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IMPACT OF ROCURONIUM AND SUCCINYLCHOLINE ON SEDATION INITIATION AFTER RAPID SEQUENCE INTUBATION

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□ **Abstract—Background: Rapid sequence intubation (RSI) involves a rapidly acting sedative plus a neuromuscular blocking agent (NMBA) to facilitate endotracheal intubation. Rocuronium and succinylcholine are NMBAs commonly used in RSI with drastically different durations of action. Objectives: Evaluate whether patients receiving RSI with a longer-acting NMBA had a greater delay in sedation or analgesia than patients that received a short-acting NMBA. Methods: This was a retrospective review of patients presenting to the emergency department requiring endotracheal intubation. Exclusions included age < 18 years, pregnancy, prior intubation, and contraindication to sedation and analgesia. Primary endpoint was time to continuous sedation or analgesia after RSI in patients receiving rocuronium or succinylcholine. Secondary endpoints included hospital length of stay (HLOS), intensive care unit length of stay (ICU LOS), and impact of an emergency medicine pharmacist (EPh). Results: A total 106 patients met inclusion criteria, 76 patients receiving rocuronium and 30 receiving succinylcholine. Mean time to sedation or analgesia was longer in the rocuronium group when compared to the succinylcholine group at 34 ± 36 min vs. 16 ± 21 min ($p = 0.002$). In the presence of an EPh, the mean time to sedation or analgesia was 20 ± 21 min, vs. 49 ± 45 min ($p < 0.001$). Time spent on ventilator, HLOS, and ICU LOS were not significantly different between groups. Conclusions: Patients receiving rocuronium in RSI had a significantly longer time to sedation or analgesia when compared to patients receiving succinylcholine. The presence of an EPh significantly decreased the time to administration of sedation or analgesia after RSI.** © **2015 Elsevier Inc.**

□ **Keywords—rapid sequence intubation; neuromuscular blocking agent; sedation; analgesia; emergency medicine pharmacist**

INTRODUCTION

Rapid sequence intubation (RSI) is defined as the use of a rapidly acting sedative as an induction agent plus a neuromuscular blocking agent (NMBA) to create optimal conditions for endotracheal intubation (1). Two of the most commonly used NMBAs in RSI are rocuronium and succinylcholine (2). Whereas both produce a similar paralytic effect, their duration of action is dramatically different, with succinylcholine typically lasting 5–15 min, and rocuronium lasting an average of 30–60 min (3,4). In contrast, many of the rapid-acting sedatives used in RSI have a much shorter duration of action. For example, the effect of etomidate, a commonly used sedative in this scenario, has been shown to last only 3–5 min (5). This creates the potential scenario where a patient who has received rocuronium in conjunction with etomidate may remain paralyzed without sedation or analgesia if a continuous sedative or analgesia agent is not promptly initiated after RSI.

One study in a pediatric population evaluated this potential complication. The study evaluated patients receiving RSI with rocuronium as the NMBA of choice and etomidate as the induction agent. The results showed the mean

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time to postintubation sedation was 46 min, with 63.1% of the population receiving sedatives more than 15 min after intubation, and 13.1% of patients receiving no additional sedation post intubation (6). The level of sedation in their study population was not evaluated, nor was the use of analgesics. However, based on the duration of action of the NMBA and the time to initiation of additional sedation, the study supports the authors' fear of these patients potentially remaining paralyzed with no sedation. In the critical care literature, patients with inadequate pain and sedation have been shown to have increased catecholamine activity, leading to an increased risk of myocardial ischemia and infarction (7). In addition, inadequate analgesia and sedation for an intubated patient can be uncomfortable and alarming. Awareness during anesthesia is well described in the literature (8). Inadequate sedation or analgesia is a serious complication that may have ramifications that last long beyond a patient's hospital stay. A case series on patients awakening from light anesthesia while remaining paralyzed illustrated their anxiety, irritability, preoccupation with death, and repetitive nightmares after an incidence of awareness during anesthesia (8). A possible cause for a delay in postintubation sedation or analgesia may be from the false perception of comfort that a paralyzed patient displays. Whereas patients who have received a short-acting paralytic may quickly demonstrate their physical discomfort after elimination of the agent, those who have received longer-acting paralytics, such as rocuronium, may be unable to convey their discomfort and distress for a prolonged period of time.

