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RESEARCH PAPER

Use of neuromuscular blockade with rocuronium bromide for intubation in cats

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Abstract

Objective To determine whether neuromuscular blockade with rocuronium bromide (RB) would improve endotracheal intubation (EI) conditions in comparison with topical lidocaine hydrochloride (LH).

Study design Randomized prospective study.

Animals Forty seven healthy cats of unspecified breed, aged 17 ± 11 months and weighing 2.8 ± 0.8 kg, undergoing elective procedures.

Methods Anesthesia was induced with xylazine (XZ) (1.1 mg kg^{-1} IM) and tiletamine-zolazepam (XTZ) (7 mg kg^{-1} IM) and EI was attempted. Cats which could not be intubated at the first attempt (n = 34), were randomly medicated with either 0.1 mL LH 10% spray on the laryngeal mucosa (n = 17) or 0.6 mg kg^{-1} intravenous RB (n = 17). Sixty seconds later, a second attempt at EI was performed. The effect of both drugs was assessed using a previously published scale (Sandor Agoston). EI conditions associated with laryngoscopy, vocal cord position and movement, cough, patient movement, time and attempts needed in order to perform EI were recorded. Heart rate and end-expired CO_2 concentration were monitored.

Results Groups were comparable in age, weight, gender and hematological parameters. Clinically acceptable EI conditions were not significantly different between RB and LH assisted groups (p = 0.31). However, there was a significant difference in cough, vocal cord movement and position between the RB and the LH groups. The group intubated at the first attempt and receiving neither RB nor LH coughed persistently (11/13). The cats receiving RB had to be ventilated for 10–28 minutes.

Conclusions and clinical relevance The present study shows that, when used in cats anesthetized with XTZ, RB paralyzes the internal laryngeal muscles keeping the vocal cords in an intermediate position (paramedial) 60 seconds after being administered. RB is an effective alternative to LH to overcome the airway protective reflexes when performing EI but requires ventilatory support until the paralysis wears off.

Keywords cat, intubation, laryngeal paralysis, lidocaine, muscle relaxants, rocuronium bromide.

Introduction

Endotracheal intubation (EI) is one of the main safety measures in veterinary clinical practice when using general anesthesia (Nicholson & Watson 2001). EI maintains an airway during general anesthesia and diminishes the risk of aspirating materials from the pharynx; it also allows positive-pressure ventilation and gas administration to the patient (Cruz 2001). In addition, some positions in head or neck surgeries make intubation essential to protect the airway. However, EI is not complication free, especially in cats (Dyson et al. 1998; Brodbelt et al. 2007). The cat's airways are small and delicate and can be easily injured (Mitchell et al. 2000; Hofmeister et al. 2007). Laryngospasm is a protective reflex of the upper airway (UA) during EI (Rex et al. 1983), and this protective response must be minimized in order to facilitate intubation.

Lidocaine hydrochloride (LH) is frequently used for topical desensitization of a cat's laryngeal mucosa (Morrell et al. 1982; Rex et al. 1983). Recovery of total laryngeal sensitivity after 2% LH administration ranges from 17 to 100 minutes; while at 10% concentrations recovery may take up to 256 minutes (Robinson et al. 1985). A significant decrease ($p < 0.001$) in the occurrence of spasms and failed attempts (2 and 10%, respectively) has been reported when evaluating the comparative benefits of the topical application of LH (Hamill et al. 1981).

Topical application of LH (10% spray) is a safe and usual alternative for laryngeal desensitization during EI. However, it can cause moderate laryngeal cell damage, characterized by laryngeal edema, hydropic degeneration, necrosis and neutrophil infiltration of epithelial cells. With preexistent mucosal ulceration, damage might become more severe and compromise the airway or even harm the patient's postoperative progress (Rex et al. 1983). Laryngeal desensitization for long periods of time, may allow the aspiration of material during the recovery phase (Robinson et al. 1985). Given these undesirable effects of topical LH it may be better to use another method to decrease laryngeal reflexes.

