Succinylcholine Versus Rocuronium for Pediatric Rapid Sequence Intubation in the Emergency Department

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Objectives: Succinylcholine and rocuronium are neuromuscular blocking agents used in the emergency department (ED) during rapid sequence intubation (RSI). Very few studies have been conducted to determine which agent is preferred for children. This study analyzed outcomes of death, post-traumatic stress disorder (PTSD) and malignant hyperthermia for children administered succinylcholine versus rocuronium for RSI in the ED.

Methods: This retrospective, propensity-matched study utilized the TriNetX database. Cohorts included children less than or equal to 17 years of age, given a paralytic agent plus etomidate or ketamine during intubation in the ED from 2004 to 2024. Cohorts were further stratified by the administration of succinylcholine or rocuronium. The outcomes measured were death, PTSD, and malignant hyperthermia. Propensity matching was done for demographics and pre-existing conditions.

Results: Before propensity matching, 2095 pediatric patients were identified. After propensity matching, 706 patients were identified in each cohort. After propensity matching, children administered succinylcholine had a lower rate of death (5.7% vs. 8.9%, RR: 0.65, 95% CI [0.43-0.93], $P = 0.019$) but no significant difference in PTSD (2.6% vs. 3.7%, RR: 0.71, 95% CI [0.32-1.68], $P = 0.399$). There was no significant difference in malignant hyperthermia. Subgroup analysis suggests that succinylcholine and etomidate were the best combination of drugs for RSI.

Conclusions: Mortality rates were lower for children administered succinylcholine for RSI when compared with rocuronium. This study demonstrates a potential association between succinylcholine use and favorable RSI outcomes in the ED, though further prospective studies are needed.

Key Words: succinylcholine, rocuronium, rapid sequence intubation, Pediatric Emergency Medicine

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Rapid sequence intubation (RSI) is frequently performed for airway management in the pediatric emergency department (PED)[1–3] with up to 80% of emergency intubations in children using RSI.[2,3] RSI is an effective method in obtaining airway access in pediatric emergencies rather than the conventional intubation.[1,2] RSI differs from conventional intubation by administering a sedative and paralytic agent simultaneously to induce rapid unconsciousness and muscle paralysis. Conventional intubation may involve administration of a sedation but no paralytic agent. RSI has a higher success rate on the first attempt of intubation (83%) compared with conventional intubation. Although RSI is commonly considered the most effective way to obtain airway access in pediatric emergencies, the incidence of failed intubation attempts is much higher in the pediatric patient population.[4] This is due to the relative infrequency of the procedure by the adult provider and the child's anatomic differences compared with adults. Children have a smaller, shorter and narrower trachea, prominent occiput, large tongue, tonsils and adenoids, superior laryngeal position, weaker hypoepiglottic ligament, large floppy epiglottis, anatomic subglottic narrowing and a more compliant chest wall, which can make pediatric intubations more difficult.[5–10]

When considering neuromuscular blocking agents (NMBA) in children for RSI, succinylcholine and rocuronium are commonly used agents. Succinylcholine is the preferred muscle relaxant because it has a rapid onset of 40 to 60 seconds and a short duration, lasting only 6-10 minutes. Rocuronium is not as rapid onset, 45 to 120 seconds, and lasts 37 to 72 minutes.[11–14] The use of succinylcholine is contraindicated in pediatric patients with chronic myopathy, extensive crush injury, malignant hyperthermia, pre-existing hyperkalemia, increased intraocular pressure, known pseudo-cholinesterase deficiency, and >2 days following burns or multiple trauma (https://www.uptodate.com/contents/succinylcholine-suxamethonium-drug-information?source=auto_suggest&selectedTitle=1~2—1~2—succinyl&search=succinylcholine). Current guidelines recommend the use of succinylcholine, if not contraindicated, or rocuronium with sugammadex immediately available for reversal in those patients with difficult airways.[1] Unfortunately, sugammadex is moderately expensive, with it being reported in the United States as $102/vial, versus neostigmine/glycopyrrolate in the