The emergency medicine pharmacist (EPh) has been shown to play an important role in patient care in the emergency department (ED) (9). Their expert understanding of medications, including those in RSI, provides useful assistance in the timely initiation of postintubation sedation or analgesia in this critically ill population. Through their direct involvement in RSI, we anticipate an improvement in time to initiation of sedation and analgesia after RSI.

Currently, limited data exist on time-to-sedation or analgesia for patients intubated in the ED. The objective of this study is to examine the time to postintubation sedation or analgesia between patients receiving rocuronium or succinylcholine after intubation. In addition, we sought to evaluate the impact of an EPh on time to sedation or analgesia after RSI, the time of mechanical ventilation, hospital length of stay, and intensive care unit length of stay for the rocuronium and succinylcholine groups.

METHOD

Study Design

This study was a retrospective chart review performed at a tertiary care, academic medical center in Lexington, Kentucky. The site is a 650-bed, acute care, academic hospital and Level I trauma center. The yearly census for the ED exceeds 65,000 patients. An EPh is present in the ED from 1:00 p.m.–11:00 p.m. daily. This study was approved by the IRB of University of Kentucky.

Patient Selection

Patients eligible for inclusion were intubated in the ED from October 2009 through December 2012. Exclusion criteria included pregnancy, patients who were intubated prior to arrival, those with incomplete medical records, and patients who did not receive sedation or analgesia after RSI due to contraindication. Additionally, patients younger than 18 years of age were excluded, as well as patients who did not receive an NMBA during intubation.

Data Collection, Demographics and Outcome

Baseline demographic data collection included age, sex, race, weight, mechanism of injury, indication for intubation, presence of EPh, and Glasgow Coma Scale score (GCS) upon arrival (Table 1). Additional demographics collected include sedatives used in intubation, intubation attempts, and continuous sedatives and analgesics (Table 2). Analgesics or anxiolytics received while in transit to the ED were also collected. Additionally, data on the duration of mechanical ventilation, intensive care unit length of stay, and hospital length of stay were

Table 1. Patient Characteristics

Characteristic	Rocuronium n = 76	Succinylcholine n = 30	*p*-Value
Chief complaint, n (%)			
MVC	37 (48.7)	16 (53.3)	0.925
MCC	14 (18.4)	4 (13.3)	0.945
GSW	8 (10.5)	1 (3.3)	0.418
Other	17 (22.4)	9 (30)	0.567
Female, n (%)	19 (25)	17 (56.6)	0.004*
Age, mean (SD)	38.4 (15.4)	39.6 (17.2)	0.735
Race, n (%)			
White	57 (75)	22 (73.3)	0.944
African American	10 (13.1)	2 (6.7)	0.542
Hispanic	8 (10.5)	4 (13.3)	0.944
Other	1 (1.3)	2 (6.7)	0.139
EPh present, n (%)	49 (64.5)	23 (76.6)	0.327
Indication for intubation, n (%)			
AMS	1 (1.3)	3 (10)	0.122
Airway protection	53 (69.7)	12 (40)	0.021*
Combative	5 (6.6)	4 (13.3)	0.847
Other	17 (22.4)	11 (36.7)	0.208
GCS, median (IQR)	13 (6–14)	13 (7–15)	0.704
Weight, kg, mean (SD)	81.2 (16.5)	81.2 (18.7)	0.991

MVC = motor vehicle crash; MCC = motorcycle crash; GSW = gunshot wound; EPh = emergency medicine pharmacist; AMS = altered mental status; GCS = Glasgow Coma Scale score; IQR = interquartile range.
* $p < 0.05$.

Table 2. Medication Use

Characteristic	Rocuronium n = 76	Succinylcholine n = 30	*p*-Value
Sedative in RSI, n (%)			
Ketamine	6	2 (6.6)	0.676
Etomidate	58 (76.3)	24 (80)	0.597
Propofol	3 (3.9)	2 (6.6)	0.931
None	0 (0)	2 (3.3)	0.628
Midazolam	9 (11.8)	1 (3.3)	0.326
Intubation attempts, mean (SD)	1.1 (0.39)	1.3 (0.53)	0.167
Continuous sedation agent, n (%)			
Propofol	41 (53.9)	18 (60)	0.728
Midazolam	28 (36.8)	8 (30)	0.66
None	6 (7.9)	2 (6.6)	0.847
Lorazepam	1 (1.3)	2 (6.6)	0.917
Continuous analgesic agent, n (%)			
Fentanyl	22 (28.9)	10 (30)	0.897
Morphine	19 (25)	5 (16.7)	0.505
None	35 (46)	15 (50)	0.64

RSI = rapid sequence intubation.

also collected and evaluated as secondary outcomes. The primary outcome was a comparison of time to initiation of continuous sedation or analgesia after RSI in patients who received either rocuronium or succinylcholine. Time was denoted from the administration of the paralytic until the administration of the first continuous infusion sedative or analgesic postintubation.

