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Intubation following high-dose rocuronium in a cat with protracted laryngospasm

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Abstract

Case summary An 11-year-old spayed female domestic shorthair cat with a history of laryngospasm at induction of general anesthesia presented for dental evaluation and treatment. The cat was premedicated with hydromorphone (0.05 mg/kg) and alfaxalone (0.5 mg/kg) intravenously, pre-oxygenated for 5 mins (3 l/min, face mask) and anesthesia was induced with alfaxalone (to effect) intravenously. Lidocaine (0.1 ml, 2%) was applied topically to the arytenoid cartilages following loss of jaw tone. Laryngospasm was not noted during or immediately following lidocaine application. However, after waiting 60 s for the onset of effect of the topical lidocaine, laryngospasm was apparent. Orotracheal intubation by direct visualization was unsuccessful after four attempts by three anesthetists (with increasing levels of experience). At this point, a failed intubation was declared and the non-depolarising neuromuscular blocking agent rocuronium (1 mg/kg IV) given, resulting in arytenoid abduction and appropriate conditions for intubation. Successful intubation occurred 9 mins after induction of anesthesia. Oxygen was continuously supplemented throughout and arterial hemoglobin saturation with oxygen was never <94%.

Relevance and novel information To the authors' knowledge, this is the first report of the use of high-dose rocuronium to successfully resolve prolonged laryngospasm at induction of general anesthesia in a cat. Despite laryngospasm and a delay in achieving orotracheal intubation, low values for arterial hemoglobin saturation with oxygen (indicative of hypoxemia) were not observed, highlighting the benefits of pre-oxygenation and apneic oxygenation. The principles of the Difficult Airway Society 2015 guidelines were followed in managing this difficult intubation.

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Case description

A 6.3 kg, 11-year-old, spayed female domestic shorthair cat presented with periodontal disease for dental evaluation and treatment. The cat had a history of chronic kidney disease (evaluated as IRIS stage 1) and had been prescribed a commercial renal diet. The cat was also receiving fluoxetine (1 mg/kg q24h PO) and trazodone (3 mg/kg q12h PO) to manage anxiety and aggression.

Initial examination of the oral cavity revealed significant gingivitis and mild calculus, which warranted closer examination under general anesthesia. The owners provided written informed consent for anesthesia and the procedure.

The cat had been anesthetized twice before for dental procedures at the hospital. In both instances a standard orotracheal intubation protocol was followed: pre-oxygenation with a face mask for 3–5 mins, intravenous

induction of general anesthesia, topical lidocaine applied to arytenoid cartilages, and attempted orotracheal intubation no sooner than 30 s after lidocaine application. Laryngospasm was reported at the induction of both anesthetics. In the second case, orotracheal intubation