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United States as $13.5/vial.[15] Suggammadex has been shown per a Cochrane review to be faster than neostigmine in reversing paralysis.[16] Suggammadex is infrequently available as a reversal agent for rocuronium in the emergency department[17,18] and more commonly utilized after surgical procedures in the operating room.[19]

The use of succinylcholine for RSI is often preferred due to the shorter duration of action when compared with rocuronium, which can be beneficial in situations of unanticipated difficult airways.[1] While succinylcholine is supported in the guidelines, there are studies focused on RSI in pediatric populations that favor rocuronium over succinylcholine for optimal intubation conditions if administered at higher doses (1.2 mg/kg).[20] These studies found the use of this dose led to optimal intubation conditions with less side effects (muscle fasciculations or myalgia) compared with succinylcholine.[21]

Awareness with recall of paralysis (AWAP) and post-traumatic stress disorder (PTSD) has been reported in adults undergoing intubation. Having experienced AWAP places patients at increased risk of PTSD.[21–23] In adults, there have been higher levels of PTSD and AWP with rocuronium versus succinylcholine.[21] Post-traumatic stress disorder has not been studied in children undergoing intubation with an NMBA.

Currently, few studies exist that compare the effectiveness of these agents in the pediatric population. This study compared succinylcholine with rocuronium for RSI in pediatric emergencies and the outcomes of death, PTSD, and malignant hyperthermia. We also did a subgroup analysis of etomidate or ketamine in combination with succinylcholine or rocuronium.

METHODS

Study Design and Setting

The TriNetX database provides deidentified electronic medical records of over 114 million patients from 69 health care organizations (HCO) across the United States. Our study was a retrospective analysis that used the TriNetX database to collect data on the use of succinylcholine or rocuronium during intubation in the emergency department and the subsequent instances of death, PTSD, or hyperthermia. Selections were made using the Unified Medical Language System (UMLS) and National Library of Medicine (NLM) keywords. The study period was December 20, 2004, through November 20, 2024, from which 2 cohorts were established. The STROBE guidelines were used for this observational study.

Selection of Participants

The inclusion criteria for the first cohort (succinylcholine cohort) were those less than 18 years of age identified having emergent endotracheal intubation (UMLS: CPT:31500) in the emergency department (UMLS:HL7V3: VisitType: EMER) who were given etomidate (NLM: RXNORM:4177) or ketamine (NLM: RXNORM:6130), and succinylcholine (NLM: RXNORM:10154). The exclusion criteria for the first cohort were any use of rocuronium (NLM: RXNORM:68139) during this event.

The inclusion criteria for the second cohort (rocuronium cohort) were those less than 18 years of age identified having emergent endotracheal intubation (UMLS: CPT:31500) in the emergency department (UMLS:HL7V3: VisitType: EMER) who were given etomidate (NLM: RXNORM:4177) or ketamine (NLM: RXNORM:6130), and rocuronium (NLM:RXNORM: 68139). The exclusion criteria for the second cohort were any use of succinylcholine (NLM: RXNORM:10154) during this event. For both cohorts, etomidate and ketamine were included as induction agents in the analysis, as together, they account for ~95% of RSI inductions in most emergency departments.[24]

For PTSD, we only evaluated PTSD in patients who were 8 to 18 years of age, so those less than 8 years were not included in this analysis. Other studies have used the age range greater than or equal to 8 years of age as the age when PTSC can be evaluated.[25,26]

Outcomes

The outcomes assessed were death, post-traumatic stress disorder (PTSD), and malignant hyperthermia. The outcome of death was identified through the TriNetX database demographics. Mortality data within the TriNetX platform were obtained from EMR data and HCOs, in conjunction with the national death registries. The outcome of PTSD was identified through the ICD-10 code of UMLS:ICD10CM: F43.10. The PTSD was measured at discharge from the hospital.

To control for potential confounders, we propensity-matched demographic characteristics of age, sex, and ethnicity. We also propensity-matched for comorbid conditions potentially affecting intubation, such as being overweight/obese (E66), diseases of the circulatory system (I00-I99), diseases of the nervous system (G00-G99), acute kidney failure and chronic kidney failure (N17-N19), and asthma (J45).

