Effect of a pharmacist on timing of postintubation sedative and analgesic use in trauma resuscitations

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Purpose. Pharmacists' impact in reducing the time interval from intubation to sedative and analgesic use during trauma patient resuscitations is investigated.

Methods. A retrospective cohort study was conducted at a level 1 trauma center to compare medication-use outcomes in consecutive cases in which trauma patients underwent rocuronium-assisted rapid-sequence intubation (RSI) and subsequent sedation and analgesia with or without a pharmacist's participation on the resuscitation team. The primary and secondary outcomes were, respectively, the time to sedative provision and the time to analgesic provision after intubation.

Results. Relative to resuscitation cases not involving a pharmacist, the presence of the pharmacist during RSI was associated with decreased mean times to provision of postintubation sedation (9 minutes versus 28 minutes, $p = 0.007$) and analgesia (21 minutes versus 44 minutes, $p = 0.057$). The cumulative proportions of patients receiving appropriate sedation 5, 10, and 15 minutes after intubation were 11%, 26%, and 41% in the pharmacist-absent group and 33%, 53%, and 63% in the pharmacist-present group ($p = 0.009$, 0.008, and 0.045, respectively); for postintubation analgesic use, the corresponding figures were 9%, 14%, and 23% in the pharmacist-absent group and 17%, 30%, and 43% in the pharmacist-present group ($p = 0.236$, 0.066, and 0.039, respectively).

Conclusion. The presence of a pharmacist during RSI procedures was associated with decreased times to postintubation sedative and analgesic use, indicating that pharmacist participation in trauma-resuscitation responses can facilitate appropriate drug therapy.

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Trauma patients may require a variety of pharmacologic therapies in the trauma bays, such as analgesia, sedation, prophylactic antibiotics, and hemostatic agents.[1,2] Some patients need rapid-sequence intubation (RSI) to secure their airway and provide ventilation. This is performed by the near simultaneous administration of an induction agent with a paralytic agent to facilitate tracheal intubation. Etomidate is the most commonly used agent for induction, and rocuronium is increasingly used for therapeutic paralysis because of potential adverse effects related to succinylcholine use in trauma patients. Etomidate causes hypnosis that lasts for five minutes, whereas rocuronium causes neuromuscular blockade for approximately one hour.[3,4] This combination can lead to undesirable circumstances in which the patient is conscious but pharmacologically paralyzed for a prolonged period after RSI if additional sedatives are not provided promptly after intubation. Guidelines published by the Society of Critical Care Medicine recommend that adequate sedation and analgesia should be provided in patients given neuromuscular blockers.[5] In addition, patient recall of being conscious while pharmacologically paralyzed is considered to be an important complication to avoid—second only to death, according to an expert panel of anesthesiologists.[6] However, national estimates in the United States indicate that less than 50% of patients are given postintubation sedatives.[7]

The incorporation of pharmacists into the emergency department (ED) and trauma bays has many advantages and has been found to be an im-

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portant adjunct of the resuscitation team, with patient safety benefits.[8] Currently, close to a third of hospitals in the United States have pharmacists practicing in the ED or trauma center,[9] where their role is to optimize and facilitate the provision of medication therapy. In trauma centers, the presence of pharmacists enables their participation on the trauma response team. In one study evaluating the types of activities performed by pharmacists during trauma responses, the provision of analgesics and the provision of sedatives were the most commonly cited medication-related activities requiring the pharmacists' intervention.[2] In trauma patients who are intubated using rocuronium for RSI, pharmacists may be able to facilitate the prompt provision of postintubation sedatives and analgesics, thereby reducing the potential for uncomfortable patient recall. This is important because inadequate sedation and analgesia have been linked to the development of posttraumatic stress syndrome.[10] Delays in the administration of sedation and analgesia can also lead to myocardial ischemia, hypercoagulability, and immunosuppression.[11]

The objective of the study described in this article was to evaluate the effect of a pharmacist's presence on the timing of postintubation sedation and analgesia. We hypothesized that when a pharmacist was present, trauma patients would receive sedatives and analgesics sooner after intubation.

Methods

Study design and setting. The investigation was a retrospective cohort study conducted in a level 1 trauma center in the United States. Institutional review board approval was obtained prior to data collection. During the study time frame, a pharmacist was present in the ED 40–70 hours per week (three pharmacists performed this role in rotation). The pharmacists were located in the ED and responded to all trauma resuscitations when present in the ED. Their primary role during the trauma resuscitations was to assist with the selection, dosing, and provision of drug therapy; this primarily included analgesics, sedatives, paralytics, prophylactic antibiotics, and hemostatic agents. In addition to participating in resuscitations, the pharmacists reviewed medication orders, served as drug therapy consultants to ED physicians and nurses, and facilitated medication distribution.

