# Etomidate Versus Midazolam for Procedural Sedation in Pediatric Outpatients: A Randomized Controlled Trial

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**Study objective:** Midazolam is widely used for procedural sedation and analgesia. Etomidate has been studied mostly in adults. Our objective is to compare the efficacy of etomidate and midazolam for achieving procedural sedation and analgesia in children.

**Methods:** A randomized, double-blind, emergency department and orthopedic clinic-based trial was carried out among patients aged 2 to 18 years with displaced extremity fractures. Patients were administered 1 $\mu$g/kg of fentanyl and either 0.2 mg/kg of etomidate or 0.1 mg/kg of midazolam. Adequate sedation was defined, for the purpose of this study, as a score of 4 or more on the Ramsay Sedation Scale. The primary outcome was induction and recovery time. The rates of adverse events, success of fracture reduction, and parent and physician satisfaction were also compared.

**Results:** From April to August 2004, 100 of 128 eligible patients were enrolled (age 8.7±3.7 years; 50% male patients). A higher proportion of patients attained adequate sedation among those who received etomidate: 46 of 50 (92%) versus 18 of 50 (36%) (Δ 56%; 95% confidence interval [CI] 38% to 69%). Time taken for induction (hazard ratio 4.9; 95% CI 2.2 to 10.9) and time taken for recovery (hazard ratio 2.8; 95% CI 1.5 to 5.1) were lower among patients who received etomidate. The rates of adverse events were similar in both groups, except for myoclonus and pain at the injection site, which was more frequent in the etomidate group.

**Conclusion:** Induction and recovery times are shorter with etomidate compared with midazolam. At the dosages used for procedural sedation and analgesia among children with displaced extremity fracture, etomidate has higher efficacy in comparison with midazolam. [Ann Emerg Med. 2006;48: 433-440.]

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## INTRODUCTION

### Background

Painful procedures in the pediatric emergency department (ED) are frequent and the underuse of analgesia and sedation among children has been well documented.[1] The ideal sedative agent for procedural sedation and analgesia would have a rapid onset of action and a brief half-life, therefore permitting easy titration on response and a rapid recovery time once the procedure is over. Also, it would induce amnesia and sedation and decrease muscular tone while having no adverse effects. Unfortunately, no single agent has all these properties. Midazolam, a benzodiazepine, is the most widely used intravenous sedative in the ED for adults, as well as children.[2-5] Although well accepted for procedural sedation and analgesia, its time of onset is relatively long, and the recovery time can be prolonged with high doses.[3,6] It also has the potential for inducing respiratory depression and hypotension.[7] A drug that offers promise for procedural sedation and analgesia is etomidate. Its use has been initially described for rapid sequence intubation in the ED in adults, as well as in children.[8-10] It offers a rapid onset of sedative effect, brief half-life, short recovery time, and minimal effect on the respiratory and cardiovascular systems.[11]

**Editor's Capsule Summary**

*What is already known on this topic*

Midazolam and etomidate are used for pediatric procedural sedation; however, the latter drug has been less studied for this purpose.

*What question this study addressed*

Does etomidate demonstrate more rapid onset and shorter recovery than midazolam for pediatric procedural sedation, and is it more effective?

*What this study adds to our knowledge*

At single intravenous doses of 0.2 mg/kg of etomidate and 0.1 mg/kg of midazolam, the former drug demonstrated faster onset and a shorter recovery. It also induced a deeper average level of sedation, which resulted in superior sedation conditions. Adverse effects were similar between the 2 drugs.

*How this might change clinical practice*

In the doses used in this study, etomidate was superior to midazolam for pediatric procedural sedation and appeared to be equally safe.

*Research we'd like to see*

Large series are needed to better establish the safety profile of etomidate. A randomized trial of the relative efficacy and safety of etomidate, propofol, and ketamine would also be of great interest.

### Importance

Balancing adequate procedural sedation and analgesia with rapid discharge after the procedure is a major challenge to emergency physicians. The use of etomidate would greatly reduce the time nurses and physicians have to stay at the patient's bedside, ensuring a faster turnover without compromising patient safety. However, there is a paucity of literature that addresses the use of etomidate for procedural sedation and analgesia specifically in large samples of outpatient children.

### Goals of This Investigation

The objective of this study was thus to compare the induction and recovery times of etomidate and midazolam in children presenting to the pediatric ED and orthopedics clinic with extremity fractures requiring procedural sedation and analgesia for reduction at a large tertiary-care facility.

## MATERIALS AND METHODS

### Study Design

The study was a prospective, double-blind, randomized, controlled clinical trial. The ethical review board at our institution approved the study. Written informed consent was obtained from a parent for all children. All children able to understand the study also provided their verbal or written assent.