Data Analyses

With a sample size of 100 patients, the study had an 80% power to detect a mean difference of 20 min between the two groups. The primary outcome and other continuous variables were evaluated using an unpaired Student's *t* test. Chi-squared and Fischer's exact tests were used to evaluate baseline characteristics and other dichotomous variables. All analyses were conducted to be two-sided with $\alpha < 0.05$.

RESULTS

From October 1, 2009 to December 31, 2012, 626 patients were evaluated for inclusion in the study. Eighty-two patients were found to be younger than 18 years of age, 62 patients had received paralytics prior to arrival, 333 patients had incomplete medical records, and 43 patients did not receive sedation or analgesia within a plausible time frame after RSI (Figure 1). Therefore, 106 patients were eligible for evaluation of study.

Rocuronium was the most common agent used in eligible patients, with 76 patients receiving rocuronium,

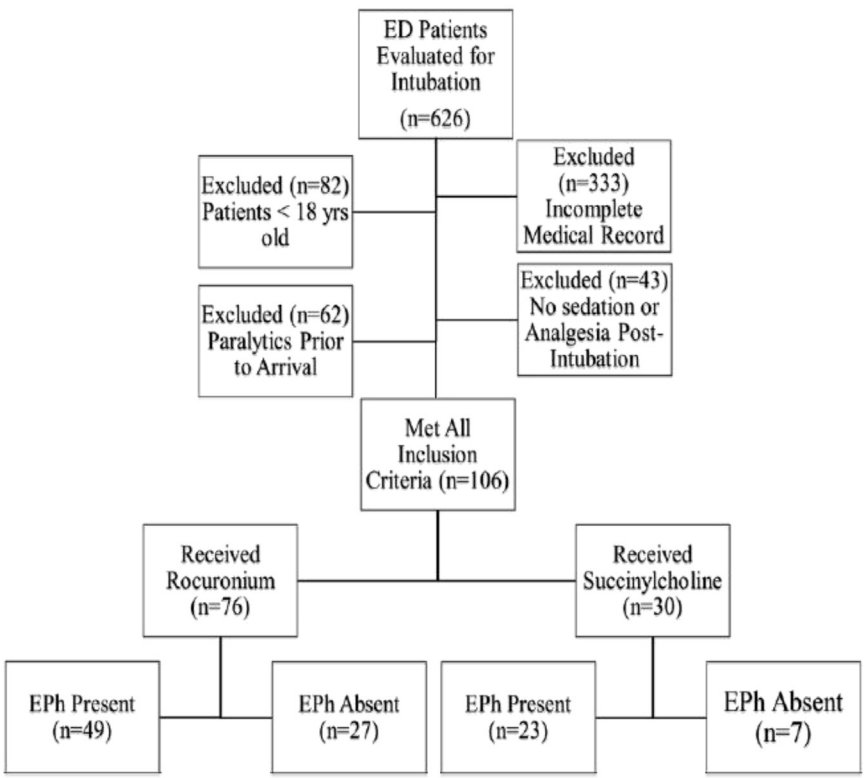

Figure 1. Patient selection. ED = emergency department; EPh = emergency medicine pharmacist.

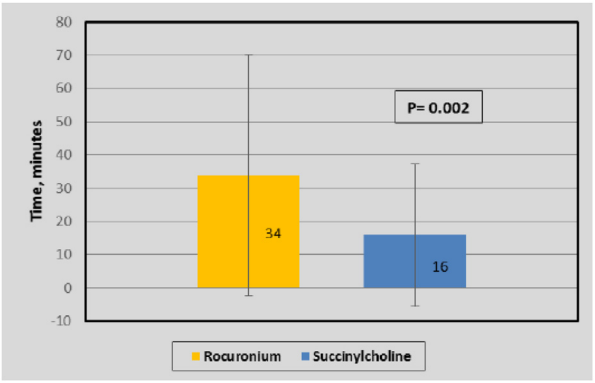

Figure 2. Mean time to sedation or analgesia: all patients.