The use of neuromuscular blockers (NMB) for endotracheal intubation is a usual practice in human anesthesia, and its efficiency has been assessed using many different scales. The Sandor-Agoston scale (Table 1) for EI assessment has been approved by an international consensus conference for good clinical research practices (Viby et al. 1996). The NMB, administered immediately after an anesthetic induction agent, paralyzes the laryngeal muscles to allow easier EI. Succinylcholine is a depolarizing NMB which has an effective, fast, and brief suppressive effect on laryngeal reflexes. In cats it has a short duration of action and muscle function recovers after 3–5 minutes (Hall et al. 2001). However, the use of succinylcholine can be accompanied by undesirable side effects, such as: muscular pain, hyperglycemia, cardiac arrhythmias, prolonged apnea, masseter muscle spasms, malignant hyperthermia, cardiac arrest, and increases in intraocular

Table 1 Sandor-Agoston values for assessment of intubation conditions*

	Intubation conditions		
	Clinically acceptable		Clinically not acceptable
Variables	Excellent†	Good‡	Poor§
Laryngoscopy	Easy (Jaw relaxed, no resistance to blade in the course of laryngoscopy)	Fair (Jaw not fully relaxed, slight resistance to blade)	Difficult (No jawrelaxation, active resistance of the patient to laryngoscopy)
Vocal cords			
Position	Abducted	Intermediate	Closed
Movement	None	Moving	Closing
Reaction to insertion of tracheal tube and/or cuff inflation			
Movements of the limbs	None	Slight	Vigorous
Cough§	None	Slight (Abdominal movement with non audible air expulsion)	Sustained (Multiple movements of abdomen and thorax with audible air expulsion; >10 seconds)

*Source: Modiffied of Viby et al. 1996. †All variables are in excellent condition. ‡All variables are in either excellent or good condition. §At least a single variable listed under poor condition.

and intracranial pressures (Hildebrand 1997; Martinez & Keegan 2007). Prolonged blockade may occur with decreased plasma cholinesterase concentration hepatic disease, pregnancy, or exposure to anticholinesterase agents such as organophosphates (Hildebrand 1997).

Rocuronium bromide (RB) is a non-depolarizing NMB, used as an alternative to succinylcholine. In a study performed in cats anesthetized with isoflurane (Auer & Mosing 2006), RB at 0.6 mg kg^{-1} showed no negative side effects on heart rate nor on blood pressure and produced a complete blockade in 90% of the cats. RB had a rapid onset (47 ± 11 seconds) and moderate duration of effect (13 ± 2.7 minutes). Paralysis of the respiratory muscles requires that the cat receives intermitent positive pressure ventilation until spontaneous respiration returns. Preoxygenation is recomended prior to the use of NMB (Hall et al. 2001) for intubation.

The objective of the present study was to investigate if neuromuscular blockade with rocuronium bromide was able to improve endotracheal intubation conditions by comparison with lidocaine hydrochloride.

Materials and methods

This study was designed as a randomized prospective study. The Animal Care Committee of the University authorized this study in compliance with the Guide for the care and use of laboratory animals (US National Institute of Health 2011). In all cases, informed consent was granted by the patient's owner. The study was performed with owned cats; 47 healthy cats of unspecified breed, destined for elective procedures to be performed in the Veterinary Hospital. The procedures were: ovariohysterectomy, $n = 21$; orchiectomy, $n = 14$; dental cleaning, $n = 5$; or clinical examination, $n = 7$. Their mean body weight (± standard deviation) was 2.8 ± 0.8 kg and their age was 17 ± 11 months. Only cats identified as healthy, through physical examination and chemical and hematological testing, were used in this study.

A combination of xylazine (Bayer, Mexico; 1.1 mg kg^{-1}, IM) and tiletamine-zolazepam (XTZ; Virbac France, imported by Virbac Mexico; 7 mg kg^{-1} IM) was administered to all cats. After 10 ± 4 minutes the cats were anesthetized and a 24-gauge intravenous catheter was placed aseptically into the cephalic vein. Saline solution (Pisa Farmaceutica, Mexico; 0.9%) was then infused (10 ± 4 minute after XTZ) at a rate of 10 mL kg^{-1} hour^{-1}, through. The cats were placed in sternal recumbency, and using the aid of a lighted laryngoscope (Welch Allyn type Miller, blade No. 0, NY, USA), a non-lubricated endotracheal tube (Mallinckrodt tube with a low volume high pressure cuff; 3.0 mm for <3.0 kg BW and 4.0 mm for >3.0 kg BW), without stylet, was introduced; and the cuff was inflated until resistance to injection was felt, and adjusted when leaks were detected during ventilation. The endotracheal tube was attached to a Bain non-rebreathing system with an oxygen flow of 0.6 L kg minute^{-1}. Oxygenation, heart rate (HR) and end-tidal CO_2 ($P_{E'}CO_2$) were monitored as described below.