### Setting and Selection of Participants

Patient enrollment took place in the ED department, as well as the orthopedic outpatient clinic, at a tertiary-care urban pediatric center with annual census of more than 60,000 visits to the ED and more than 15,000 to the orthopedic outpatient clinic. All sedation and analgesia were performed in the same room, adjacent to the ED and orthopedics outpatient clinic. It is equipped with reanimation equipment, portable radiograph machine, and plaster casts. Enrollment took place between 8 AM and 11 PM 7 days a week. Healthy children with a physical status score of I or II (American Society of Anesthesiologists), aged between 2 and 18 years, and presenting to the hospital with a displaced extremity fracture requiring procedural sedation and analgesia for closed reduction were eligible for participation in the study. Exclusion criteria included respiratory tract infection, hemodynamic instability, significant recent head injury, known seizure disorder, significant underlying heart or lung disease or craniofacial anomaly, underlying adrenocortical dysfunction, pregnancy, allergy to study drugs, fasting criteria not met (solids less than 6 hours and clear liquids less than 2 hours earlier),[12,13] or inability to obtain IV access.

### Interventions

After giving informed consent, eligible patients could receive intravenous morphine (0.05 to 0.1 mg/kg; maximum 5 mg/dose)[14] at the emergency physician's or orthopedist's discretion. If the procedure could be done immediately, intravenous fentanyl (1 μg/kg; maximum 50 μg/dose) was administered. If necessary, additional doses of fentanyl, 0.5 μg/kg per dose (maximum 50 μg/dose), at a minimal interval of 2 minutes were administered throughout the procedure after the evaluation of the level of pain of the patient by the investigator (see below), up to a total maximum of 2 μg/kg. All sedation and analgesia were performed by the principal investigator.

Patients were subsequently randomized to receive either midazolam (0.1 mg/kg=0.1 mL/kg; maximum 5 mg)[2,3,14-16] or etomidate (0.2 mg/kg=0.1 mL/kg; maximum 10 mg),[11,17-21] both in a slow intravenous push (60 to 90 seconds). Randomization was done by the pharmacy department with preestablished computer-derived random-number tables. Study drug vials were prepared by the pharmacy department before the beginning of the study, were kept in a safety box in the ED, and looked identical. At randomization, the principal investigator chose the next numbered vial available.

All sedation and analgesia were done under continuous cardiorespiratory monitoring based on recommended guidelines[12,13] and under the surveillance of a pediatric respiratory therapist, an ED nurse, and the principal investigator. Parents were not allowed inside the room, as is our usual procedure. We did not use supplemental oxygen on patients, except in case of desaturation. Desaturation was

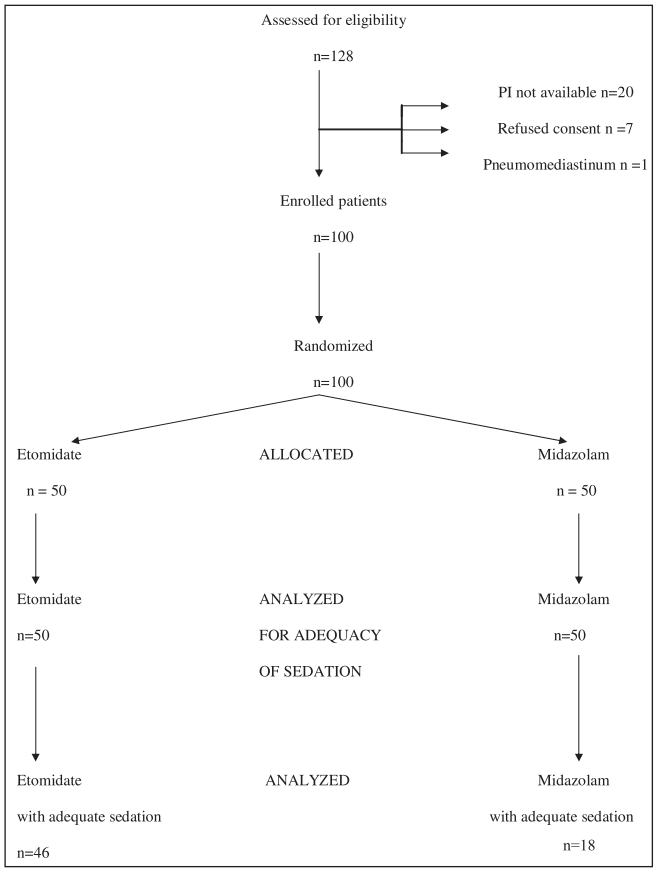


**Figure 1.** Description of patient enrollment and randomization. *PI*, Principal investigator.

defined as a persistent saturation lower than 93% for more than 10 seconds. Other adverse events or desaturation not responding to $O_2$ and head positioning were treated with naloxone or flumazenil.

The fracture reduction began after adequate induction was attained, as determined by the principal investigator (moderate to deep sedation=Ramsay score ≥4).[22] For patients who could not achieve a Ramsay score of ≥4 with maximal doses of fentanyl and the study drug, the reduction was nonetheless carried out. For patients for whom no sedation could be achieved (Ramsay score 1 or 2), nitrous oxide was added at the performing physician's discretion, and the patient was removed from further study intervention (Figure 1). After each reduction attempt, a radiograph was performed with the portable machine. If after a number of attempts at reduction the performing physician deemed a closed reduction impossible, the procedure was then stopped (failed procedure).The patient was then either treated by the orthopedist or sent directly to the operating room for open or closed reduction under general anesthesia.

