gas sampling line and transported the sample to an external analyzer (Figure 1 B). The gas sample was then analyzed by an infrared sensor built into the machine, and capnograms were displayed on a monitor. The monitors were turned on at least for 5 min for warm-up before use and were evaluated for correct functioning and display of the parameters measured and reported. For capnography in particular, a built-in calibration cycle was completed, after which correct display of EtCO₂ readings was tested by introducing a breath into the breathing circuit system. Prior to anesthetic induction, parameters taken for comparison at various time points included resting heart rate (manual) and respiratory rate (manual). These baseline parameters were compared with those subsequently obtained from physiologic monitors including EKG and capnography immediately after endotracheal intubation and at extubation.

Statistical analysis. A priori power analysis based on the results of preliminary experiments of each intubation method was calculated by using G*Power (version 3.1.9.2; Heinrich–Heine University Düsseldorf, Düsseldorf, Germany), and results suggested that 4 rabbits in each group would provide a power of 90% by using one-way ANOVA between means at an α level of 0.05. Time to successful endotracheal intubation was compared by using one-way ANOVA, given that data were normally distributed according to the Shapiro–Wilk test; Bonferroni posthoc testing was conducted to determine differences among groups. Physiologic parameters including heart rate, respiratory rate, and EtCO₂ readings were analyzed among groups through repeated-measures ANOVA; if the data did not assume compound symmetry in the variance–covariance matrix according to results from a Mauchly test of sphericity, Greenhouse–Geisser correction was applied to calculate appropriate *P* values. When differences were significant, Sidac posthoc testing was applied to isolate significance among groups and time points. A *P* values less than 0.05 was considered to be statistically significant, and all statistical analyses were performed by using Prism (version 7, GraphPad Software) and SPSS Statistics for Windows (version 18.0, IBM Armonk, NY).

Results

The time to recumbency (mean $\pm$ 1 SD) was 2.7 ± 0.9 min after intramuscular administration of anesthetic drugs. Approximately 90 s after rabbits became recumbent, the anesthetic depth in all rabbits was sufficiently deep for intubation, as assessed by relaxed jaw tone, absence of righting reflex, and lack of voluntary movement in response to interdigital web pinching. The time to complete endotracheal intubation was 46.4 ± 12.6 s in the MC group, 147.2 ± 44.2 s in the SC group, and 385.0 ± 114.1 s in the LS group. Figure 2 depicts the intubation time

(A) Mainstream Capnography **(B) Sidestream Capnography**

Figure 1. Schematic comparison of (A) mainstream and (B) sidestream capnography.

Figure 2. Time to complete endotracheal intubation in mainstream capnography (MC), sidestream capnography (SC), and laryngoscopy (LS) groups. Note that only 3 animals in the LS group were successfully intubated; times differed significantly ($P < 0.05$) between groups.

for each animal in all 3 groups; only 3 animals in the LS group were intubated successfully. The time to complete endotracheal intubation differed significantly ($P < 0.05$) among all 3 groups. Prolonged intubation times in 3 animals in the LS group necessitated supplementary sevoflurane administration to regain an anesthetic depth appropriate for intubation. However, only 1 of these 2 rabbits was intubated successfully within the required time limit of 540 s.

Table 1 presents data for heart rate, respiratory rate, and EtCO_2 values during the measurement period. There was no statistical significance of time-by-group interaction in heart rate ($P = 0.473$), respiratory rate ($P = 0.306$), and EtCO_2 ($P = 0.286$) among groups. However, intragroup values for heart rate and respiratory rate at intubation were significantly decreased from preintubation values (heart rate: MC group, $P = 0.001$; SC group, $P = 0.002$; and LS group, $P = 0.309$; respiratory rate, MC group, $P = 0.004$; SC group, $P = 0.029$; and LS group, $P = 0.025$). At extubation, heart rate and respiratory rate were not significantly different from their preintubation values. In all groups, intragroup capnographic readings were greater at intubation

than at preintubation (MC group, $P = 0.002$; SC group, $P = 0.003$; and LS group, $P = 0.325$). Capnographic readings at extubation did not differ from preintubation values.

All rabbits recovered uneventfully between 3 and 10 min after reversal with atipamezole. No postanesthetic complications were observed in any of the animals.

Discussion

Many of the medical and surgical procedures performed in laboratory and pet rabbits require general anesthesia through injectable or inhalant anesthetics or both. Maintaining a patent airway during general anesthesia regardless of the type of anesthetic used is a top priority for safe anesthesia in any species. Inhalant anesthetics are administered through an endotracheal tube or a facemask. Compared with a facemask, endotracheal intubation ensures a more secure airway for the administration of inhalant anesthetics and supplemental oxygen. Endotracheal intubation provides additional benefits, including more efficient ventilatory support, quicker anesthetic stabilization, and prevention of environmental contamination with waste anesthetics because it is an airtight system. In addition, a patent airway allows for more accurate capnographic monitoring, thus allowing clinicians to accurately monitor and respond to changes in a patient's respiratory status.