The patients ($n = 13$) in which intubation was possible on the first attempt (Non assisted group: NAG) were connected to the breathing circuit and the scheduled surgical-medical procedure was performed. In cats where intubation was not successful at the first attempt ($n = 34$), due to vocal cord and/or arytenoids cartilage adduction, sternal recumbency was maintained and oxygen was administered by mask. They were then randomly allocated, according to the order in which they arrived at the hospital into one of the following two groups ($n = 17$ each): a lidocaine group (LG) that received LH (AstraZeneca, Mexico) on the laryngeal mucosa (0.1 mL, 10% spray), or a rocuronium group (RG) that received RB (Schering-Plough, Mexico) as a rapid bolus IV (0.6 mg kg^{-1} over 5 seconds). Sixty seconds after LH or RB administration, EI was attempted with the aid of laryngoscopy. Once EI was achieved, the endotracheal tube was connected to a non rebreathing anesthetic circuit as above and the scheduled surgical or medical procedure was performed.

The assessment of EI conditions included five variables: a) ease of laryngoscopy, b) position and c) movement of the vocal cords, d) patient movement and e) cough during insertion of the endotracheal tube or when inflating the tube cuff. The scores for each variable were 'excellent', 'good' or 'poor' where excellent and good were 'clinically acceptable' and poor was 'clinically unacceptable' (Table 1). When any variable was assessed as 'poor', EI conditions were considered 'clinically unacceptable'. In addition, time taken and number of attempts for EI were also recorded.

Heart rate and $P_{E'}CO_2$ concentration were recorded before and during the procedure by a sidestream multi-parameter monitor (Welch Allyn, Atlas # 622 NP-E1, NY, USA). HR was measured using a lead II electrocardiogram, $P_{E'}CO_2$ was evaluated before EI, via a CO_2 monitor adapter in a face mask; this mask was replaced for the endotracheal tubes when EI was fulfilled. $P_{E'}CO_2$ was evaluated with a sampling rate of 50 mL minute^{-1}. Manual ventilation was applied when apnea was present or $P_{E'}CO_2$s were >40 mmHg (4.7 kPa) at 15 breaths per minute, with an approximate tidal volume of 10 mL kg^{-1}. Tidal volume was evaluated clinically from the reservoir bag of the breathing circuit.

Endotracheal intubation was carried out according to Hartsfield et al. (2007) with the aid of a professional assistant. Anesthesia, treatments and monitoring were performed by an experienced veterinary anesthetist (MGTM); assessment of EI and its variables was carried out by a veterinarian experienced in feline physiology (AMS). This last veterinarian was not present when the experiment was designed nor when the treatment was applied, so he was unaware of which treatment had been used; when a second EI attempt was required, he left the room and LH or RB was applied, one minute later the EI was performed.

Differences among groups were analyzed using chi-squared and ANOVA (with Duncan's multiple range test; Statistical Analysis System software, SAS/STAT version 9.0.0, SAS Institute Inc., NC, USA), for discrete and continuous variables, respectively. Results were expressed as a proportion of cats which showed an EI condition in each group, continuous variables are expressed as mean (±SD) and range. The differences were considered significant if $p < 0.05$.

Results

No significant statistical differences ($p > 0.05$) were observed in relation to gender or mean weight, age, hematocrit and total proteins among groups (Table 2). EI was performed at the first attempt and without pharmacological assistance in (13/47) of the patients, while in the remaining cats; EI was performed with LH or RB.

The proportion of cats whose EI conditions were clinically acceptable (excellent and good), or clinically unacceptable (poor), showed no significant statistical differences ($\chi^2 > 0.05$; Fig. 1) between the LG and RG but these groups were significantly different from the group which received neither treatment.

In the analysis of the variables considered for EI conditions assessment, there was no difference among treatments in the 'laryngoscopy' variable ($\chi^2 > 0.05$). All patients in this study had relaxed jaws, and none of the cats showed any resistance to laryngoscopy. Significant differences ($\chi^2 < 0.01$) were found among all groups in the 'cough' variable during tube insertion or cuff inflation. None of the cats in the RG coughed, whereas, in the LG, 1/17 of the patients had sustained coughing and 5/17 had small diaphragmatic movements. In the NAG, 11/13 cats had sustained coughing, which was considered as clinically unacceptable.