**Outcome Measures**

On a standardized data sheet, the principal investigator recorded the total number of fentanyl doses administered, the number of attempts until successful reduction, the duration of the painful procedure, the time to return to baseline level of consciousness, and the time of discharge from the hospital. All adverse events, including nausea, vomiting, myoclonus, desaturation, and apnea, as well as other events possibly related to the procedural sedation and analgesia, were also recorded. In addition, vital signs, depth of sedation (Appendixes E1 and E2, available online at http://www.annemergmed.com), and level of pain were recorded before the first dose of fentanyl was given and then every 2 minutes until the end of the painful procedure. Thereafter, the scales were recorded every 5 minutes until the patient had returned to his or her baseline level of consciousness. The patient was then discharged at the discretion of the attending physician working in the ED, as is the usual practice in our center.

The primary outcome of the study was the comparison of the induction and recovery times of midazolam and etomidate. Induction time was defined as the time between sedative administration and attainment of a Ramsay score ≥4, whereas recovery time was defined as the time between the administration of the sedative (study drug) and the return to baseline of the patient's level of consciousness. This outcome was available only for patients who were adequately sedated (Ramsay score ≥4).

Secondary outcomes were the comparison of the efficacy of sedation of the 2 study drugs by using objective scales at the beginning of the painful procedure, the success rates of fracture reduction, rate of adverse events, and physician and parental satisfaction at discharge. Oversedation was defined as having a Ramsay score of 6 (no response to light glabellar tap) on 2 consecutive evaluations. Highest Ramsay score at any given time during the procedural sedation and analgesia was also documented for each patient. Secondary outcomes were calculated for all study patients (n=100).

Two types of sedation scales were used. All were documented by the same investigator. The Ramsay score,[23] a simple and rapid measure commonly used in clinical practice, was used to measure the primary outcome (Appendix E1, available online at http://www.annemergmed.com). Although not validated in children,[24] this scoring system has been used in research studies on procedural sedation in children.[25,26] The COMFORT scale is the only sedation scale that has been validated in children aged 0 to 18 years,[24] albeit for critically ill, intubated children.[27] We used a modified version of the scale previously used for nonventilated children [28] for our outpatient population (Appendix E2, available online at http://www.annemergmed.com).

Parent satisfaction, as well as performing physician's level of satisfaction, was evaluated at the end of the reduction with a 5-point Likert scale. Parents were also contacted by telephone 48 hours after discharge to evaluate the occurrence of late adverse events.

The principal investigator documented the level of pain of the study subjects by using a 0- to 100-mm visual analog scale, with the lower limit being "no pain" and the upper limit being

**Table 1.** Demographic distribution of the enrolled study population.

| Demographic Distribution | Etomidate Group (n=50) | Midazolam Group (n=50) | Δ (95% CI) |
|---|---|---|---|
| Boys (%) | 25 (50) | 25 (50) | 0 |
| Mean weight (SD), kg | 35.7 (15.4) | 31.2 (13.4) | 4.4 (−1.3 To 10.1) |
| Mean age (SD), mo | 108 (45.6) | 100 (42.7) | 8 (−10 To 26) |
| Age distribution, y | | | |
| ≤3 | 2 (4) | 1 (2) | |
| 4–6 | 15 (30) | 13 (26) | |
| 7–13 | 29 (58) | 26 (52) | |
| >13 | 4 (8) | 10 (20) | |
| Reductions by orthopedists (%) | 26 (52) | 31 (62) | −10 (−28 To 9) |
| Forearm fracture (%) | 40 (80) | 35 (70) | 10 (−7 To 26) |
| Received morphine before procedural sedation and analgesia (%) | 8 (16) | 4 (8) | 8 (−5 To 21) |

"most pain."[29] The visual analog scale has been validated in acute pain in adults [30,31] and is usually used for studies in children older than 7 years who rate their own pain.[32-34]

At the end of the procedure, the principal investigator tried to guess which of the study drugs the patient received.

To estimate sample size, in the absence of previous studies in the pediatric population, information on similar studies carried out among adult patients was used. In adults, induction times ranged from 5 to 15 minutes for midazolam and 4 to 7 minutes for etomidate. Recovery times for midazolam ranged from about 40 minutes to 70 minutes, and that for etomidate ranged from 10 minutes to 40 minutes. According to our previous experience, we anticipated the induction times for midazolam to be about 10 minutes and about 5 minutes for etomidate. Similarly, we anticipated the recovery times to be about 40 and 20 minutes, respectively. Following an ED physician survey in our center, the sample size was calculated with a clinically significant difference in induction time of 5 minutes and 20 minutes for recovery. To detect this level of significance with 80% power at $\alpha=0.05$, we required 33 patients in each arm. We therefore expected that a sample size of 50 patients would have more than adequate power.