Endotracheal intubation is not readily achievable in all species, and rabbits are known as one of the most challenging species to intubate. These difficulties are primarily related to the inability to visualize the laryngeal airway sufficiently. These difficulties can lead to a prolonged delay in endotracheal tube insertion, the inability to insert an endotracheal tube successfully, or incorrect placement of the endotracheal tube (for example, accidental esophageal intubation). Furthermore, postextubation airway complications due to difficult intubation (for example, laryngeal or sublaryngeal tracheal injury) can markedly increase patient morbidity and mortality.^{7,14} Therefore, it is essential to identify a technique that will reliably enable clinicians to effectively, efficiently, and atraumatically accomplish endotracheal intubation in rabbits—and other small laboratory species that pose similar difficulties in regard to intubation.

Table 1. Physiologic variables in rabbits throughout the intubation procedures

	Group	Before intubation	At intubation	At extubation
Heart rate (bpm)	MC	248.2 ± 30.4 ^a	214.8 ± 33.5 ^a	232.4 ± 23.5
	SC	241.0 ± 29.6 ^a	201.0 ± 31.0 ^{a,b}	234.0 ± 23.6 ^b
	LS	241.8 ± 36.0	209.2 ± 41.7	235.6 ± 35.0
Respiratory rate (breaths per min)	MC	52.0 ± 9.4 ^a	28.4 ± 6.2 ^{a,b}	50.0 ± 6.4 ^b
	SC	48.4 ± 9.3 ^a	23.8 ± 5.9 ^{a,b}	40.8 ± 8.0 ^b
	LS	54.2 ± 9.0 ^a	23.2 ± 4.2 ^{a,b}	44.4 ± 6.5 ^b
EtCO ₂ (mm Hg)	MC	33.2 ± 10.1 ^a	45.3 ± 9.4 ^{a,b}	36.7 ± 6.6 ^b
	SC	32.0 ± 7.3 ^a	49.6 ± 6.0 ^{a,b}	39.5 ± 7.6 ^b
	LS	30.9 ± 8.6	54.5 ± 7.5	40.5 ± 3.6

EtCO₂, endtidal CO₂; LS, laryngoscopy; MC, mainstream capnography; SC, sidestream capnography

Data are reported as mean ± 1 SD. The MC and SC groups each contained 5 rabbits; only 3 rabbits were intubated in the LS group. Within each experimental group, neither heart rate, respiratory rate, nor EtCO₂ differed between before intubation and at extubation.

^aSignificant difference ($P < 0.05$) between values before intubation and at intubation in each group.

^bSignificant difference ($P < 0.05$) between values at intubation and at extubation in each group.

Numerous intubation techniques for rabbits have been described.^{2,4,8,9,12,15,17,18,21,23} However, none of these are without limitations, including the necessary level of technical expertise and experience and requirements for specialized equipment and their associated cost. Therefore, we wanted to identify a method of intubation that could be performed simply and reliably and that did not require specialized equipment beyond what might likely be found in modern veterinary practice or laboratory settings. Given the initial findings regarding the use of sidestream capnography to facilitate intubation in rabbits,¹⁰ we decided to further investigate the utility of the capnography for endotracheal intubation in rabbits. In addition to confirming the previous findings,¹⁰ we wanted to investigate the utility of mainstream capnography as an alternative method of intubation in rabbits and to compare its effectiveness with those of sidestream capnography and laryngoscopy-guided endotracheal intubation in rabbits.

The current investigation demonstrated mainstream capnography to be a useful technique for intubating rabbits, with significantly faster airway establishment than intubation facilitated by using sidestream capnography or laryngoscopy. The time to intubate was approximately 3 times faster with MC compared with SC. The superior results obtained by using MC compared with SC can be ascribed to the differences in how gas samples are acquired and processed prior to being analyzed by each type of capnograph. Specifically, a sidestream capnography uses small-bore tubing to aspirate a gas sample from within the breathing system and to transport the gas sample to an external analyzer, which displays the CO₂ values as graphical and numerical data. The time needed for the gas to reach the analyzer depends on the gas sampling rate, the length and diameter of the sampling tube, and the volume of the analyzing chamber. The transit time can result in a delay of as long as several seconds between when the airway sample is acquired and analyzed and when results are displayed on the monitor. In mainstream capnography, the CO₂ analyzer is housed in an airway adapter, which is inserted between the endotracheal tube and the breathing circuit. Therefore, airway CO₂ concentrations are displayed in real-time on the monitor. When attempting endotracheal intubation, orienting the tip of the tube in relation to the airway to facilitate intubation is a dynamic process that requires both the assistant and the intu-

bator to communicate promptly and coordinate the maneuvers effectively. A delay in recognizing when the tube is positioned near or in the airway because of a lag in CO₂ readings can lead to a missed window of opportunity and challenges the intubator in getting the tube aligned optimally to facilitate the intubation. In contrast, mainstream capnography allows the intubator to position the endotracheal tube in response to real-time capnographic changes, thus allowing quick and accurate adjustment in endotracheal placement and advancement.