and 30 patients receiving succinylcholine as their NMBA in RSI. The mean dose of rocuronium was 1.1 ± 0.27 mg/kg, and the mean dose of succinylcholine was 1.5 ± 0.43 mg/kg. Patients received etomidate as the induction agent in 77% (n = 83) of RSI cases. The mean dose of etomidate received was 0.3 ± 0.08 mg/kg. Other induction agents included ketamine (n = 7), propofol (n = 5), and midazolam (n = 11). The mean time to sedation or analgesia after RSI was significantly longer for the rocuronium group when compared to the succinylcholine group, with 34 ± 36 min and 16 ± 21 min, respectively ($p = 0.002$) (Figure 2). When comparing the time to sedation or analgesia for the absence and presence of an EPh, we found a significant difference. With the presence of an EPh and regardless of drug, the mean time sedation or analgesia was 20 ± 21 min, whereas in the absence, the mean time to sedation or analgesia was 49 ± 45 min ($p < 0.001$) (Figure 3). When comparing time to sedation or analgesia between rocuronium and succinylcholine in the presence of an EPh, a difference was seen, with 23 ± 22 vs. 12 ± 14, respectively ($p = 0.024$). In the absence of an EPh, the difference between rocuronium and succinylcholine was 55 ± 46 vs. 28 ± 33, respectively ($p = 0.132$). In evaluation of the rocuronium group with and without the presence of an EPh, the mean time to sedation or analgesia with EPh present was 23 ± 22, whereas in the absence, it was 55 ± 46 ($p = 0.002$).

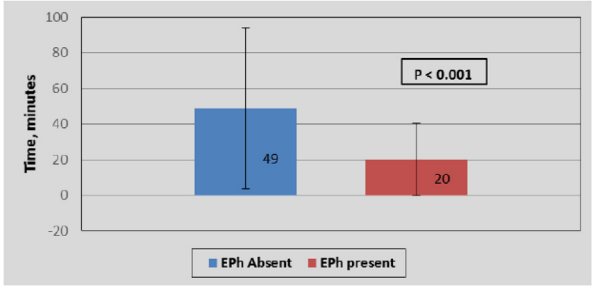

Figure 3. Mean time to sedation or analgesia: presence of an emergency medicine pharmacist (EPh).

Finally, the comparison of time to sedation or analgesia in the succinylcholine group with and without an EPh was 13 ± 14 and 28 ± 3, respectively ($p = 0.306$). The other secondary outcomes of time on ventilator, hospital, and ICU length of stay were not significant between the groups (Table 3). The mean GCS prior to intubation was 13 for both groups.

DISCUSSION

The primary outcome of this study illustrated a statistically significant difference in time to sedation or analgesia after RSI between patients who received rocuronium or succinylcholine, with the rocuronium group having a considerably greater time to sedation or analgesia than the succinylcholine group, at 34 ± 36 min vs. 16 ± 21 min ($p = 0.002$). This time difference supports our theory that the use of long-acting NMBAs like rocuronium in RSI may have adverse consequences on patients' care in the postintubation period. This time difference is consistent with the findings of Watt et al., which showed a time to sedation after RSI with rocuronium and succinylcholine to be 27 ± 29 vs. 15 ± 13 min, respectively ($p < 0.001$) (10). Health care team members may be using a patient's clinical symptoms as the queue that the induction and the paralytic have worn off, and additional sedation or analgesic medications are needed. Succinylcholine's duration of action is 5–15 min, which closely mirrors the duration of many of the induction agents. Although the goal should be to provide adequate sedation and analgesia from the time of NMBA administration forward, patients who receive succinylcholine are less likely to remain under-sedated when used in conjunction with a short-acting induction agent. Rocuronium, when dosed at 0.6 mg/kg, has a duration of action of approximately 30 min (3). However, the dose recommended for RSI is 1.2 mg/kg (11). At this dose, its duration of action approaches 60 min (3). The mean dose of rocuronium used in this study was 1.1 ± 0.27 mg/kg. With > 75% of patients receiving short-acting etomidate, it is reasonable to assume that this patient population was at risk for under-sedation and inadequate analgesia. Finally, because the mean

Table 3. Secondary Outcomes

Outcome	Rocuronium n = 76	Succinylcholine n = 30	*p*-Value
Time on ventilator, days, mean (SD)	8.2 (16.9)	5.0 (5.6)	0.314
HLOS, days, mean (SD)	20.6 (24.7)	20.5 (23.7)	0.979
ICU LOS, days, mean (SD)	9.8 (13.5)	8.3 (8.6)	0.564

HLOS = hospital length of stay; ICU LOS = intensive care unit length of stay.

