AEJ ANESTHESIA EJOURNAL
Volume 8- No. 9 2020

Rocuronium vs Succinylcholine: Emergency Airway Management of the COVID-19 Patient

Ryan Shores, DNP, CRNA*
Katherine Fowler, DNP, CRNA*
John McDonough, EdD, Dr. (habil) NSA, CRNA, APRN*
Amy Suralis, DNP, CRNA*
Denise Schindele, BA, CCRN, RNA*^
Tilmann Müller-Wolff, MA, BSc, RNA, CCRN*^

Affiliation:
**University of North Florida*
^Klinikum Ludwigsburg, Germany

Funding/Conflict of Interest Disclosure:
None

KEYWORDS: COVID-19, Airway management; Rapid sequence induction; Rocuronium; Succinylcholine

Abstract

Severe acute respiratory syndrome-coronavirus-2 (SARS CoV-2) infection leading to the COVID-19 pandemic has created a new paradigm and challenge for airway management. Anesthesia providers perform tracheal intubation in a variety of settings where the best possible approach and plan for tracheal intubation is determined including patient anatomy, pathophysiology and urgency. SARS CoV-2 is a highly contagious RNA virus that has caused widespread infections, severe respiratory disease, and deaths. The purpose of this article is to describe current international standards of COVID-19 airway management, review the multi-system pathophysiology of COVID-19 patients, as well as evidence-based pharmacologic options available for intubating COVID-19 patients. This review supports rapid sequence induction with minimal airway manipulation using rocuronium 1.2-1.5 mg/kg with an option of sugammadex (16 mg/kg) reversal as a safer and superior choice to succinylcholine.

INTRODUCTION

Severe acute respiratory syndrome-coronavirus-2 (SARS CoV-2) infection leading to the COVID-19 pandemic has created a new paradigm and challenge for airway management. Anesthesia providers perform tracheal intubation routinely in a variety of settings where the best possible approach and plan for tracheal intubation is determined including patient anatomy, pathophysiology and urgency. SARS CoV-2 is a highly contagious RNA virus that has caused widespread infections, severe respiratory disease, and deaths.[1] A study conducted in Lombardy, Italy revealed that 88% of COVID-19 patients who were critically ill needed mechanical ventilation.[14] In Italy, March 2020 up to 15% of all COVID-19 infected individuals were active healthcare staff.[4] Alternative and safer airway management techniques must be used. In order to protect and prevent more healthcare providers from becoming infected with COVID patients needing airway management have been preferentially intubated, initiating full ventilator support and then placed in the prone position for twelve hours per day to improve oxygenation and alveolar recruitment.[4-6]

The American Association of Nurse Anesthetists (AANA), American Society of Anesthesiologists (ASA), and Anesthesia Patient Safety Foundation (APSF) suggest using rapid sequence induction (RSI) for endotracheal intubation in COVID-19 patients.[7,8] The RSI technique for COVID-19 patients includes a sedative-hypnotic and rapid-acting muscle relaxant. Some practitioners recommend the use of ketamine 1-2 mg/kg to enhance bronchodilation.[7] Muscle relaxation during RSI can be achieved with succinylcholine or rocuronium. Choice of drug for muscle relaxation during RSI is multifactorial in COVID patients. Obviously a drug with a rapid onset is desired after full preoxygenation and denitrogination.[7,8] The other primary consideration is the ability to reverse and/or recover from muscle relaxation in the event tracheal intubation is unsuccessful. Succinylcholine is rapidly metabolized by plasma pseudocholinesterase and does not need a reversal agent.[9] Rocuronium has a longer duration of action. Without reversal, an RSI intubating dose (1.2 mg/kg) would result in extended paralysis.[10] The reversal agent sugammadex, specific for rocuronium and vecuronium, can provide rapid recovery of muscle relaxation even with larger doses of rocuronium.[11] This article will discuss existing evidence supporting the merits of a pharmacologic plan utilizing rocuronium with sugammadex reversal in lieu of succinylcholine when providing endotracheal intubation in the COVID-19 patient population.