In addition, our results demonstrated that both methods of capnography-guided intubation were more reliable, effective, and efficient than laryngoscopy-guided intubation, which was unsuccessful in 2 of the 5 animals. Intubation times in rabbits that were successfully intubated by using laryngoscopy were significantly longer than those obtained with either method of capnography. In addition, supplemental administration of sevoflurane through a facemask was required in 3 of the 5 rabbits in the LS group. Even with supplement sevoflurane administration, 2 of the 3 rabbits could not be intubated. Even though the order in which the rabbits were intubated was randomized, we performed a posthoc review of the order of intubation to check for any potential bias associated with acquired technical proficiency. The 2 animals that could not be intubated were the 4th and 12th experimental subjects in the study. This order further argues against any bias associated with acquired technical proficiency.

The physiologic variables that we measured to evaluate differences between intubation techniques (that is, heart rate, respiratory rate, and EtCO₂) did not reveal significant differences between experimental groups at the corresponding time points. However, for intragroup comparison, significant reductions in heart rate and respiratory rate and significant increases in EtCO₂ occurred after intubation in all groups and likely reflect the cardiovascular and respiratory depression associated with increased anesthetic depth. Conversely, the rebound of physiologic variables after extubation similar to those at preintubation probably reflects the dissipation of an anesthetic effect and the return to full consciousness. Despite obvious changes in heart rate and EtCO₂ between time points in LS group, no significance was detected in these variables—likely due to the small sample size and broad standard deviation as a result of 2 failures of intubation in this group. The apparent mild respiratory acidosis

(EtCO₂ > 40 mm Hg) in all groups after intubation was associated with the decreased respiratory rate, but SpO₂ was at least 96% at all times in 100% oxygen. We therefore recommend that intubated rabbits under injectable general anesthesia should receive supplemental oxygen, given their increased likelihood of respiratory depression due to anesthesia.

As an incidental and interesting observation during preliminary trials for capnography-guided intubation, an uncuffed endotracheal tube was associated with increased risk of failure during intubation than using a cuffed one. We initially preferred the uncuffed tube because of its softer material, which we considered to be less damaging to delicate tissue of the airways. However, the uncuffed tube frequently bent at insertion, possibly associated with increased resistance associated with laryngeal spasm and epiglottal entrapment. The bending of the uncuffed tube made passing the tube further down the trachea difficult. After replacing uncuffed tubes with cuffed ones, intubation was accomplished much more consistently and smoothly, with minimal resistance of the tube against the push to introduce into the trachea. Therefore, we used cuffed tubes for all animals for the main study. A short and flimsy stylet may lead to less successful endotracheal intubation, due to lack of strength to sufficiently overcome bending of the tube. A wire stylet placed within the endotracheal tube could result in a different outcome in intubating the rabbits, but no conclusive information is currently available regarding whether a different type of stylet or a cuffed tube can facilitate endotracheal intubation in rabbits. Further studies may be warranted to investigate whether these factors play a role in improving the success of intubation.

In summary, capnography-guided intubation allowed for faster and more consistent endotracheal intubation in rabbits compared with intubation performed by using a laryngoscope in the current study groups. Furthermore, endotracheal intubation accomplished was much more quickly with MC as compared with SC, thus making MC preferred method of capnography-guided intubation. We feel that, because capnographs have become much more affordable recently and because increasing numbers of practitioners use capnography for routinely monitoring anesthetized animals, using MC or SC for endotracheal intubation in rabbits is now a viable alternative. Finally, the utility of MC- or SC-guided endotracheal intubation in rabbits demonstrated in the current study could prove to be applicable in other species in which endotracheal intubation is challenging, such as hamsters, guinea pigs, and rats. Further studies are warranted to evaluate the clinical relevance of capnography-guided intubation in these species.