Patient selection and data collection. A list of adult trauma patients who were intubated in the ED was obtained from a quality-improvement database. The database is maintained by an emergency physician who is in charge of maintaining this procedural competency for resident physicians in the emergency medicine training program. Consecutive intubations of trauma patients over a roughly two-year period (July 16, 2009–June 30, 2011) were evaluated. Cases were excluded from the analysis if the patients did not receive rocuronium for RSI or their medical records did not contain all desired data. Patients were categorized into two groups: (1) pharmacist present at the trauma resuscitation and (2) pharmacist absent at the trauma resuscitation

Data collected included patient demographics, reason for intubation, trauma type, mechanism of injury, presence of traumatic brain injury, vital signs, ED disposition, ED length of stay, analgesic and sedative use in the ED, and time from intubation to sedative and analgesic use. The quality-improvement database and the patients' medical records were used for data collection.

Outcomes and data analysis. The primary and secondary outcomes evaluated were the time to sedative provision after intubation and the time to analgesic provision after intubation, respectively, with and without a pharmacist. These times were defined as the duration of time in minutes between intubation and postintubation sedative (primary outcome) or analgesic (secondary outcome) provision. The cumulative proportion of patients who received sedatives and analgesics at each 5-minute increment up to 30 minutes after intubation was compared between the two groups.

Continuous variables were compared between the two groups (pharmacist present or pharmacist absent) using Student's t test. Categorical variables were compared between the two groups using a chi-square test. The method of Cohen[11] was used to estimate our target sample size. To find a large effect-size difference in the time to medication use ($d = 0.8$, where $d = [\text{mean}_a - \text{mean}_b]/\sigma$) using a two-tailed α of 0.05, we estimated that at least 26 patients would be required in each group. All analyses were two-tailed with an a priori α of <0.05. All analyses were conducted in Stata 11 (StataCorp LP, College Station, TX).

Results

Study cohort. There were a total of 358 intubations performed in adult trauma patients in the ED during the study time frame, and 112 patients received rocuronium for RSI. Of these patients, 12 were excluded due to incomplete records and thus the remaining 100 patients were included in the study cohort; the pharmacist was absent (i.e., did not participate in the trauma response) in 70 cases and present in 30 cases. There were no significant baseline differences between these two groups with respect to patient demographics, trauma characteristics, patient disposition, and vital signs (Table 1).

Preintubation medications. In the overall cohort, induction for RSI was performed using etomidate ($n = 97$, 97%), propofol ($n = 2$, 2%), or ketamine ($n = 1$, 1%). Prior to intubation, 10% ($n = 10$) received analgesics in the pharmacist-present

group and 13% (n = 13) received analgesics in the pharmacist-absent group (p = 0.729). As per the study selection criteria, all patients received rocuronium for therapeutic paralysis. The mean ± S.D. dose of rocuronium was 1.1 ± 0.3 mg/kg in the pharmacist-absent group and 1.2 ± 0.3 mg/kg in the pharmacist-present group (p = 0.906).

Postintubation sedation. After intubation, 81% (n = 57) in the pharmacist-absent group and 70% (n = 21) in the pharmacist-present group received some sedative (propofol or midazolam) in the ED (p = 0.206). Of the patients (n = 22) who did not receive postintubation sedation, 73% (n = 16) had traumatic brain injury and 18% (n = 4) were hypotensive (systolic blood pressure of <90 mm Hg). When the pharmacist was present, the mean ± S.D. time to postintubation sedation was significantly shorter than when a pharmacist was absent (9 ± 12 minutes versus 28 ± 29 minutes, p < 0.007). The cumulative proportions of patients in the two groups who had received sedation at each

Table 1.
Demographic, Clinical, and Case Data on Patients Who Received Rocuronium for Rapid-Sequence Intubation, by Study Cohort[a,b]