Analysis

Statistical analysis and propensity matching were conducted within the TriNetX software. The listed comorbidities were 1:1 propensity-matched based on the score generated via the greedy nearest neighbor algorithm with a set caliper of 0.1 used for the pooled SDs. The proper balance of the covariates was analyzed using the standard mean difference, with an absolute value of > 0.1 indicating a positive residual imbalance. A priori statistical significance was established with a 2-tailed alpha < 0.05. Within the TriNetX database, a user-identified input matrix was employed for the covariates, which is then put into a logistical regression analysis for dichotomous data and linear regression for continuous data, which was used to obtain the individual subject propensity scores. The database randomizes the order of the rows, which were obtained from the greedy nearest neighbor algorithm, which helps to minimize bias within the calculation. The greedy nearest neighbor matching is the algorithm utilized for propensity matching within the TriNetX database. The univariate analysis was done to compare the outcomes within the designated time frames for each cohort and reported as risk ratios (RR), a 95% CI, and *P* values.

A subgroup analysis was performed comparing succinylcholine and rocuronium in the etomidate and ketamine cohorts, evaluating mortality with propensity matching. The etomidate cohort excluded those who were given ketamine, and the ketamine cohort excluded those given etomidate at the time of RSI. In addition, a post hoc analysis was performed to identify the percentage of patients with acute trauma and asthma in the succinylcholine and rocuronium RSI groups.

A post hoc analysis was done on acute trauma patients to determine whether there was higher mortality in those

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intubated with succinylcholine or rocuronium. This study, utilizing deidentified data from TriNetX, has been determined to be exempt by the UTMB IRB. The UTMB IRB determined that this project does not involve intervention or interaction with human subjects and is deidentified per the deidentification standard defined in Section §164.514(a) of the HIPAA Privacy Rule. This formal determination by a qualified expert was refreshed in December 2020.

RESULTS

Characteristics of Study Subjects

In this study, 712 patients were identified for cohort 1 (succinylcholine), and 1383 patients were identified for cohort 2 (rocuronium) before propensity matching. After propensity matching, 706 patients were identified per cohort. Before propensity matching, there were significant age differences ($P < 0.001$) between the succinylcholine (9.5 ± 6.3 y) and the rocuronium (7.7 ± 6.3 y) cohorts. The percentage of Hispanic and Latino patients ($P = 0.018$) was significantly higher in the rocuronium group. The comorbidities before propensity matching, except for asthma and overweight/obesity, were significantly higher in the rocuronium group compared with the succinylcholine group; diseases of the circulatory system ($P < 0.001$), diseases of the nervous system ($P < 0.001$), and acute/chronic kidney failure ($P = 0.023$). After propensity matching, there was no significant difference between the groups in demographics and comorbid conditions (Table 1).

Mortality

Before propensity matching, the rate of death in cohort 1 (succinylcholine) was 5.6%, and in cohort 2 (rocuronium) was 8.6% (RR: 0.65, 95% CI [0.65-0.93], $P = 0.016$). After propensity matching, the rate of death in cohort 1 (succinylcholine) was 5.7%, and in cohort 2 (rocuronium) was 8.9% (RR: 0.64, 95% CI [0.43-0.93], $P = 0.019$) (Table 2).

Post-Traumatic Stress Disorder

Before propensity matching, the rate of PTSD in cohort 1 was 2.5% and in cohort 2 was 3.4% (RR: 0.75, 95% CI [0.36-1.58], $P = 0.445$). After propensity matching, the rate of PTSD in cohort 1 (succinylcholine) was 2.6% and in cohort 2 (rocuronium) was 3.7% (RR: 0.71, 95% CI [0.32-1.68], $P = 0.399$) (Table 2).

Malignant Hyperthermia

When evaluating the rate of hyperthermia, no patients in the succinylcholine group had malignant hyperthermia; however, at least one occurrence of malignant hyperthermia was identified in the rocuronium cohort before propensity matching. This difference was not statistically significant.

Subgroup Analysis of Etomidate Versus Ketamine

The subgroup analysis of the etomidate and ketamine cohorts showed the lowest mortality rate with succinylcholine in combination with etomidate. The mortality for succinylcholine and etomidate was 7.0%, succinylcholine and ketamine was 8.2%, rocuronium and etomidate was 8.6%, and rocuronium and ketamine was 16.4% (Comparison of succinylcholine and etomidate vs. rocuronium and ketamine, χ^2 statistic 11.08 with a P value < 0.001).