REVIEW OF LITERATURE

CINAHL, PubMed, and Cochrane Database of Systematic Reviews were searched using key words, *rapid sequence induction*, *COVID, SARS-CoV-2, rocuronium, succinylcholine, sugammadex, and airway management*. Inclusion criteria included prospective and retrospective articles that evaluated rocuronium and succinylcholine for onset times and/or recovery. Additional relevant literature included recent data analyses, monographs, case analyses, and guidelines specific to COVID.

SARS-CoV-2 Pathophysiology and Respiratory Compromise

SARS CoV-2 emerged in press headlines December 2019 due to the aggressive pneumonia outbreak in Wuhan, China.[1] This pneumonia progressed to severe adult respiratory distress syndrome (ARDS) and was highly communicable. By March 11, 2020 the virus had spread to over 100 countries. The World Health Organization (WHO) declared SARS CoV-2 a pandemic and named the disease COVID-19.[1]

The SARS-CoV-2 virus is known for causing severe acute respiratory symptoms (eg, dry cough, dyspnea, adult respiratory distress syndrome (ARDS).[12] The virus gains access into the host through angiotensin converting enzyme 2 (ACE2) receptors in the pulmonary epithelium.[13] Once SARS-CoV-2 enters the alveolar epithelium, it elicits an intense inflammatory response that can lead to pneumonia, and in many cases ARDS. There are several host factors that make certain people more susceptible to a severe form of the disease. These include increased age, and comorbidities such as hypertension, chronic kidney disease, cardiovascular disease, and diabetes.[13–15] One of the unique factors of SARS-CoV-2 is that it has a long incubation period, up to 14 days.[12] Most people start with symptoms of dry cough, malaise, and fever. [12,16] Dyspnea usually develops days after first symptoms emerge, and progresses to pneumonia and ARDS quickly thereafter.[17]

SARS-CoV-2 can affect other organ systems as well. One of the most common complications is acute renal insufficiency, in as many as 20-30% of patients with severe SARS-CoV-2.[15,17] The cause of this is multifactorial, including cytotoxic effects of viral accumulation in the renal tissue after entrance in circulation, possibly through renal ACE2 receptors, deposits of inflammatory mediators in the kidney, and end-organ effects of hypoxia, shock, and rhabdomyolysis.[13] In a study by Cheng et al, 15% of patients admitted to the hospital diagnosed with COVID-19 had new elevated baseline serum creatinine level ranging up to 359 micromoles/liter. The authors concluded that the mortality for all patients with COVID-19 was 12.5% but those with elevated serum creatinine increased to 30.9% .[13]

Pharmacology of Muscle Relaxants and Reversal

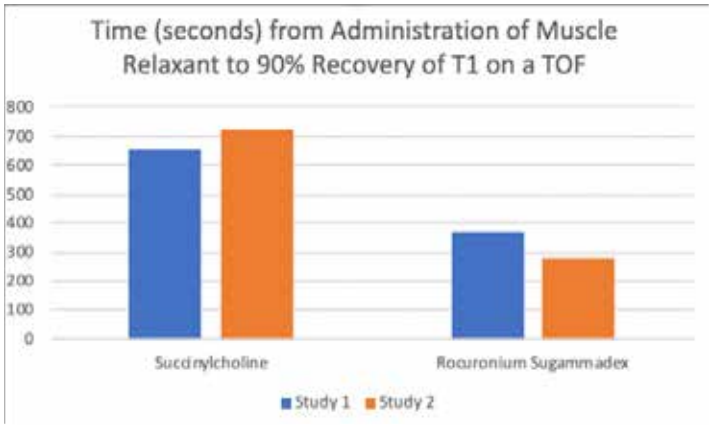
Because of increased likelihood of acute renal injury in this population, succinylcholine should be avoided as part of RSI and endotracheal intubation.[18] Rapid sequence induction can be accomplished with the use of high dose rocuronium (1.2 to 1.5 mg/kg). Succinylcholine is a depolarizing skeletal muscle relaxant that has been used by anesthesia providers since 1952 for endotracheal intubation.[9] It binds, as an agonist, to nicotinic receptors at the neuromuscular junction resulting in temporary flaccidity of striated muscles. It is rapidly hydrolyzed by plasma pseudocholinesterase into succinylmonocholine, within 4-6 minutes. This time can be extended by drug-drug interactions, or if the patient has a deficiency in pseudocholinesterase. The likelihood of this deficiency is low (1:2500).[9] It is also well-known that succinylcholine can produce acute lethal hyperkalemia leading to ventricular tachycardia and fibrillation in certain populations (eg, active infection, paralysis, or immobility) and is a trigger for malignant hyperthermia leading to death if untreated.[9] As many COVID patients suffer from acute renal injury, lethal hyperkalemia could be possible.