Variable	Pharmacist-Absent Group (n = 70)	Pharmacist-Present Group (n = 30)	p
Demographics			
Mean ± S.D. age, yr	48 ± 20	52 ± 18	0.335
Male	48 (69)	21 (70)	0.887
Mean ± S.D. weight, kg	75 ± 25	76 ± 32	0.981
Race/ethnicity			0.629
White	42 (60)	21 (70)	
Hispanic	21 (30)	7 (23)	
Other	7 (10)	2 (7)	
Trauma Characteristics and ED Case Disposition			
Reason for intubation			0.375
Airway protection	55 (79)	20 (67)	
Patient control	12 (17)	7 (23)	
Other	3 (4)	3 (10)	
Trauma type			0.932
Blunt	65 (93)	28 (93)	
Penetrating	5 (7)	2 (7)	
Injury mechanism			0.287
Fall	18 (26)	9 (30)	
Motor vehicle collision	10 (14)	7 (23)	
Pedestrian struck by vehicle	8 (11)	0	
Gunshot	4 (6)	2 (7)	
Motorcycle collision	5 (7)	0	
Stab	1 (1)	0	
Other	24 (35)	12 (40)	
Traumatic brain injury	47 (67)	18 (60)	0.493
ED length of stay			0.129
<1 hr	15 (21)	8 (27)	
1–4 hr	35 (50)	19 (63)	
>4 hr	20 (29)	3 (10)	
Died in ED	3 (4)	1 (3)	0.824
Baseline vital signs and scores, mean ± S.D.[c]			
Systolic blood pressure, mm Hg[d]	142 ± 30	149 ± 34	0.296
Heart rate, beats/min	105 ± 29	97 ± 31	0.221
Respiratory rate, breaths/min	22 ± 9	20 ± 5	0.204
Glasgow Coma Scale score	9 ± 5	10 ± 5	0.500
Oxygen saturation, %	97 ± 4	95 ± 10	0.207

[a]ED = emergency department.
[b]All data except p values are no. (%) of patients unless specified otherwise.
[c]Prior to intubation.
[d]The rate of hypotension (<90 mm Hg) within one hour after intubation was similar (approximately 10%) in both groups.

5-minute increment are shown in Table 2.

Postintubation analgesia. After intubation, the presence of a pharmacist was associated with a higher frequency of analgesic (fentanyl, morphine, or hydromorphone) usage relative to the pharmacist-absent cases, but the difference was not significant (60% [18 of 30 patients] versus 47% [33 of 70 patients], $p = 0.239$). Of the 49 patients who did not receive postintubation analgesia, 69% ($n = 34$) had traumatic brain injury and 12% ($n = 6$) were hypotensive. The mean time from intubation to analgesic provision was 44 ± 47 minutes in the pharmacist-absent group and 21 ± 24 minutes in the pharmacist-present group ($p = 0.057$). For both groups, the cumulative proportion of patients who had received analgesia at each 5-minute increment is shown in Table 2.

Discussion

The key finding of this study was that a pharmacist's presence during trauma resuscitations was associated with decreased average times to sedative and analgesia provision after intubation. The study was conducted in a subset of patients who received rocuronium, which is a long-acting neuromuscular blocker at the doses used in this study. In our institution, rocuronium is commonly used in the trauma setting to facilitate intubation and is considered to be equivalent to succinylcholine with regard to intubation success.[12] Given concerns with succinylcholine in trauma patients, such as increased intracranial or intraocular pressure, as well as hyperkalemia, its use is often avoided in these patients. However, a disadvantage of rocuronium use at doses recommended for RSI (i.e., >1 mg/kg) is that it can cause paralysis for more than one hour. This prolonged lack of patient movement due to pharmacologic paralysis can lead to a delay in the provision of sedatives and analgesics by health care providers. In a previously published study of pediatric patients given long-acting paralytics, the mean time from induction of sedation to postintubation sedative use was 46 minutes[13]; this is concerning because the sedative used for RSI was etomidate, which typically produces hypnosis for only 5 minutes. Similarly, etomidate was used in 97% of the cases in our study. The combination of a long-acting paralytic (rocuronium) and a short-acting sedative (etomidate) can lead to patient awareness during pharmacologic paralysis if postintubation sedation is not provided promptly after intubation.

The results of our study indicate that there were considerable delays in providing sedatives and analgesics when the pharmacist was not present. These delays might have been due to the staff's lack of knowledge of the pharmacokinetics and pharmacodynamics of the medications used or to their perception of sedation in patients who are pharmacologically paralyzed. There are also logistical reasons that are likely to be contributory to delays in postintubation sedation and analgesia. For instance, provision of sedatives and analgesics requires providers to leave the bedside and obtain medications from controlled-access cabinets; this may not be possible in certain circumstances due to limited nursing staff. Even after medications are obtained, the priming of medication tubing and programming of infusion pumps can lead to delays. In our study, the pharmacist's presence enabled the nursing staff to remain at the patient's bedside while medications were retrieved for administration.