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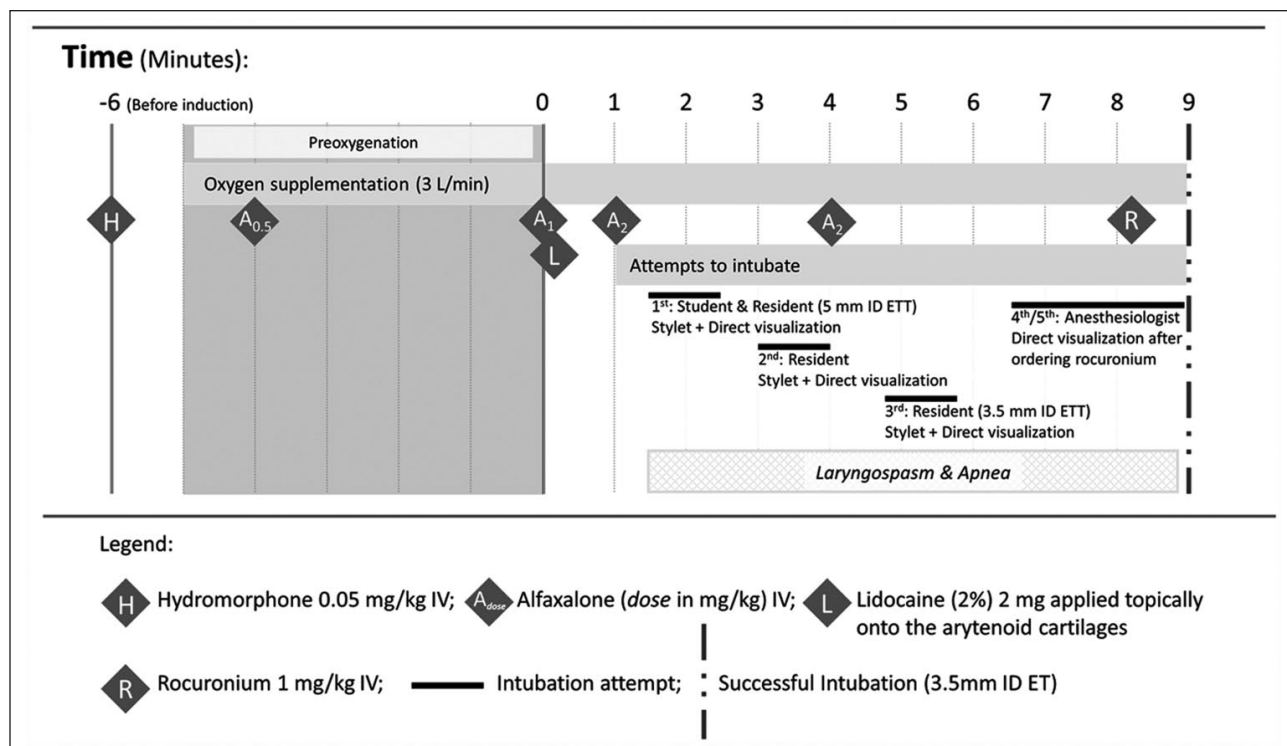


Figure 1 Timeline of events from premedication to successful intubation. Saturation determined by pulse oximetry was between 94% and 98% throughout this period. ID = internal diameter; ETT = endotracheal tube

was achieved, with a documented delay of 7 mins between the induction of anesthesia and placement of the endotracheal tube (duration of intubation not noted in the first case). Other than laryngospasm, the anesthetic procedures and recovery were uneventful.

During the currently reported case, events occurred as follows (Figure 1). The cat was initially premedicated with hydromorphone (Hydromorphone HP 10; Sandoz [0.05 mg/kg IV]) through a cannula placed in a cephalic vein. This was followed by alfaxalone (Alfaxan; Jurox [0.5 mg/kg IV]) 2 mins later, to provide a moderate level of sedation, allow pre-oxygenation and begin physiologic monitoring (electrocardiography, arterial blood pressure measurement [oscillometric technique] and pulse oximetry [probe placed across pelvic digital pad]). Following 5 mins of pre-oxygenation with a face mask (100% oxygen, 3 l/min), a further 1 mg/kg alfaxalone was given IV and lidocaine (Lurocaine 2%; Vétroquinol [0.1 ml, 2%]) was applied topically to the arytenoid cartilages under direct visualization (jaw tone absent). Full and symmetrical abduction and adduction of the arytenoids was observed during inspiration and expiration, respectively, during and after lidocaine application. To allow sufficient time for the lidocaine to take effect, pre-oxygenation continued for another 60 s. The cat had a subjectively normal respiratory rate (rate not recorded) and effort during this time.

Orotracheal intubation was attempted following additional alfaxalone, given until loss of palpebral reflexes

(2 mg/kg IV), with a 5 mm internal diameter (ID) endotracheal tube (same size as placed previously, with a small amount of sterile lubricant applied to the external surface). Given the history of difficult intubation, a catheter (5 Fr Red rubber catheter; Bard Medical) was prepared as a stylet for the first intubation attempt and a Diplomate anesthetist (DP) directly supervised the procedure.