### Primary Data Analysis

Patients were included for study analysis on an intention-to-treat basis. Differences in continuous and categorical variables were analyzed using Student *t* tests and $\chi^2$ tests, respectively. Significance was assessed at the 5% level. Initial analysis involved the comparison of the study times using Kaplan-Meier curves. Differences in survival times between the 2 groups were evaluated using the log-rank tests. To estimate hazard ratios, nonparametric univariate Cox proportional hazards modeling was carried out. A ratio significantly greater than 1 will indicate a lower study time (ie, lower induction, or recovery time) for the "treatment drug" (ie, etomidate), and a ratio significantly lower than 1 will indicate a higher study time for etomidate. Hazard ratios, with their respective 95% confidence intervals (CIs), were calculated. All analysis was done using Stata (version 8; Stata Corporation, College Station, TX).

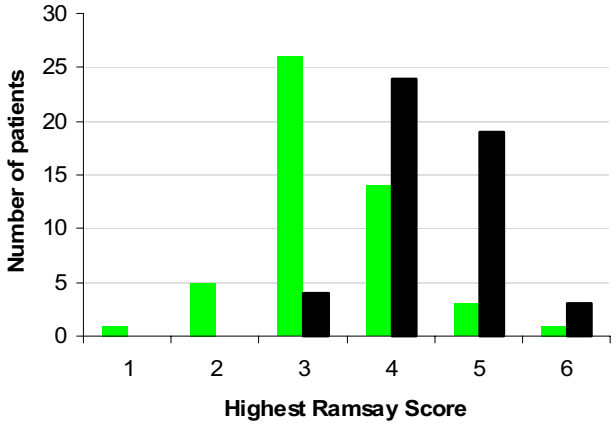


**Figure 2.** Distribution of the highest Ramsay score attained after either midazolam or etomidate. Green bars indicate midazolam; black bars indicate etomidate.

## RESULTS

During the study period (April 22, 2004, to August 23, 2004), 128 eligible children were identified for participation. Twenty-eight of these patients were not enrolled, because of refusal by parents, unavailability of the principal investigator, or a pneumomediastinum discovered on further evaluation (Figure 1). One hundred patients, 50 per group, were enrolled and were randomized. Baseline characteristics of the 2 groups were similar (Table 1).

In the etomidate group, 46 patients (92%) achieved an adequate level of sedation (Ramsay score ≥4) compared with 18 (36%) patients in the midazolam group (Δ 56%; 95% CI 38% to 69%) (Figure 2). When the subgroup of patients who reached an adequate level of sedation (Ramsay score ≥4) was analyzed, the median induction time was 2 minutes in the etomidate group compared with 4 minutes in the midazolam group (Δ 2 minutes; 95% CI −3.5 to −1.5 minutes). The median recovery time in this subgroup was 11.8 minutes for the etomidate group compared with 24 minutes for the midazolam group (Δ 12.2 minutes; 95% CI −15.5 to −6.5 minutes). Kaplan-Meier survival analysis showed that overall induction