Rocuronium, an aminosteroidal nondepolarizing neuromuscular blocking agent, is another choice commonly used by anesthesia providers for endotracheal intubation. It antagonistically attaches to nicotinic receptors, preventing acetylcholine binding, thereby preventing muscle cell depolarization.[10] Rocuronium is primarily metabolized in the liver and undergoes biliary excretion. Rocuronium does not have the precautions or contraindications that are unique to succinylcholine. The recommended dose producing standard intubating conditions is 0.6 mg/kg, however intubating conditions have been reported as suboptimal and unpredictable.[10] Administration of 1.2 mg/kg of rocuronium is recommended for optimal RSI intubating conditions however muscle relaxation can exceed 60 minutes .[10] Reversal with an anticholinesterase such as neostigmine would be ineffective at this higher dose, but could be achieved with sugammadex. Sugammadex is a modified gamma cyclodextrin. It binds to rocuronium and to a lesser degree vecuronium, to form a complex that can no longer actively bind to nicotinic receptors. The complex molecule is excreted unchanged in the urine without affecting acetylcholine concentrations. A sufficient dose of sugammadex (16 mg/kg to reverse a rocuronium dose of 1.2 mg/kg) delivers a sufficient and complete reversal.[11] Sugammadex: rocuronium binding is 1:1, so dosing in the presence of COVID would be unaffected.[11]

COVID-19 Intubation Pharmacologic Plan

Current literature supports rapid sequence induction with minimal or no manual positive pressure ventilation is preferred over standard induction techniques.[7]which causes coronavirus disease 2019 (COVID-19.[8] The choice of muscle relaxant during RSI is primarily determined by a need for a rapid onset of quality intubating conditions. A recent 2015 Cochrane systematic review comparing succinylcholine to rocuronium determined that rocuronium was "slightly less effective than succinylcholine for creating excellent and acceptable intubation conditions."[20] Most studies included in the systematic review compared succinylcholine to a rocuronium dose closer to the standard intubating dose of 0.6mg/kg. However, sugammadex provided rapid and complete reversal of even higher doses of 1.2 mg/kg.[11] More recent studies have indicated no significant differences in time to intubation, vocal cord movement, or patient movement when rocuronium doses of 1.2 mg/kg are utilized.[21-24] Evidence suggests that a rocuronium-sugammadex combination would also improve recovery time compared to succinylcholine alone. A 2010 systematic review found significant improvement in recovery time using rocuronium-sugammadex compared to succinylcholine (p<0.0001) (See Figure 1).[26] Another study examining 110 adults ages 18-65 undergoing general anesthesia, compared succinylcholine 1 mg/kg to rocuronium 1.2 mg/kg from induction administration to full recovery when sugammadex was utilized for reversal. Individuals in the rocuronium group were given sugammadex 16 mg/kg three minutes after rocuronium administration. End point measures were a T4 of 10% and 90% of the T1 on a train of four measurement with accelerometry. Succinylcholine mean recovery times were 7.1 and 10.9 minutes. The rocuronium/sugammadex group was 4.4 and 6.2 minutes. It was important to note that the study included a three minute wait before administering sugammadex, which indicated that recovery endpoints were reached at an average of 1.4 and 3.2 minutes once sugammadex was administered.[23] Another randomized, controlled, double-blinded study compared succinylcholine 1 mg/kg to rocuronium 1 mg/kg in 61 adults ages 18-60 requiring rapid sequence induction. Patients were given rocuronium, then sugammadex 16 mg/kg was administered as soon as tracheal intubation was achieved. Primary measures were duration from tracheal intubation to return of spontaneous ventilation and T4 return of 90% of T1. Average time for the succinylcholine group was 406 seconds for return of spontaneous ventilation and 518 seconds for T1=90%. Average time for the rocuronium/sugammadex group was 216 seconds for return of spontaneous ventilation and 168 seconds respectively. It is important to note that when comparing the time from muscle relaxant administration to T1=90%, the mean times were 719 seconds for the succinylcholine group and 282 seconds for the rocuronium/sugammadex group.[24]