Laryngospasm was apparent when visualizing the larynx during this first attempt. This was accompanied by apnea. The catheter was easily passed through the larynx by a final-year veterinary student, but the endotracheal tube (manipulated by an anesthesia resident, under direct visualization) could not be guided through the laryngeal opening. Additional alfaxalone (1 mg/kg IV) was administered to deepen the plane of anesthesia and a second intubation attempt was made, by the resident alone. Again, the red-rubber catheter was easily placed, but laryngospasm persisted and intubation with the endotracheal tube was not possible. The attempt was abandoned and oxygen provided by face mask while a 3.5 mm ID endotracheal tube was prepared. Another bolus of alfaxalone (2 mg/kg IV) was given and intubation was attempted using the 3.5 mm ID tube with the catheter stylet. This was unsuccessful.

At this point the Diplomate anesthetist evaluated the airway and ordered the neuromuscular blocking (NMB) agent rocuronium (Rocuronium Bromide Injection; Hospira [1 mg/kg]) to be prepared. During

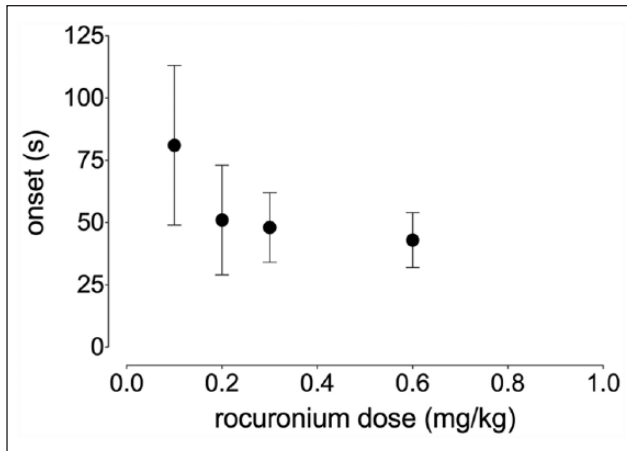


Figure 2 Plot of time to onset of neuromuscular blockade (defined as maximal reduction in first twitch of train-of-four) at four doses of rocuronium (intravenously) in healthy adult cats. From Martin-Flores et al.⁴ Data are mean \pm SD ($n = 8$)

this preparation (<30 s), a brief attempt at intubation was made before the face mask was reapplied. Rocuronium was given IV and, approximately 45 s following its administration, the arytenoid cartilages were abducted and orotracheal intubation was achieved with a 3.5 mm ID endotracheal tube (no stylet). Intubation was completed 9 mins after the induction of general anesthesia. At no point during the intubation attempts did the cat show cyanosis or desaturate (pulse oximeter readings were between 94% and 98%). During the intubation attempts, apart from the occasional inspiratory effort (accompanied by a wheeze, reflecting airway obstruction), the cat was apneic.

The cat was connected to an anesthetic machine with a coaxial Bain breathing system and anesthesia maintained with isoflurane carried in oxygen. Manual positive pressure ventilation began immediately after connection to the breathing system and the first displayed value of expired CO_2 (sidestream capnography) was 60 mmHg.

Manual ventilation was subjectively difficult initially and compliance appeared to be reduced. Thoracic radiography (single lateral view) revealed atelectasis and insertion of the endotracheal tube to the level of the tracheal bifurcation. The endotracheal tube was retracted approximately 2 inches and two metered doses (200 μg) of salbutamol (Ventolin; GSK) were given via the endotracheal tube. Following transfer of the cat to dentistry, the endotracheal tube was replaced with a larger tube (5 mm ID). After these interventions, resistance to manual ventilation reduced. At this point, mechanical positive pressure ventilation was started (tidal volume; 10 ml/kg peak inspiratory pressure; 10 cmH_2O respiratory rate; 12 breaths per minute) to maintain an expired CO_2 of approximately 30 mmHg (assuming an

under-estimation of arterial CO_2 by capnography). Total anesthesia time was 2.5 h, after which a visual train of four (TOF) evaluation indicated a return of all four twitches and reversal of the NMB agent was not performed. Recovery was uneventful.