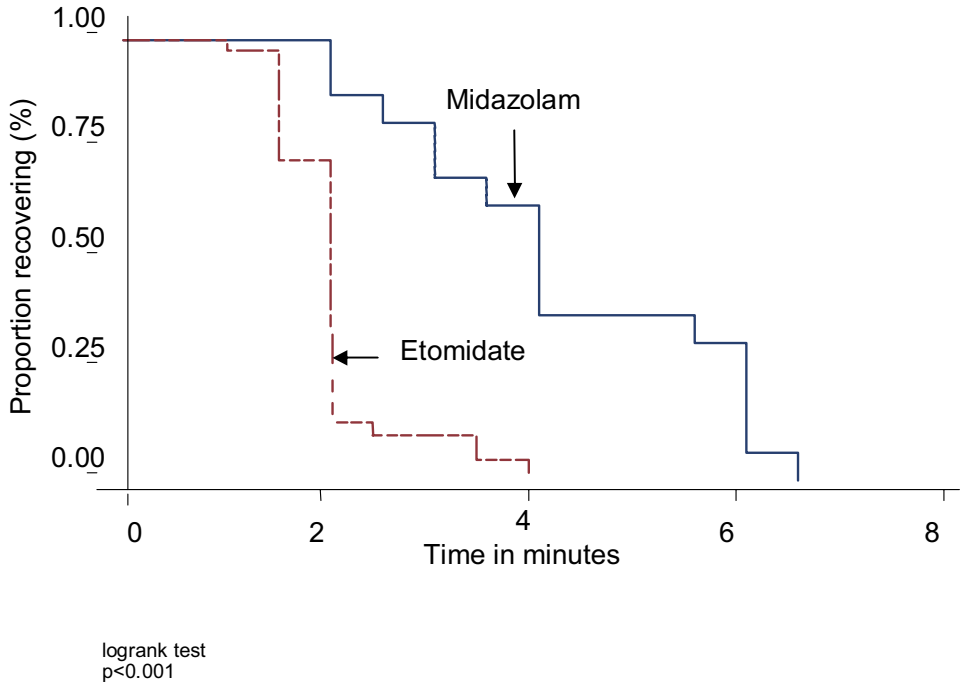


**Figure 3.** Comparison of induction times between etomidate and midazolam.

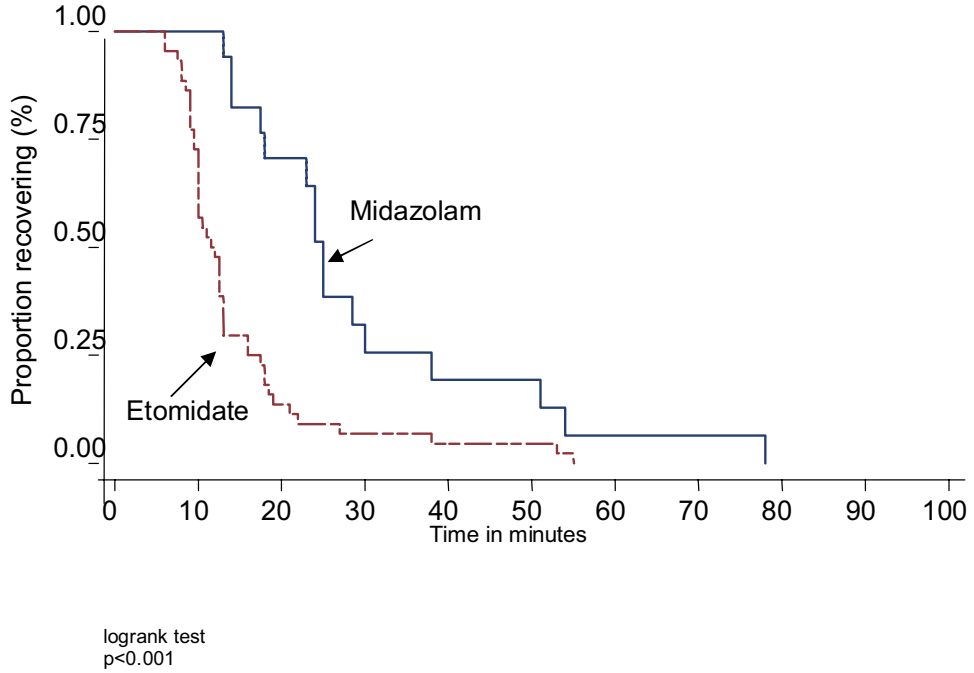


**Figure 4.** Comparison of recovery times between etomidate and midazolam.

and recovery times were lower for those patients administered etomidate (Figures 3 and 4).

Univariate Cox proportional regression modeling indicated that induction time was higher for those receiving midazolam (hazard ratio 4.9; 95% CI 2.2 to 10.9). Similarly, the recovery time was prolonged among patients receiving midazolam (hazard ratio 2.8; 95% CI 1.5 to 5.1).

No difference in success rate of fracture reduction on the first attempt between the groups was observed: 27 of 50 (54%) patients in the etomidate group compared with 25 of 50 (50%) patients in the midazolam group (Δ 4%, 95% CI −15% to 23%). Similarly, the overall success rate of reduction was comparable in both groups: 48 of 50 (96%) versus 47 of 50 (94%) patients; Δ 2%, 95% CI −8% to 13% in the etomidate

**Table 2.** Rates of adverse events during procedural sedation and analgesia, recovery, and within 48 hours after the discharge.

| Adverse Events | Etomidate (%) (n=50) | Midazolam (%) (n=50) | Δ (95% CI) |
|---|---|---|---|
| **During procedural sedation and analgesia** | | | |
| Pain on injection | 23(46) | 6(12) | 34 (16–49) |
| Myoclonus | 11(22) | 0 | 22 (10–35) |
| Desaturation | 10(20) | 11(22) | 2 (−18 To 14) |
| Oversedation | 0 | 1(2) | −2 (−10 To 5) |
| **During the recovery period** | | | |
| Agitation | 0 | 3(6) | −6 (−16 To 2) |
| Nausea | 3(6) | 0 | 6 (−2 To 16) |
| Vomiting | 1(2) | 0 | 2 (−5 To 10) |
| **Within 48 hours** | | | |
| Vomiting | 4/49(8)* | 4(8) | −0.2 (−11 To 12) |

*One patient in the etomidate group was unable to be contacted after 48 hours.

and midazolam groups, respectively. All failed procedures were reduced and treated in the operating room.

The most commonly reported adverse effect was pain at the site of injection during intravenous sedative administration, and this was reported more often in the etomidate group (Table 2). Myoclonus was only seen in the etomidate group. In all but 1 case, it was mild and brief. One patient, a healthy 9-year-old boy, presented a moderate degree of myoclonus best described as diffuse muscle rigidity that lasted approximately 30 seconds.