The RG did not have limb movement, while 2/17 of the LG had slight movement and 12/13 of the NAG showed movement, either slight (6/12) or vigorous (6/12), which was considered to be clinically unacceptable.

The variables associated with vocal cords showed significant statistical differences ($p < 0.01$), in movement as well as in position. The LG had excellent conditions in all patients (abducted vocal cords) whereas in the RG all cats had good vocal cord position (intermediate), as shown in Fig. 2 (panel: b

Table 2 Demographic characteristics (mean ± standard deviation and range) per group with non assisted or assisted endotrachal intubation

		Assisted		
Variable	Non assisted* (n = 13)	Lidocaine (n = 17)	Rocuronium (n = 17)	p-value (F-test)
Age (months)	19.8[a] ± 10.2 (5–52)	18.5[a] ± 13.6 (5–48)	15.2[a] ± 7.4 (6–30)	0.49
Weight (kg)	3.0[a] ± 0.70 (1.5–4.9)	3.0[a] ± 1.0 (1.5–4.9)	2.9[a] ± 0.6 (1.5–3.8)	0.90
Hematocrit (%)	37[a] ± 6 (25–49)	35[a] ± 5 (27–45)	35[a] ± 5 (30–47)	0.50
Total proteins (g L^{-1})	70[a] ± 3 (62–83)	72[a] ± 6 (62–81)	70[a] ± 4 (64–76)	0.30
Gender (F:M)	7:6[A]	10:7[A]	9:8[A]	0.68

*Intubated cats at first attempt. F:M: female:male proportion. A = No significant statistical differences among groups ($p > 0.05$); Chi-square test. a = No significant statistical differences among groups ($p > 0.05$); Duncan test.

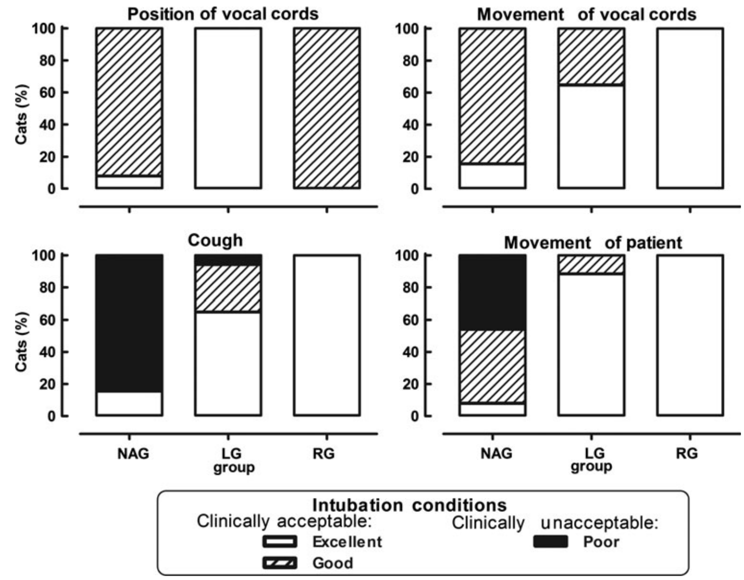

Figure 1 Cats assisted pharmacologicaly in order to facilitate endotracheal intubation (0.1 mL topically on the laryngeal mucosa; 0.6 mg mL^{-1} IV). The figure ilustrates the frequency of clinicaly acceptable (excellent and good) and unacceptable (poor) intubating conditions, according to the Sandor-Agoston scale. Results of the laryngoscopy assessments in all cats were scored excellent (clinicaly acceptable), therefore no figures have been included.

and c). In the NAG 12/13 cats had good vocal cord position. Vocal cord movement maintained synchronicity with the ventilation cycle in 11/13 cats from the NAG and 6/17 of the LG. Patients from the RG showed no movement.