Discussion

This case report describes the successful use of high-dose rocuronium to facilitate orotracheal intubation in a cat with laryngospasm. Additionally, this case illustrates application of the principles of the Difficult Airway Society 2015 guidelines for management of difficult intubation, averting a 'can't intubate, can't oxygenate' scenario.¹

Laryngospasm is a common complication encountered when intubating cats. Physical, chemical and thermal stimulation of the larynx and upper airway can produce this reflex, though the trigger in this case was unknown.² Both topical lidocaine and intravenous rocuronium have been shown to be similarly effective in facilitating tracheal intubation in cats where initial attempts to intubate were unsuccessful.³

The dose of rocuronium used in this report, 1 mg/kg, is higher than that reported in the feline literature (0.1–0.6 mg/kg) for intubation/laryngospasm.^{3,4} This dose was selected to achieve a rapid and complete neuromuscular blockade to quickly resolve laryngospasm. In people, a high dose of rocuronium (3–4 times the 95% effective dose [ED_{95}]) is used when rapid relaxation of the larynx is desired.^{1,5,6} A dose-finding study in cats observed a trend to faster onset of effect and reduced inter-individual variability (improved consistency) with increasing rocuronium doses (0.1–0.6 mg/kg), and visual examination of these data suggests that higher doses may result in a faster onset of effect (Figure 2).⁴ The ED_{90} of rocuronium in cats has been variably reported as 0.09–0.25 mg/kg.^{7,8} High doses of rocuronium have not been clinically evaluated in cats, though an experimental study using an intravenous dose of 1.5 mg/kg reported a duration of action (until recovery of 75% of a twitch response) of approximately 30–40 mins.⁸ With the knowledge and equipment to provide mechanical ventilation, monitor NMB, and access to a reversal agent, it was felt that any increase in duration of blockade was an acceptable adverse effect given the alternatives of creating a 'can't intubate, can't oxygenate' scenario or performing a tracheostomy.

The time to achieve adequate intubation conditions in this report (approximately 45 s) is similar to that reported with a dose of rocuronium of 0.6 mg/kg (IV, mean \pm SD 43 \pm 11 s), though a direct comparison of these onset times is limited as the outcome measures were different (subjective evaluation of laryngeal abduction in this case vs depression of twitch response from the fibular nerve).⁴ It has been suggested that the laryngeal muscles are

more resistant to the effects of rocuronium than fibular or radial nerves, which could explain the apparent similarity in onset time between the reported case and earlier work.^{4,6} In contrast, a feline study using subjective evaluation of intubating conditions as an outcome found a slower time to peak effect (60 s) with 0.6 mg/kg rocuronium IV.³ Furthermore, arytenoid cartilage position was classified as 'intermediate' at this dose,³ with apposition of the vocal folds.⁴ Together, these results suggest that evaluation of higher doses of rocuronium (3–4 times the ED₉₅) in cats is warranted.

Reversal of the NMB agent was not performed in this case as visual evaluation of the TOF response suggested the return of normal function; however, this is a controversial area of practice as current human guidelines suggest reversal of NMB agent as a standard of care.^{9,10} This is based on difficulty assuring adequate laryngeal and respiratory function in the presence of an apparently normal TOF response (visual evaluation is imprecise), with an associated risk of pneumonia. It was felt that 2.5 h after rocuronium administration, the likelihood of residual blockade was low. The clinical duration of rocuronium in people increases approximately three times, from 24 to 67 mins, as the dose is increased three-fold (from 0.4 to 1.2 mg/kg [four times the ED₉₅]).⁶ Extrapolating from available feline data and assuming a similar linear relationship between dose and duration, the mean \pm SD clinical duration of 0.6 mg/kg of rocuronium is reported as 18.3 ± 2.4 mins, so the dose used in this case could be expected to last approximately 40 mins.^{4,8} The cat was continuously monitored from extubation until the return of sternal recumbency. As a precaution against laryngospasm following extubation, materials necessary to induce anesthesia and perform orotracheal intubation were prepared before removal of the endotracheal tube.