The desaturation rate was similar between the groups (Table 2). No patient experienced apnea. All patients responded quickly to free oxygen administration or head repositioning. No patient required bag-valve manual ventilation or antidote administration. These events were not associated with any hemodynamic instability.

The only patient considered oversedated (Ramsay score 6 on 2 or more evaluations) was a healthy 13-year-old boy in the midazolam group who had not received morphine or other premedication and who received fentanyl at 1.5 μk/kg overall during procedural sedation and analgesia (Table 2). He desaturated to 91% but responded rapidly to 28% oxygen administration by mask. No patient in the etomidate group was considered oversedated, as defined above. Three patients in the etomidate group and no patients in the midazolam group reached a Ramsay score of 6 on a single occasion (Figure 2).

The total dose of fentanyl administered in the etomidate group (1.4 μg/kg ±0.4) was lower than that received by the midazolam group (1.7 μg/kg ±0.4): Δ −0.3, 95% CI −0.4 to −0.1, which did not affect the mean visual analog scale at the start of the reduction, which was similar in both groups (Δ −2.9 mm; 95% CI −11.0 to 5.1 mm).

Patients in the etomidate group were significantly more sedated, with a mean Ramsay score at the beginning of the reduction of 4.2±0.7 compared with 3.2±0.7 in the midazolam group: Δ 1.0; 95% CI 0.7 to 1.3. The COMFORT scale was similar at the beginning of the painful procedure, 20.7±5.7 compared with 21.3±5.2 in the etomidate and the midazolam groups, respectively (Δ −0.6; 95% CI −2.8 to 1.6).

The physician satisfaction questionnaire did not reflect any preference between the 2 drugs, with 37 of 50 (74%) patients in the etomidate group being satisfied or very satisfied compared with 31 of 49 (63%) patients in the midazolam group (Δ 11%; 95% CI −7% to 28%). Similarly, parents in both groups were equally satisfied with the sedation because 37 of 50 (74%) reported that they would strongly or very strongly choose the same sedative drug.

The primary investigator correctly guessed the study drugs given to 43 of 50 (86%) patients in the midazolam group and 40 of 50 (80%) patients in the etomidate group (Δ 6%; 95% CI −9% to 21%).

## LIMITATIONS

A primary limitation of this study is the etomidate-associated myoclonus hindering reliable blinding for the study, which may have introduced bias.

Another limitation of the study was that only 36% of the patients in the midazolam group were able to reach an adequate level of sedation (Ramsay score ≥4). The patients who did not achieve adequate sedation underwent fracture reduction nonetheless but could not be used for further subanalysis for this outcome (using the nonparametric Cox proportional hazards modeling). We used currently recommended doses,[2,3,14-16,25] and titration as a means to achieve adequate sedation was not possible because of the blinding.

## DISCUSSION

The findings from this double-blind, randomized, controlled trial suggest that in children requiring procedural sedation and analgesia, the use of etomidate resulted in shorter induction and recovery times compared with midazolam. Similarly, we observed that in comparison to midazolam, etomidate adequately sedated a significantly greater proportion of patients. The success of fracture reduction was, however, similar for both groups.

Etomidate use had been initially described for rapid sequence intubation in the ED in adults, as well as in children.[8-10] There is a paucity of literature that addresses the use of etomidate for procedural sedation specifically in large samples of children. Dickinson et al [17] reported an 83% success rate for fracture reduction among 53 children in a retrospective medical record review. There were no major adverse effects at a mean total dose of 0.24 mg/kg, and 64% of patients were discharged after an average observation time of 94 minutes. McDowall et al [19] retrospectively compared the efficacy of etomidate (n=101) (initial dose of 0.3 mg/kg) to propofol and ketamine in children undergoing painful procedures in an oncology clinic. Although etomidate was

the only agent associated with myoclonus, it caused significantly less agitation and tachycardia than ketamine and less hypoxia than propofol. Kienstra et al,[18] in the only randomized clinical trial to date in children using etomidate, reported significantly shorter induction times (difference in the means of 2.1 minutes; 95% CI 0.35 to 3.86 minutes), sedation times (difference in the means of 31.3 minutes; 95% CI 24.0 to 38.5 minutes), and fewer adverse effects when compared with pentobarbital. Similar reduction in procedural sedation and analgesia times were reported by Burton et al [35] in a comparison of etomidate and midazolam in 46 adults undergoing anterior shoulder reduction. The median time of procedural sedation and analgesia for patients administered etomidate was 10 minutes (95% CI 8 to 15 minutes) compared with 23 minutes (95% CI 16 to 30 minutes) for patients administered midazolam (difference medians for procedural sedation and analgesia of 13 minutes; 95% CI 5 to 22 minutes).