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References

- Alexander DJ, Clark GC. 1980. A simple method of oral endotracheal intubation in rabbits (*Oryctolagus cuniculus*). *Lab Anim Sci* 30:871–873.
- Bateman L, Ludders JW, Gleed RD, Erb HN. 2005. Comparison between facemask and laryngeal mask airway in rabbits during isoflurane anesthesia. *Vet Anaesth Analg* 32:280–288. <https://doi.org/10.1111/j.1467-2995.2005.00169.x>.
- Corleta O, Habazettl H, Kreimeier U, Vollmar B. 1992. Modified retrograde orotracheal intubation technique for airway access in rabbits. *Eur Surg Res* 24:129–132. <https://doi.org/10.1159/000129198>.
- Crotaz IR. 2010. Initial feasibility investigation of the V-Gel airway: an anatomically designed supraglottic airway device for use in companion animal veterinary anaesthesia. *Vet Anaesth Analg* 37:579–580. <https://doi.org/10.1111/j.1467-2995.2010.00566.x>.
- Dorsch JA, Dorsch SE. 2008. Gas monitoring, p 685–727. In: Dorsch JA, and Dorsch SE, editors. *Understanding anesthesia equipment*. Philadelphia (PA): Lippincott, Williams, and Wilkins.
- Fick TE, Schalm SW. 1987. A simple technique for endotracheal intubation in rabbits. *Lab Anim* 21:265–266. <https://doi.org/10.1258/002367787781268837>.
- Grint NJ, Sayers IR, Cecchi R, Harley R, Day MJ. 2006. Postanesthetic tracheal strictures in 3 rabbits. *Lab Anim* 40:301–308. <https://doi.org/10.1258/00236770677611415>.
- Imai A, Eisele PH, Steffey EP. 2005. A new airway device for small laboratory animals. *Lab Anim* 39:111–115. <https://doi.org/10.1258/0023677052886484>.
- Johnson DH. 2010. Endoscopic intubation of exotic companion mammals. *Vet Clin North Am Exot Anim Pract* 13:273–289. <https://doi.org/10.1016/j.cvex.2010.01.010>.
- Kim JS, Park JH, Han JS, Jang BJ. 1998. Endotracheal intubation using capnography in rabbits. *Korean journal of laboratory animal science* 14:101–102. [Article in Korean].
- Kodali BS. [Internet]. 2001. Types of capnographs. [Cited 10 November 2017]. Available at: <http://www.capnography.com/>
- Miranda A, Pêgo JM, Correia-Pinto J. 2016. Animal facility videoendoscopic intubation station: tips and tricks from mice to rabbits. *Lab Anim* 51:204–207. <https://doi.org/10.1177/0023677216652342>.
- Morgan TJ, Glowaski MM. 2007. Teaching a new method of rabbit intubation. *J Am Assoc Lab Anim Sci* 46:32–36.
- Phaneuf LR, Barker S, Groleau MA, Turner PV. 2006. Tracheal injury after endotracheal intubation and anesthesia in rabbits. *J Am Assoc Lab Anim Sci* 45:67–72.
- Schuyt HC, Leene W. 1977. An improved method of tracheal intubation in the rabbit. *Lab Anim Sci* 27:690–693.
- Schuyt HC, Leene W. 1978. An improved method in rabbit intubation and thymectomy. *Eur Surg Res* 10:362–372. <https://doi.org/10.1159/000128027>.
- Smith JC, Robertson LD, Auhll A, March TJ, Derring C, Bolon B. 2004. Endotracheal tubes versus laryngeal mask airways in rabbit inhalation anesthesia: ease of use and waste gas emissions. *Contemp Top Lab Anim Sci* 43:22–25.
- Star EG. 1979. [The endotracheal intubation of rabbits with xy-lazine and ketamine.] [Article in German]. *Res Exp Med (Berl)* 176:1–6. <https://doi.org/10.1007/BF01852105>.
- Stephens DeValle JM. 2009. Successful management of rabbit anesthesia through the use of nasotracheal intubation. *J Am Assoc Lab Anim Sci* 48:166–170.
- Su HP, Hou CJ, Chen WH, Wang KJ, Chiu YH, Sun HS. 2013. A miniature lighted stylet for fast oral endotracheal intubation in rabbits. *Vet J* 195:254–256. <https://doi.org/10.1016/j.tvjl.2012.06.016>.
- Tran HS, Puc MM, Tran JL, Del Rossi AJ, Hewitt CW. 2001. A method of endoscopic endotracheal intubation in rabbits. *Lab Anim* 35:249–252. <https://doi.org/10.1258/0023677011911705>.
- Varga M. 2017. Airway management in the rabbit. *Journal of exotic pet medicine* 26:29–35. <https://doi.org/10.1053/j.jepm.2016.10.014>.
- Worthley SG, Roque M, Helft G, Soundararajan K, Siddiqui M, Reis ED. 2000. Rapid oral endotracheal intubation with a fibre-optic scope in rabbits: a simple and reliable technique. *Lab Anim* 34:199–201. <https://doi.org/10.1258/002367700780457554>.