Post Hoc Analysis

The post hoc analysis demonstrated that acute trauma, associated with a higher mortality after ED RSI,[23] was present in 29.1% of the patients in the succinylcholine cohort and 27.2% in the rocuronium cohort. Asthma was documented in 7.1% of the succinylcholine cohort and 7.6% of the rocuronium cohort. This suggests that the succinylcholine and rocuronium cohorts were relatively similar in terms of indications for intubation.

Limitations

Several limitations should be considered when interpreting these results. First, as a retrospective analysis, our study is subject to inherent biases and confounding factors that may not have been fully accounted for despite propensity matching. Second, the use of electronic medical records and coding systems may introduce inaccuracies or missing data. In addition, the TriNetX database, while extensive, may not capture all relevant clinical details or follow-up information, potentially affecting the accuracy of our outcomes assessment. We were unable to account for variations in individual clinician practices, doses of rocuronium and succinylcholine, institutional protocols, or specific patient characteristics that might influence the choice of NMBA and subsequent outcomes. In addition, we did not control for the use of specific induction agents such as ketamine or etomidate; however, we did look at their outcomes based on their use. There is a potential for missed death events when a patient is treated at an HCO not affiliated with the TriNetX network and subsequently experiences a fatal outcome outside of this network. However, this represents only a minor issue, as currently, 94% of HCOs within the TriNetX network are also linked to the US death registries. This percentage is steadily increasing as more HCOs continue to be linked with the registries. The results need to be interpreted with the caveat that RSI in the PED is likely impacted by many other factors outside of paralytic choice and factors in the propensity model. We were not able to identify the dose of the medications given, level of training, provider, number of intubation attempts, types of laryngoscopy performed, success versus failure, time to intubation, and alternative airway management due to the limitations of our database. We also were not able to obtain information from the database on hospital-specific medication preference for RSI. We excluded patients with a documented history of PTSD before hospitalization. While a discharge diagnosis of PTSD does not necessarily indicate a causal relationship with neuromuscular blocking agents, it is notable that PTSD had not been previously documented in these cases.

In reference to mortality, we could not determine whether the mortality occurred immediately after intubation or later over the following days due to database restrictions. Most of the deaths occurred early, within 4 days, with the largest number on the first day. We think that it is important to include the later deaths as children with severe anoxic injuries may die later, and we chose to analyze this up to 60 days.

In most emergency departments, sugammadex as a reversal agent for rocuronium is not available due to cost and lack of established protocols,[17,19,27] while it is readily available in most operating rooms[19,28,29] This may limit the generalizability of these findings to settings, like the operating

TABLE 1. Demographics and Pre-Existing Conditions Before Propensity Score Matching

		Before Propensity Score Matching					After Propensity Score Matching				
Cohort		**Mean ± SD**	**Patient**	**% of Cohort**	***P***	**Std diff.**	**Mean ± SD**	**Patient**	**% of Cohort**	***P***	**Std diff.**
Demographics											
1	Age at Index	9.5 ± 6.3	712	100	< 0.001	0.283	9.5 ± 6.3	706	100	0.551	0.032
2		7.7 ± 6.3	1,383	100			9.3 ± 6.5	706	100		
1	White		359	50.4	0.917	0.005		357	50.6	0.749	0.017
2			694	50.2				363	51.4		
1	Female		273	38.3	0.956	0.003		271	38.4	0.827	0.012
2			532	38.5				275	39.0		
1	Unknown Ethnicity		169	23.7	< 0.001	0.172		163	23.1	0.616	0.027
2			233	16.8				171	24.2		
1	Not Hispanic or Latino		432	60.7	0.233	0.055		432	61.2	0.586	0.029
2			876	63.3				422	59.8		
1	Hispanic or Latino		111	15.6	0.018	0.111		111	15.7	0.884	0.008
2			274	19.8				113	16.0		
1	Black or African American		159	22.3	0.381	0.040		158	22.4	0.898	0.007
2			286	20.7				156	22.1		
1	Male		423	59.4	0.765	0.014		419	59.3	0.746	0.017
2			831	60.1				413	58.5		
1	Other Race		48	6.7	< 0.001	0.170		48	6.8	0.755	0.017
2			161	11.6				51	7.2		
1	Asian		23	3.2	0.084	0.082		23	3.3	0.256	0.061
2			67	4.8				16	2.3		
Diagnosis											
1	Overweight and obesity		27	3.8	0.839	0.009		27	3.8	0.777	0.015
2			50	3.6				25	3.5		
1	Diseases of the circulatory		47	6.6	< 0.001	0.256		47	6.7	0.745	0.017
2	system		199	14.4				44	6.2		
1	Diseases of the nervous system		126	17.7	< 0.001	0.184		126	17.8	0.834	0.011
2			349	25.2				123	17.4		
1	Acute kidney failure and		10	1.4	0.023	0.111		10	1.4	1	< 0.001
2	chronic kidney disease		42	3.0				10	1.4		
1	Asthma		62	8.7	0.197	0.060		62	8.8	0.499	0.036
2			145	10.5				55	7.8		