Although we showed that the level of sedation before the painful procedure, as judged by the Ramsay score, was deeper in the etomidate group compared with the midazolam group, this difference was not apparent with the COMFORT scale. The latter scale is more extensive and usually used for critically ill, intubated patients. We believe that the Ramsay scale, used to calculate our primary outcome, more accurately reflected the change in levels of sedation.

Except for myoclonus and pain on injection, the rate of adverse events experienced by both groups of patients in this study was similar. The 22% rate of observed myoclonus is similar to that reported by McDowall et al[19] (17%) and Burton et al[35] (21%). Although well accepted for procedural sedation and analgesia, midazolam has the potential for inducing respiratory depression and hypotension.[7] Common adverse effects, including oversedation, have been reported in children.[25] In the present study, desaturation rates in the 2 groups were comparable but higher than previously reported. These differences could be attributed to the strict cutoff for desaturation we adopted (93%) and also to the fact our patients were not preoxygenated. Only 1 patient in the midazolam group was considered oversedated but responded well to frequent stimulation. No patient in our study required bag-valve manual ventilation or endotracheal intubation.

To our knowledge, this is the first randomized controlled trial that evaluated the utility of etomidate in the pediatric ED for procedural sedation and analgesia. Our findings suggest that etomidate may be more efficacious than midazolam. Future studies should evaluate the cost-benefits of using this drug for routine pediatric procedural sedation and analgesia.

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*Author contributions:* LD, AD, BN, BB, DA, and CS conceived the study, designed the trial, and obtained research funds. LD was responsible for the conduct of the trial, patient recruitment, and data collection. BB and DA provided statistical advice on study design and analyzed the data. LD drafted the manuscript and all authors contributed to its revision. LD takes the responsibility for the paper as a whole.

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## REFERENCES

1. Petrack EM, Christopher NC, Kriwinsky J. Pain management in the emergency department: patterns of analgesic utilization. *Pediatrics*. 1997;99:711-714.
2. Pena BM, Krauss B. Adverse events of procedural sedation and analgesia in a pediatric emergency department. *Ann Emerg Med*. 1999;34:483-491.
3. Krauss B, Green SM. Sedation and analgesia for procedures in children. *N Engl J Med*. 2000;342:938-945.
4. Kennedy RM, Porter FL, Miller JP, et al. Comparison of fentanyl/midazolam with ketamine/midazolam for pediatric orthopedic emergencies. *Pediatrics*. 1998;102:956-963.
5. Sievers TD, Yee JD, Foley ME, et al. Midazolam for conscious sedation during pediatric oncology procedures: safety and recovery parameters. *Pediatrics*. 1991;88:1172-1179.
6. Morton NS. Total intravenous anaesthesia (TIVA) in paediatrics: advantages and disadvantages. *Paediatr Anaesth*. 1998;8:189-194.
7. Nordt SP, Clark RF. Midazolam: a review of therapeutic uses and toxicity. *J Emerg Med*. 1997;15:357-365.
8. Bergen JM, Smith DC. A review of etomidate for rapid sequence intubation in the emergency department. *J Emerg Med*. 1997;15:221-230.
9. Sokolove PE, Price DD, Okada P. The safety of etomidate for emergency rapid sequence intubation of pediatric patients. *Pediatr Emerg Care*. 2000;16:18-21.
10. Guldner G, Schultz J, Sexton P, et al. Etomidate for rapid-sequence intubation in young children: hemodynamic effects and adverse events. *Acad Emerg Med*. 2003;10:134-139.
11. Falk J, Zed PJ. Etomidate for procedural sedation in the emergency department. *Ann Pharmacother*. 2004;38:1272-1277.
12. American Academy of Pediatrics Committee on Drugs. Guidelines for monitoring and management of pediatric patients during and