As mentioned previously, less than one half of U.S. patients who are intubated in the ED receive any postintubation sedation.[7] In our study, the rate of postintubation sedative use was close to 80% in the overall cohort of trauma patients. However, not all patients who receive RSI may require sedatives or analgesics after intubation. For instance, some patients in our study did not receive any sedatives or analgesics while in the ED regardless of the pharmacist's presence; in some cases, this might have been partly due to the nature of the patient's injuries (i.e., a perceived lack of need for sedation and analgesia in patients with traumatic brain injury). How-

Table 2.
Timing of Postintubation Sedative and Analgesic Use, by Study Cohort

Postintubation Time, min	Pharmacist-Absent Group ($n = 70$)	Pharmacist-Present Group ($n = 30$)	p
Sedative use			
5	8 (11)	10 (33)	0.009
10	18 (26)	16 (53)	0.008
15	29 (41)	19 (63)	0.045
20	38 (54)	19 (63)	0.402
25	39 (56)	19 (63)	0.479
30	40 (57)	20 (67)	0.373
Analgesic use			
5	6 (9)	5 (17)	0.236
10	10 (14)	9 (30)	0.066
15	16 (23)	13 (43)	0.039
20	17 (24)	13 (43)	0.057
25	17 (24)	13 (43)	0.057
30	17 (24)	13 (43)	0.057

[a]All data except p values are cumulative no. (%) of patients who received medication at each time point.

ever, close to 70% of the overall cohort had traumatic brain injury, and many such patients did receive sedative and analgesic medications. Also, clinicians may avoid sedatives and analgesics to avoid drug-induced hypotension, but as the rate of hypotension during the first hour after intubation was about 10% in both study cohorts, that does not explain the lack of use of sedatives and analgesics. Therefore, we cannot be certain regarding the reasons why these medications were not provided in the evaluated cases, and there was no specific documentation addressing the lack of use. Nonetheless, patients who required these medications received them much sooner when the pharmacist was present.

The study had a number of notable limitations related to the study design.

First, as in any chart-based investigation, there was the possibility of erroneous documentation in the medical record.

Second, the outcomes of this study were the mean times to sedative and analgesic provision, and it was assumed that delays would lead to patient awareness or recall of being awake while pharmacologically paralyzed. In an ideal study design, patients would be randomly assigned to an intervention or a control group and interviewed after recovery to determine their recall of events in the ED, but such randomization would not be ethical. Based on the duration of effect of the medications administered to the study cohorts, it is very likely that patient awareness of paralysis occurred. Although we do not know how great a reduction in the time interval from administration of a neuromuscular blocker to initiation of sedation should be to be clinically relevant, common sense seems to dictate that achieving the shortest interval is clinically important.

Third, this study did not evaluate the cost-effectiveness of having a pharmacist present during trauma resuscitation. It is likely that this would not be considered a cost-effective role if the sole purpose of the pharmacist's presence were to assist with trauma care. However, in EDs with existing pharmacy services, the incorporation of the pharmacist into the trauma-resuscitation process would not add additional cost.

In addition, the groups had similar characteristics; therefore, we did not identify any confounders and the need for a multivariate analysis was not necessary.

We included in the analysis all patients who received the treatment of interest (rocuronium-assisted RSI) at the study site during the study time frame, thereby minimizing the possibility of selection bias. The study was conducted in a level 1 trauma center; therefore, the results should be extrapolated with caution to other settings.

Finally, although the presence of a pharmacist during trauma resuscitations was associated with decreased times to sedative and analgesic use, we cannot be certain regarding causation. For instance, it is possible that the pharmacist's presence, in and of itself, prompted other staff to be more cognizant and responsive regarding the need for analgesic and sedative medications. However, in our institution's trauma bay, it is usual practice for a pharmacist to retrieve medications from controlled-access cabinets and provide them to the trauma care team; therefore, we believe that the observed decrease in the average time to medication provision was most likely directly related to the pharmacist's formal integration into the trauma-resuscitation process. On a related note, as multiple pharmacists were involved in this study, there was the possibility of variability in performance of trauma response activities; the data collected were not stratified by individual pharmacist.

Conclusion

The presence of a pharmacist during trauma resuscitations was associated with decreased times to postintubation sedative and analgesic use, indicating that pharmacist participation in trauma-resuscitation responses can facilitate appropriate drug therapy.

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