Figure 1. Time (seconds) from Administration of Succinylcholine or Rocuronium/sugammadex to 90% Recovery of T1 on a Train of Four (TOF)



Note: Time from administration of rocuronium to administration of sugammadex was 180 seconds in Study 1 and 114 seconds in Study 2

CONCLUSION

This literature review suggests that patients with SARS-CoV-2 could benefit from a pharmacologic intubation plan that includes RSI using rocuronium 1.2 mg/kg with sugammadex 16 mg/kg. Current literature is limited by small sample sizes and lack of high-quality studies. Other considerations include the availability of sugammadex and provider comfort with these agents. In some cases, patients emergently intubated are done so by non-anesthesia personnel with limited knowledge of both the pharmacologic implications of commonly used medications and disease process of SARS-CoV-2. The evidence in this review should be considered when determining implications of the pharmacologic plan on outcome of intubating patients with SARS-CoV-2.

REFERENCES

1. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. JAMA. 2020;323(18):1843-1844. doi:10.1001/*JAMA*.2020.3786
2. Westhoff M, Schönhofer B, Neumann P, et al. Noninvasive mechanical ventilation in acute respiratory failure. *Pneumologie*. 2015;69(12):719-756. doi:10.1055/s-0034-1393309
3. Dubb R, Kaltwasser A M-WT. Maschinelle Beatmung und NIV. *Anästhesie Und Intensivmedizin Für Die Fachpflege*. 2016;745-795. doi:10.1007/978-3-662-50444-4_56
4. Arndt D, Heininger S, Hinzmann D, et al. Schutz und Erhalt der psychischen Gesundheit von Mitarbeitern in notaufnahmen und auf intensivstationen während der COVID-19-Pandemie. *Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin (DIVI)*. 2020;2:54-64.
5. Kluge S, Janssens U, Welte T, Weber-Carstens S, Marx G, Karagiannidis C. Recommendations for critically ill patients with COVID-19. *Medizinische Klin - Intensivmed und Notfallmedizin*. 2020;115(3):175-177. doi:10.1007/s00063-020-00674-3
6. Schwabbauer N, Berg B, Blumenstock G, Haap M, Hetzel J, Riessen R. Nasal high-flow oxygen therapy in patients with hypoxic respiratory failure: Effect on functional and subjective respiratory parameters compared to conventional oxygen therapy and non-invasive ventilation (NIV). *BMC Anesthesiol*. 2014;14(1):1-7. doi:10.1186/1471-2253-14-66
7. Cook TM, El-Boghdadly K, McGuire B, McNarry AF, Patel A, Higgs A. Consensus guidelines for managing the airway in patients with COVID-19: Guidelines from the Difficult Airway Society, the Association of Anaesthetists the Intensive Care Society, the Faculty of Intensive Care Medicine and the Royal College of Anaesthetists. *Anaesthesia*. 2020;75(6):785-799. doi:10.1111/anae.15054
8. ASAHQ. Intubation in COVID-19. https://www.asahq.org/in-the-spotlight/coronavirus-covid-19-information/caesar. Updated February 2, 2020. Accessed April 13, 2020.
9. FDA. Anectine ® (Succinylcholine Chloride Injection,USP). 2018;37(Iv):433-458. Accessed March 3,2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/008453s027lbl.pdf
10. TEVA. Package insert Rocuronium Bromide Injection. http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/078717s000lbl.pdf. Updated February 2, 2008. Accessed April 13, 2020.
11. Package insert Sugammadex. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022225lbl.pdf. Updated February 1, 2015. Accessed April 13, 2020.