*Number of patients between 1 and 10 represented by ≤ 10 to maintain deidentification.
Cohort 1 indicates succinylcholine; cohort 2, rocuronium; Std diff., standard difference.

rooms, where reversal agents are readily available. It should be noted that it takes ~2 to 3 minutes for sugammadex to reverse the paralysis from rocuronium,[22] and considerably longer for neostigmine, making it an unsuitable agent for reversal in the event of post-RSI complications.[29] Reversal of NMB has been indicated in the ED for neurological evaluation in cases of head injury or seizure. However, it is often impractical during emergency airway management, as many patients present with impaired hemodynamics and respiratory compromise. In such cases, reversal of NMB may be dangerous, as the patient may not be able to rapidly resume spontaneous ventilation.[30,31] In addition, reversal of NMB is not recommended by the Difficult Airway Society guidelines, which instead recommend pursuing alternative airway management strategies.[32]

DISCUSSION

Our study was robust, with 706 propensity-matched pairs of pediatric patients receiving rocuronium or succinylcholine for RSI. The findings of this study demonstrate a lower rate of death between the two groups, with those patients who received succinylcholine having a lower rate of death compared with those who received rocuronium. This study demonstrates a potential association between

TABLE 2. Outcomes of Succinylcholine Versus Rocuronium Before and After Propensity Score Matching

	Before Propensity Score Matching				After Propensity Score Matching			
Outcomes	**Cohort 1 (%)**	**Cohort 2 (%)**	**RR (95% CI)**	***P***	**Cohort 1 (%)**	**Cohort 2 (%)**	**RR (95% CI)**	***P***
Death	5.6	8.6	0.65 (0.46-0.93)	0.016	5.7	8.9	0.64 (0.43-0.93)	0.019
PTSD*	2.5	3.4	0.75 (0.36-1.58)	0.445	2.6	3.7	0.71 (0.32-1.68)	0.399

*Analysis restricted to 8 to 17 years old.
PTSD indicates post-traumatic stress disorder; RR, relative risk.

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succinylcholine use and favorable RSI outcomes in the ED, though further prospective studies are needed to determine causality. There was no significant difference in the rate of PTSD when comparing groups.

There have been other studies in pediatric patients where succinylcholine and rocuronium were compared for intubation conditions, success on the first intubation attempt, and hemodynamics, but only one study examined death in the ED, and that was in an adult study by Demasi.[33] Demasi's study included a large number of patients: 475 patients who received succinylcholine and 1864 patients who received rocuronium for intubation in the emergency department or intensive care unit.[33] They found no patients who had cardiac arrest or deaths in the patients who had received succinylcholine, but 13 cardiac arrests during intubation in the group receiving rocuronium.[33] In this study, there was a higher number of patients with the risk factors for diseases of the circulatory,nervous system, and kidney system in the rocuronium group, so perhaps rocuronium was used in sicker patients; however, with propensity matching as done in our study, these differences were mitigated. Succinylcholine versus rocuronium has been studied in adults in the outpatient setting.[34] A randomized trial that compared succinylcholine versus rocuronium among 1248 patients in the out-of-hospital setting found a higher incidence of successful intubation on the first attempt with succinylcholine (79.4%) compared with rocuronium (74.6%). Severe complications such as cardiac arrest were observed more frequently in the succinylcholine group (23.2% vs. 18.2%), but the difference was not statistically significant.[34]