In all cats from the NAG and LG, EI was achieved at the first attempt, while in RG, only 8/17 of the patients were intubated on their first attempt, while the rest required 2 or 3 attempts; showing significant statistical differences ($p < 0.01$), with the NAG and LG groups. However, the time spent to achieve EI showed no significant statistical differences ($p > 0.05$), since the mean time for the NAG, LG and RG were 9 ± 2, 9 ± 1 and 10 ± 2 (8–12) seconds, respectively. In the RG, the cats were apneic for 20 ± 8 (10–28) minutes after having administered the medication, so these animals were manually ventilated for this period. Orchiectomy and clinical examinations (n = 21) ended before cats returned to spontaneous ventilation, therefore they were assisted until their recovery (recovery time: 5 ± 2 minutes from the end of the procedure).

Starting 4 minutes before administering the RB or LH until 10 minutes after; cats anesthetized with XTZ from all groups had both HR and $P_{E}'CO_2$ concentrations within physiological range (Table 3). The indicators of respiratory function showed no significant statistically differences ($p > 0.05$) among groups, which showed that manual and spontaneous ventilation were similar.

Discussion

In the present study, all cats subjected to EI with RB had clinically acceptable conditions, according to the Sandor Agoston scale (Viby et al. 1996). EI conditions with RB were better than the conditions present without pharmacological assistance, in

Figure 2 Representative larynx of cats, placed in sternal recumbency, to evaluate endotracheal intubation conditions (EI). Panel (a): laryngeal spasm in cats, not medicated, in which intubation at the first attempt was not possible; panel (b): Laryngeal opening after desensitization with lidocaine hydrochloride (0.1 mL of 10% topically); panel (c): Laryngeal relaxation after paralysis with rocuronium bromide (0.6 mg kg^{-1} IV). AC, Arytenoid cartilage; G, Glottis; VC, Vocal cords; E, Epiglottis.

Table 3 Heart rate (HR) and end-expired CO_2 ($P_{E'}CO_2$) tension in cats anesthetized with xylazine and tiletamine-zolazepam

	Minutes before and after medication							
Group	**−4**	**−2**	**0**	**2**	**4**	**6**	**8**	**10**
HR (beats minute^{-1}*)								
Non assisted	140 ± 21	145 ± 22	137 ± 27	139 ± 12	141 ± 19	138 ± 26	140 ± 17	139 ± 15
Lidocaine†	136 ± 19	141 ± 14	139 ± 17	141 ± 21	143 ± 21	143 ± 19	137 ± 21	140 ± 19
Rocuronium†	148 ± 27	150 ± 27	147 ± 25	140 ± 22	139 ± 21	133 ± 35	142 ± 16	141 ± 20
$P_{E'}CO_2$ (mmHg*)								
Non assisted	29 ± 4	27 ± 7	28 ± 7	28 ± 5	28 ± 6	30 ± 5	30 ± 5	29 ± 3
Lidocaine†	28 ± 5	28 ± 6	29 ± 7	29 ± 4	29 ± 5	29 ± 5	30 ± 6	29 ± 5
Rocuronium†	31 ± 4	30 ± 6	29 ± 6	30 ± 6	31 ± 4	32 ± 5	31 ± 4	31 ± 5

*Mean ± standard deviation. †Lidocaine hidrochloride or rocuronium bromide (0.1 mL topical on laryngeal mucosa; 0.6 mg mL^{-1} IV) was administered at 0 and endotrachal intubation was performed one minute later.

addition they were clinically similar to the conditions present with the use of topical LH, which is commonly used in cats for EI (Hamill et al. 1981; Morrell et al. 1982; Dyson 1988). The use of neuromuscular blockade for EI is a routine practice in human medicine and has been used by some clinicians as a routine approach for EI in cats (Hall et al. 2001). Succinylcholine has been the drug most commonly used for this technique. This is the first report of EI in cats using RB and could be considered in cases where LH cannot be recommended due to previous pathologies or pathologies induced by LH in the pharyngeal-laryngeal mucosa (Rex et al. 1983; Chadwick 1985).

In this study, EI conditions in cats from the NAG were assessed as clinically acceptable in only 2/13 of the patients (5/13 cough; 6/13 movement of limb and cough). Therefore 45/47 of cats required some type of pharmacological assistance for clinically acceptable conditions. Our results concur with previous statements that in order to decrease laryngeal responses, it is best to use pharmacological aids in all patients to be intubated (Robinson et al. 1985; Dyson 1988). Laryngoscopy, position, and vocal cord movement in cats from the NAG were evaluated before performing the EI and, although there was good relaxation and minimal response to laryngoscopy, the larynx and trachea remained reactive (Rex et al. 1983).