GCS of the rocuronium group was 13 (6–14) upon presentation, the majority of patients were coherent prior to being intubated.

The acute intubation of a critically ill patient is a time-sensitive and high-stress situation that actively involves physicians, pharmacists, nurses, respiratory therapists, and other health care personnel. With such an emphasis placed on the securement of the endotracheal tube, post-intubation care may become an afterthought to team members involved in the intubation. However, the presence of an EPh would hypothetically improve the time to sedation or analgesia after RSI by including a team member who provides a primary focus on medications. This hypothesis was shown to be true in the current study, as there was a decreased time to sedation or analgesia for intubations occurring while an EPh was present in the ED vs. when they were absent, at 20 ± 21 min vs. 49 ± 45 min, respectively ($p < 0.001$). When evaluating patients intubated in the presence of an EPh, there is still a statistically significant difference in time to sedation or analgesia between patients that received succinylcholine or rocuronium, with their time to sedation or analgesia being 13 ± 14 and 23 ± 22, respectively ($p = 0.024$). Patients intubated in the absence of an EPh trended toward a statistical significance in time to sedation or analgesia; however, this lack of significance is likely due to low enrollment in the succinylcholine-without-EPh-presence group. This discrepancy has two possible explanations. First, there was a national shortage of succinylcholine for a period during this study interval, and many of the RSI boxes contained only rocuronium, whereas the limited supply of succinylcholine was kept in a refrigerated Pyxis station (CareFusion Corporation, San Diego, CA). Often, the EPh would obtain succinylcholine prior to the arrival of the patient and have it available to the provider if its use was indicated. In the absence of the EPh, the provider may not want to send a nurse to the Pyxis for succinylcholine, and simply just use rocuronium. Second, the presence of an EPh has been shown to help not only with medication administration, but appropriate documentation as well. A number of EPh-absent succinylcholine patients were excluded simply due to lack of adequate medication documentation in the electronic and paper charts.

Mechanical ventilation is a painful intervention and has the potential to provoke anxiety in patients (12). Literature from the critical care population illustrates that inadequate or absent sedation can increase coagulability, increase the risk of self-extubation, and lead to myocardial ischemia (7,13). These are all adverse outcomes associated with patient care, and have the ability to affect the prognosis and length of stay for a hospitalized patient. Although extensive reporting exists on the adverse outcomes associated with inadequate sedation or analgesia, there are limited data exploring the relationship between a delay in sedation or analgesia after RSI, and adverse outcomes. However, in both cases, an absence or inadequacy in sedation or analgesia is present, which has the potential to elicit similar complications. Self-extubation by the patient may result in severe hemodynamic or airway complications, including hypotension, dysrhythmias, bronchospasm, aspiration, and laryngeal bleeding (14). In one study, a patient's unplanned extubation was associated with a significantly increased risk of hospital-acquired pneumonia ($p = 0.002$) (15). This contributed to significantly longer mechanical ventilation, intensive care unit stay, and hospital stay in this patient population. Our study did not show a difference in time spent on ventilator or length of stay. However, statistical significance is not required to make this occurrence clinically significant. Inadequate sedation or analgesia is a preventable complication; thus, if a single patient incurred a prolonged stay as a result of medication delay, it is one occurrence too many.

The focus of this study was time to initiation of continuous infusion analgesics or sedatives, and did not assess patients that received only intermittent sedatives or analgesics after RSI. Intermittent bolus administration may be appropriate in patients with hemodynamic instability, as it provides analgesia or sedation for a brief period of time. Although blood pressure was not collected in this study, a hypotensive effect seen with many sedatives may give clinicians pause to initiate an agent in this patient population. The use of intermittent boluses allows clinicians to evaluate the effects on the patient's hemodynamics prior to initiating a continuous infusion agent.