Rocuronium potentially has more awareness with recall of paralysis (AWP) and post-traumatic stress disorder (PTSD) following intubation since it lasts longer than succinylcholine, so the patient may wake up from sedation but still be paralyzed, and it may not be apparent there is a need for additional sedation. AWP is the recollection of sensory perceptions while under the influence of an NMBA. PTSD has been studied in adults who receive rocuronium or succinylcholine for intubation but not studied in children. A 2022 study on adults by Fuller compared rocuronium versus succinylcholine concerning AWP and PTSD[21] and they concluded that rocuronium exposure led to increased levels of perceived threat placing patients at greater risk of PTSD.[21] AWP can lead to PTSD, as noted in a recent multicenter study that demonstrated PTSD symptoms are indeed more common after definite or possible awareness with recall with the PTSD Checklist-Specific (PCL-S), PCL-S is a validated measure of PTSD symptoms after a defined incident (eg, surgery).[16] Other literature has supported similar conclusions. Pappal et al[35] studied a total of 383 mechanically ventilated adult patients, of whom 10 (2.6%) experienced AWP.[35]

Clinical practice patterns related to the management of sedation and neuromuscular blockade in the ED place patients at high risk for AWP and PTSD. These include (1) high frequency of neuromuscular blockade use in the ED, with an increase in the use of longer-acting agents such as rocuronium[22,36,37] underdosing of intravenous analgesia and sedation[22,36–40] (2) high proportion of patients who receive no sedation after intubation[22,36–40] delays in administration of sedation after neuromuscular blockade,[41–43] and (3) inconsistent monitoring and documentation of sedation depth.[21,22,36,41,44,45] In adults, clinical data in ED sedation practices show that 20% to 45% of patients do not receive any analgesia and sedation after intubation, with up to 33% of patients not having any sedation depth assessment while mechanically ventilated in the ED.[21,38–41,46] The reality of clinical practice in the ED emphasizes the importance of mitigating PTSD in pediatric patients after being intubated, with ongoing sedation for amnesia following intubation as an area of improvement.

To our knowledge, our study is the first study to examine succinylcholine and rocuronium with subsequent PTSD in children during RSI. Literature suggests that PTSD can only be appropriately measured in children 8 years and older, therefore we evaluated PTSD in children between the ages of 8 and 17 years.[25] Our study found no significant difference in the incidence of PTSD between succinylcholine versus rocuronium before or after propensity matching. However, there were more occurrences of PTSD reported in the group that received rocuronium.

Malignant hyperthermia (MH) has been noted with succinylcholine. The incidence of MH in children, with anesthetics such as succinylcholine, is 3 in 100,000, and mortality may be as high as 11%.[46,47] Case studies do exist reporting MH with rocuronium but it has been debated if this was actual MH.[48] According to the Malignant Hyperthermia Association of the United States (MHAUS), rocuronium is a safe and nontriggering agent for MH.[49] In our study, there was at least 1 patient reported with MH in the rocuronium cohort, and this was probably not likely due to the NMB agent. There were no patients with MH in the succinylcholine group.

The subgroup analysis of the etomidate and ketamine cohorts, with propensity matching, suggests that succinylcholine with etomidate was the preferred combination of drugs for RSI in children, showing the lowest mortality rate. Other studies have shown no difference in combinations of etomidate and rocuronium or succinylcholine versus ketamine with rocuronium or succinylcholine.[43,45,46] This is the first study exclusively in children examining etomidate versus ketamine with succinylcholine or rocuronium and the mortality in children.

In summary, mortality rates were lower in children administered succinylcholine for RSI when compared with rocuronium. This study demonstrates a potential association between succinylcholine use and favorable RSI outcomes in the ED, though further prospective studies are needed to determine causality.

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