During attempts to intubate, desaturation was not observed. Two factors are likely to have contributed to this outcome: pre-oxygenation and apneic oxygenation. Pre-oxygenation increases physiologic stores of oxygen by replacing nitrogen with oxygen and this reservoir of oxygen delays the time to hypoxemia. Pre-oxygenation is recommended in cases where prolonged or difficult intubation is anticipated.¹¹ In dogs, preoxygenation (100% O₂) for 3 minutes prolongs the time to desaturation (< 90% arterial hemoglobin saturation) by approximately 5 minutes, compared to 1 minute with room air.¹² Apneic oxygenation is a technique for providing oxygen in the presence of apnea. During apnea, a negative pressure is created in the alveoli as oxygen is absorbed. This draws gas down the pressure gradient from the upper to the lower airways. If gas in the upper airway is 100% oxygen, the pressure gradient is maintained, supporting oxygenation.^{13,14} However, without ventilation, CO₂ accumulates,

causing respiratory acidosis.^{13,14} The authors postulate that the stylet may have maintained a small opening between the arytenoids that, when combined with the occasional inspiratory effort, supported oxygenation of the cat but was insufficient to allow removal of CO₂, explaining the observed hypercapnia immediately following intubation.

Managing an unanticipated difficult tracheal intubation is a potentially life-threatening situation. While the Difficult Airway Society 2015 guidelines algorithm does not directly apply to veterinary species (Figure 3), as NMB to facilitate intubation is not usually necessary and supraglottic airway devices (SAD) are only available for a few species, the authors found the principles of approaching difficult airway management, as described in the guidelines, to be invaluable. These principles are: planning airway management (including pre-oxygenation), clear communication, early recognition and declaration of problems, and timely progress to a successful outcome. This approach facilitates decision-making under difficult circumstances, in the presence of cognitive overload, and thereby avoid fixating on a technical task (eg, placing an endotracheal tube) rather than the overall goal, which is to maintain oxygenation throughout and minimize trauma from repeated intubation attempts. In this case, a catheter guide was prepared in advance, the number of attempted intubations limited to four attempts (as per the guidelines), failed intubation was declared before hypoxemia occurred and the alternative plan (NMB) instituted. Had intubation failed following NMB, a SAD would have been placed, leading to the 'Stop and think' step of the algorithm, with the possibility of allowing the patient to recover (following reversal of the NMB agent) or proceeding with a tracheostomy (Figure 3). A feline-specific SAD (v-gel; Docsinnovent) was available but was not placed before giving a NMB agent as it would not have corrected the laryngospasm. A tracheostomy was briefly considered, but it was felt that the time to prepare and perform a tracheostomy was longer than the speed of onset of rocuronium. Pre-oxygenation was fundamental in allowing the necessary time for the interventions and contributed to a positive outcome. The authors encourage readers to review Figure 3 and the accompanying paper,¹ and consider how they might proceed under similar circumstances, with the equipment and drugs available to them.

There are several potential areas for improvement in the management of this case. Better tracking of time may have reduced the time to intubation. While a student did successfully pass the catheter initially, and was directly assisted by a resident, perhaps the outcome would have been different had a more experienced anesthetist attempted intubation initially. Given the anesthetic history, NMB without applying topical lidocaine may have prevented laryngospasm and facilitated earlier