This study did not assess the adequacy of continuous sedation or analgesia after RSI; rather, it only looked at the time period until it was initiated. Therefore, it cannot be assumed that once patients were initiated on sedation or analgesia, the amnestic, anxiolytic, and analgesic properties of the continuous infusion agent were optimized. Additionally, in 7.5% (n = 8) of the cases, patients received a continuous infusion analgesic alone in the immediate postintubation period. One possible explanation for this omission may have been the patients' hemodynamic instability in the immediate postintubation period. However, the use of analgesia only, or "analgosedation" is an appropriate and utilized strategy in the critically ill intubated patient (16).

Limitations

Given that this was a retrospective chart review, we relied heavily on the proper documentation of ED patients. Many of the patients in this study were critically ill upon presentation and likely required numerous nursing and health care contributions that could have potentially

detracted from proper documentation. This was evident in the large number of patients we excluded due to inadequate charting. Inadequate documentation came in numerous forms. Because the majority of patients arrived as trauma alerts, much of the charting of medications and procedures was completed on paper charting. Often, the charting would lack specific dosing and time of administration of medications, instead simply listing drug names that were administered during RSI and the postintubation period. Other times, the details of RSI medication, dose, and time of administration were very precise, but the documentation of continuous sedatives or analgesics was done without reference to time. The authors cannot explain this deficiency in charting other than to assume the nurse responsible for charting was required to participate in the care of the patient, and could not accurately complete their documentation responsibilities. Furthermore, the lapse in documentation after RSI supports the hypothesis that great emphasis and attention to detail is placed on the time up to successful endotracheal intubation, and less on the postintubation period. We struggled to enroll significant numbers of patients who presented outside the hours of the EPh. A possible explanation for this is the role the EPh plays in medication documentation. Because all medications in the ED at University of Kentucky are on override, an electronic physician order is not necessary, and verbal orders suffice. Often, adequate documentation of medications given in RSI and the postintubation period requires retroactive charting that may be forgotten by nursing, but able to be completed by the EPh. Thus, we found more frequent documentation of RSI medications when an EPh was present. Secondary outcomes of ventilator time and length of stay were not statistically significant, however, they were likely not powered to show a difference. Another limitation of the study is the assumption that patients who had a longer time to sedation or analgesia had any recollection or adverse outcome associated with this period of time. When considering a patient who has a > 30-day hospital stay for multiple trauma, it is unlikely that a 30-min period of inadequate sedation or analgesia results in clinically measurable outcomes. The most optimal way to assess this would be with patient interviews, which were not performed. Finally, we did not collect vital signs, so we cannot comment on the postintubation care and optimization of continuous infusion agents for patients outside of our study window. Future research is needed in this area, as we could not assess it based on the data collected.

CONCLUSIONS

Patients who received rocuronium for RSI in the ED have a significantly longer time to sedation or analgesia after intubation when compared to those who received succinylcholine. This puts the group that received rocuronium at an increased risk of remaining paralyzed without sedation or analgesia. Proper attention to postintubation sedation and analgesia is the responsibility of all health care individuals involved, but can be better assisted with the presence of an EPh.

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ARTICLE SUMMARY

1. Why is this topic important?

This is important because it illustrates the disconnect that providers may have by assuming that if a patient is not moving, then they are properly sedated and are experiencing no pain. Rapid sequence intubation (RSI) is a stressful and high-pressure situation, but attention to detail does not stop after successful placement of the endotracheal tube.

2. What does this study attempt to show?

This study shows us that, indeed, patients that receive a longer-acting neuromuscular blocking agent (NMBA) during RSI remain paralyzed for a longer period of time, without sedation or analgesia, than similar patients that received a short-acting NMBA. The presence of an emergency medicine pharmacist was associated with a reduction in time to administration of a continuous sedative or analgesic agent.

3. What are the key findings?

The key findings from this study are that patients receiving longer-acting NMBAs like rocuronium during RSI have a longer duration to postintubation sedation than patients receiving short-acting NMBAs like succinylcholine. This time difference is long, and mirrors the duration of action for each of the neuromuscular blocking agents. The presence of an emergency medicine pharmacist may decrease this time delay; however, it does not remove it completely.

4. How is patient care impacted?

Patient care is impacted through their delay in sedation and analgesia after RSI. During this time, the patient may experience extreme pain and discomfort. Due to the use of a longer-acting NMBA, the patient remains paralyzed and unable to express their distress. Inadequate sedation and analgesia during intubation is well documented as contributing to poor outcomes during hospitalization.