Vocal cord position is present in some scales, such as those of Lund & Stovner (1969), Fahey et al. (1981) and Sandor Agoston (Viby et al. 1996). In cats, some reports have assessed intubation; for example, Dyson (1988) reported laryngeal relaxation and intubation conditions and Sano et al. (2003) described EI in cats induced with propofol, but neither of these reports evaluated the cats' vocal cord position.

Saglam & Tas (2011) used a scale to evaluate EI in cats; laryngeal responses and vocal cord visibility are grouped in four assessment levels. That study, with cats anesthetized with ketamine, midazolam and succinylcholine ($n = 7$), reported EI conditions as good and excellent; but described vocal cords as relaxed and open. In our study, 60 seconds after the RB injection was administered the vocal cords were in an intermediate position (Fig. 1, panel c) in all cases (17/17). RB has been extensively used in human anesthesia (Perry et al. 2002), where it is common to find vocal cords that are abducted, immobile and in an intermediate position (Eikermann et al. 2002; Almeida et al. 2004; Politis et al. 2005). In a different study in cats which used the same RB dose as our study, the loss of neuromuscular response to stimulation of the ulnar nerve was maximal at 46 ± 11 seconds with a duration time from 10 to 24 minutes (Auer & Mosing 2006). Although the larnygeal muscles are usually paralyzed earlier than the muscles of the thoracic limb it is possible that this was not the case with rocuronium in cats and our results reflect a partial paralysis of these muscles at 60 seconds (Ibenbunjo & Hall 1994). However, this vocal cord position is the same as the one observed in a cat's cadaver and in laryngeal paralysis induced by damage to the cat's laryngeal nerves (Campbell & Holmberg 1984).

In our work, the apnea time of RG cats ranged from 10 to 38 minutes, which is similar to that reported by Auer & Mosing (2006). In our study, the values of $P_{E'}CO_2$ ranged from 23 to 37 mmHg and were close to the average previously reported for anesthetized cats (Clark 2003; Mendes & Selmi 2003). Hypercapnia may increase the activity of intrinsic laryngeal muscles (Adachi et al. 1998) but this was not the case during this study.

In the LG there were six patients with abduction (inspiring phase) and adduction (expiring phase) of the vocal cords during ventilation; which made it necessary to wait for abduction before attempting intubation. In the RG, all patients (17/17) had immobile vocal cords, which allowed EI to be performed immediately, but care must be taken due to the intermediate position of the vocal cords.

Patients from the RG did not cough. However, cats in the NAG (11/13) and the LG (6/16) groups had sustained coughing and diaphragmatic movements during EI or cuff inflation. Coughing is undesirable, since it may increase intragastric pressure (Minton et al. 1986; Libonati et al. 1985) that could increase the risk of aspiration (Libonati et al. 1985). In addition, the prevention of cough allows a smooth transition from general anesthesia with EI (Huang et al. 1998).

When evaluating the quality of EI in cats, the number of attempts needed are considered (Dyson 1988), where increasing numbers could increase the potential for laryngeal damage. In the LG all patients were intubated on the first attempt while nine patients of the RG needed more than one attempt. The reason more than one attempt was needed was related to the necessity of approaching the endotracheal tube by the glottis's ventral median plane in order to laterally displace the relaxed arytenoid cartilages and vocal cords. However, in our study, the increase in the number of attempts was not associated with laryngeal damage neither was it an inconvenience since the time spent to perform the EI was less than 12 seconds in all cases. There were no statistical differences in intubation times when comparing the three groups. However, relaxation of the skeletal musculature induced by RB requires control of ventilation, optimal tidal volume and avoidance of pulmonary atelectasis (Auer & Mosing 2006).

In summary, the results of the present study show that in terms of decreasing the airway's protective response in cats anesthetized with xylazine, tiletamine and zolazepam, rocuronium bromide at 0.6 mg kg^{-1} was as effective as 0.1 mL kg^{-1} 10% topically applied lidocaine. This suggests that rocuronium bromide could be an alternative to facilitate intubation in domestic cats, especially where topical lidocaine hydrochloride may carry a higher risk of side effects, due to the presence of laryngeal or pharyngeal pathologies. However, rocuronium bromide would not be suitable where ventilatory support is unavailable or for procedures shorter than the effect of the rocuronium.

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