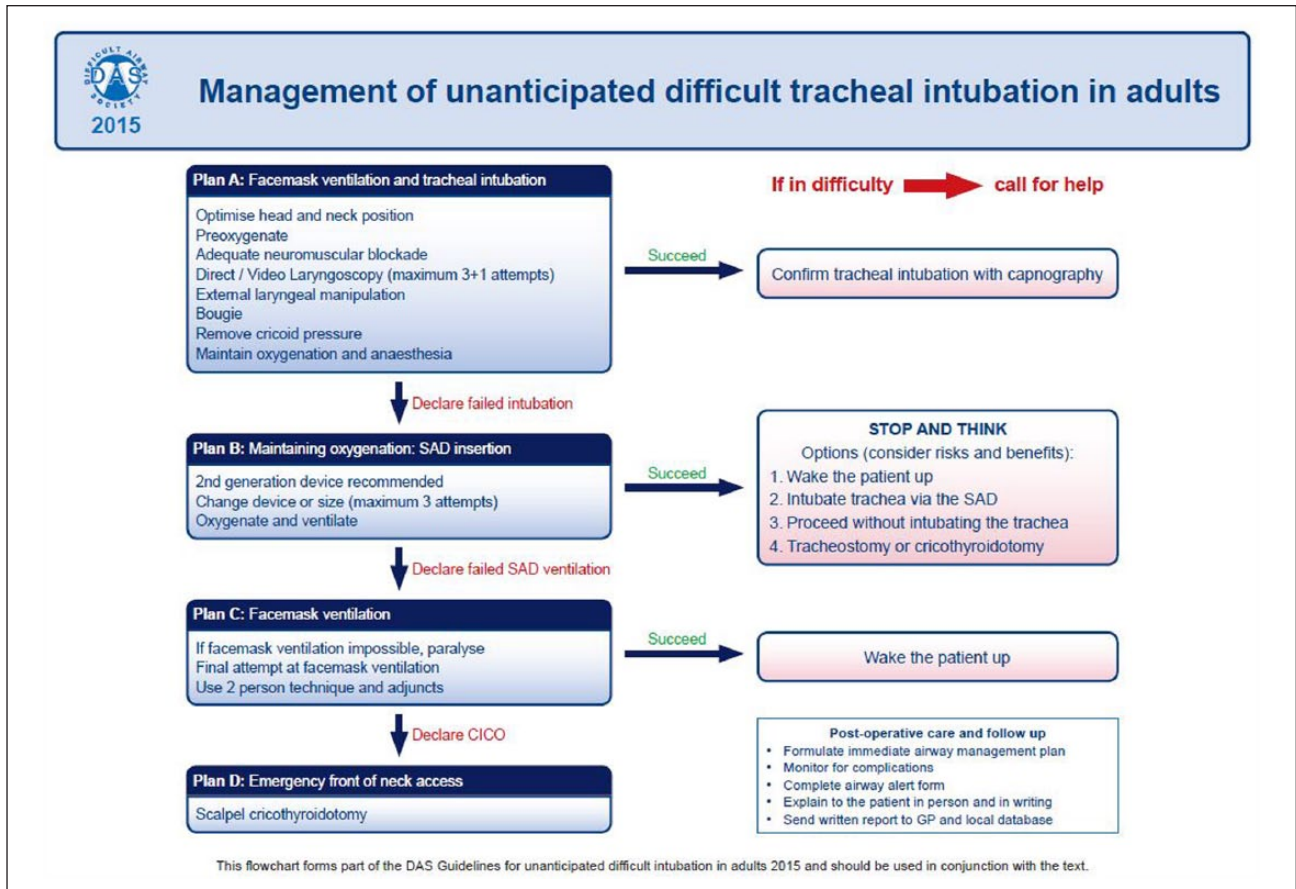


Figure 3 Management of unanticipated difficult tracheal intubation in adults. Reproduced from: Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults¹

intubation. Potential endobronchial intubation could have been avoided by premeasuring the insertion depth of the endotracheal tube to the thoracic inlet (incisors to the point of the shoulder).

Conclusions

This case appears to be one of the rare instances where standard airway-management techniques were unsuccessful. Rocuronium 1 mg/kg successfully and rapidly achieved conditions for orotracheal intubation, following a prolonged period of laryngospasm with multiple, unsuccessful intubation attempts. Pre-oxygenation and apneic oxygenation maintained oxygenation during the time taken to secure an airway. The principles of a human difficult airway management algorithm were successfully applied and are likely to have contributed to a successful outcome. The development of a feline-specific difficult airway algorithm would be beneficial in guiding management of difficult intubations.

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