12. Park SE. Epidemiology, virology, and clinical features of severe acute respiratory syndrome -coronavirus-2 (SARS-CoV-2; Coronavirus Disease-19). *Clin Exp Pediatr.* 2020;63(4):119-124. doi:10.3345/cep.2020.00493
13. Cheng Y, Luo R, Wang K, et al. Kidney impairment is associated with in-hospital death of COVID-19 patients. medRxiv. https://doi.org/10.1101/2020.02.18.20023242. Updated February 20, 2020. Accessed March 2, 2020.
14. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. *JAMA*. 2020;323(16):1574-1581. doi:10.1001/jama.2020.5394
15. Disease EK, Palevsky APM, Radhakrishnan J, Townsend RR. Coronavirus disease 2019 (COVID-19): Issues related to kidney disease and hypertension. https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-issues-related-to-kidney-disease-and-hypertension. Updated June 16, 2020. Accessed March 3, 2020.
16. Centers for Disease Control and Prevention. Symptoms of coronavirus. CDC. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html. Updated February 8, 2020. Accessed April 12, 2020.
17. Anesi GL. Coronavirus disease 2019 (COVID-19): Critical care and airway management issues. UpToDate. https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-critical-care-issues/print?search=neumonía en el embarazo&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2. Updated February 1, 2020. Accessed March 28, 2020.
18. London AMJ. Coronavirus disease 2019 (COVID-19): Anesthetic concerns, including airway management and infection control. https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-patients-airway-management-anesthesia-machine-ventilation-and-anesthetic-care/print?search=coronavirus&source=search_result&selectedTitle=7~150&usage_type=default&display_rank=7. Updated February 1, 2020. Accessed April 12, 2020.
19. Martyn JAJ, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic States. *Anesthesiology*. 2006;104(1):158-169. doi:10.1097/00000542-200601000-00022
20. Dtt T, Ek N, Vah M, Js L, Ga W, Jj P. Rocuronium versus succinylcholine for rapid sequence induction intubation. *Cochrane Database Syst Rev.* 2015;2015(10):CD002788. doi:10.1002/14651858.CD002788.pub3.Copyright

21. Patanwala AE, Stahle SA, Sakles JC, Erstad BL. Comparison of succinylcholine and rocuronium for first-attempt intubation success in the emergency department. *Acad Emerg Med*. 2011;18(1):10-14. doi:10.1111/j.1553-2712.2010.00954.x
22. Perša L, Kamenik M, Nevenka, Škvarč K, Mekiš D. Rocuronium versus succinylcholine for rapid sequence intubation in patients with bowel obstruction. *Signa Vitae.* 2019;15(2):52-58. doi:10.22514/SV152.102019.8
23. Lee C, Jahr JS, Candiotti KA, Warriner B, Zornow MH, Naguib M. Reversal of profound neuromuscular block by sugammadex administered three minutes after rocuronium: A comparison with spontaneous recovery from succinylcholine. *Anesthesiology.* 2009;110(5):1020-1025. doi:10.1097/ALN.0b013e31819dabb0
24. Sørensen MK, Bretlau C, Gätke MR, Sørensen AM, Rasmussen LS. Rapid sequence induction and intubation with rocuronium-sugammadex compared with succinylcholine: A randomized trial. *Br J Anaesth*. 2012;108(4):682-689. doi:10.1093/bja/aer503
25. Malhotra S. Practice Guidelines for Management of the Difficult Airway. *Pract Guidel Anesth.* 2016;(2):127-127. doi:10.5005/jp/books/12644_18
26. Chambers D, Paulden M, Paton F, et al. Sugammadex for reversal of neuromuscular block after rapid sequence intubation: A systematic review and economic assessment. *Br J Anaesth.* 2010;105(5):568-575. doi:10.1093/bja/aeq270