after sedation for diagnostic and therapeutic procedures. *Pediatrics*. 1992;89:1110-1115.
13. Gross JB, Bailey PL, Caplan RA, et al. Practice guidelines for sedation and analgesia by non-anesthesiologists: a report by the American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. *Anesthesiology*. 1996; 84:459-471.
14. Algren JT, Algren CL. Sedation and analgesia for minor pediatric procedures. *Pediatr Emerg Care*. 1996;12:435-441.
15. Cote CJ. Sedation for the pediatric patient: a review. *Pediatr Clin North Am*. 1994;41:31-58.
16. Shields RE. A comprehensive review of sedative and analgesic agents. *Crit Care Nurs Clin North Am*. 1997;9:281-288.
17. Dickinson R, Singer AJ, Carrion W. Etomidate for pediatric sedation prior to fracture reduction. *Acad Emerg Med*. 2001;8:74-77.
18. Kienstra AJ, Ward MA, Sasan F,et al. Etomidate versus pentobarbital for sedation of children for head and neck CT imaging. *Pediatr Emerg Care* 2004;20:499-506.
19. McDowall RH, Scher CS, Barst SM. Total intravenous anesthesia for children undergoing brief diagnostic or therapeutic procedures. *J Clin Anesth*. 1995;7:273-280.
20. Rothermel LK. Newer pharmacologic agents for procedural sedation of children in the emergency department: etomidate and propofol. *Curr Opin Pediatr*. 2003;15:200-203.
21. Rupprecht T, Kuth R, Bowing B, et al. Sedation and monitoring of paediatric patients undergoing open low-field MRI. *Acta Paediatr*. 2000;89:1077-1081.
22. American College of Emergency Physicians. Clinical policy for procedural sedation and analgesia in the emergency department: American College of Emergency Physicians. *Ann Emerg Med*. 1998;31:663-677.
23. Ramsay MA, Savege TM, Simpson BR, et al. Controlled sedation with alphaxalone-alphadolone. *BMJ*. 1974;2:656-659.
24. De Jonghe B, Cook D, Appere-De-Vecchi C, et al. Using and understanding sedation scoring systems: a systematic review. *Intensive Care Med*. 2000;26:275-285.
25. Havel CJ Jr, Strait RT, Hennes H. A clinical trial of propofol versus midazolam for procedural sedation in a pediatric emergency department. *Acad Emerg Med*. 1999;6:989-997.
26. Moro-Sutherland DM, Algren JT, Louis PT, et al. Comparison of intravenous midazolam with pentobarbital for sedation for head computed tomography imaging. *Acad Emerg Med*. 2000;7:1370-1375.
27. Ambuel B, Hamlett KW, Marx CM, et al. Assessing distress in pediatric intensive care environments: the COMFORT scale. *J Pediatr Psychol*. 1992;17:95-109.
28. van Dijk M, de Boer JB, Koot HM, et al. The reliability and validity of the COMFORT scale as a postoperative pain instrument in 0 to 3-year-old infants. *Pain*. 2000;84:367-377.
29. Scott J, Huskisson EC. Graphic representation of pain. *Pain*. 1976;2:175-184.
30. Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. *Acad Emerg Med*. 2001;8: 1153-1157.
31. Gallagher EJ, Bijur PE, Latimer C, et al. Reliability and validity of a visual analog scale for acute abdominal pain in the ED. *Am J Emerg Med*. 2002;20:287-290.
32. O'Hara M, McGrath PJ, D'Astous J, et al. Oral morphine versus injected meperidine (Demerol) for pain relief in children after orthopedic surgery. *J Pediatr Orthop*. 1987;7:78-82.
33. Smith GA, Strausbaugh SD, Harbeck-Weber C, et al. Comparison of topical anesthetics with lidocaine infiltration during laceration repair in children. *Clin Pediatr (Phila)*. 1997; 36:17-23.
34. Powell CV, Kelly AM, Williams A. Determining the minimum clinically significant difference in visual analog pain score for children. *Ann Emerg Med*. 2001;37:28-31.
35. Burton JH, Bock AJ, Strout TD, et al. Etomidate and midazolam for reduction of anterior shoulder dislocation: a randomized, controlled trial. *Ann Emerg Med*. 2002;40:496-504.

## APPENDIX E1

Ramsay score to assess sedation from 1 to 6.[23]

Awake
1=Anxious, agitated, or both
2=Cooperative, oriented, and tranquil
3=Responds to command only
Asleep
4=Brisk response to light glabellar tap
5=Sluggish response to light glabellar tap
6=No response

## APPENDIX E2

Modified COMFORT scale to assess sedation.*[28]

**Alertness**
Deeply asleep 1
Lightly asleep 2
Drowsy 3
Fully awake and alert 4
Hyperalert 5

**Calmness/Agitation**
Calm 1
Slightly anxious 2
Anxious 3
Very anxious 4
Panicky 5

**Respiratory Response**
Quiet breathing, no crying 1
Sobbing or gasping 2
Moaning 3
Crying 4
Screaming 5

**Physical Movement**
No movement 1
Occasional slight movement 2
Frequent slight movement 3
Vigorous movement limited to extremities 4
Vigorous movement including torso and head 5

**Blood Pressure (BP)**
BP below baseline 1
BP consistently at baseline 2
BP elevations of less 15% from baseline 3
BP elevations of 15% from baseline 4
BP elevations of more than 15% from baseline 5

**Pulse Rate (PR)**
PR below baseline 1
PR consistently at baseline 2
PR elevations of less 15% from baseline 3
PR elevations of 15% from baseline 4
PR elevations of more than 15% from baseline 5

**Muscle Tone**
Totally relaxed muscle tone 1
Reduced muscle tone 2
Normal muscle tone 3
Increased muscle tone and flexion of fingers and toes 4
Extreme muscle rigidity and flexion of fingers and toes 5

**Facial Tension**
Facial muscles totally relaxed 1
Facial muscle tone normal; no facial muscle tension evident 2
Tension evident in some muscles 3
Tension evident throughout facial muscles 4
Facial muscles contorted and grimacing 5

*Note that each response category ranges from 1 (low distress) to 5 (high distress). The total score thus ranges from a minimum of 8/40 (oversedation) to a maximum of 40/40 (undersedation).