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A Randomized Comparison of Nitrous Oxide Plus Hematoma Block Versus Ketamine Plus Midazolam for Emergency Department Forearm Fracture Reduction in Children

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ABSTRACT

OBJECTIVES. Ketamine provides effective and relatively safe sedation analgesia for reduction of fractures in children in the emergency department. However, prolonged recovery and adverse effects suggest the opportunity to develop alternative strategies. We compared the efficacy and adverse effects of ketamine/midazolam to those of nitrous oxide/hematoma block for analgesia and anxiolysis during forearm fracture reduction in children.

METHODS. Children 5 to 17 years of age were randomly assigned to receive intravenous ketamine (1 mg/kg)/midazolam (0.1 mg/kg; max: 2.5 mg) or 50% nitrous oxide/50% oxygen and a hematoma block (2.5 mg/kg of 1% buffered lidocaine). All of the children received oral oxycodone 0.2 mg/kg (max: 15 mg) at triage before reduction. Videotapes were obtained before (baseline), during (procedure), and after (recovery) reduction and scored using the Procedure Behavioral Checklist by an observer blinded to study purpose. The primary outcome measure was the mean change in Procedure Behavioral Checklist score from baseline to procedure, with greater change indicating greater procedure distress. Other outcome measures of efficacy included recovery times and visual analog scale scores to assess patient distress, parent report of child distress, and orthopedic surgeon satisfaction with sedation. Adverse effects were assessed during the emergency visit and by telephone 1 day after reduction. Data were analyzed using repeated measures, that is, analysis of variance, χ², and t tests.

RESULTS. There were 102 children (mean age: 9.0 ± 3.0 years) who were randomly assigned. There was no difference in age, race, gender, and baseline Procedure Behavioral Checklist scores between ketamine/midazolam (55 subjects) and nitrous oxide/hematoma block (47 subjects). Mean changes in Procedure Behavioral Checklist scores were very small for both groups. The mean change in Procedure Behavioral Checklist was less for nitrous oxide/hematoma block, and patients and
parents reported less pain during fracture reduction with nitrous oxide/hematoma block. Recovery times were markedly shorter for nitrous oxide/hematoma block compared with ketamine/midazolam. Orthopedic surgeons were similarly satisfied with the 2 regimens. Of the ketamine/midazolam subjects, 11% had O₂ saturations <94%. Other adverse effects occurred in both groups, but more often in ketamine/midazolam both during the emergency visit and at 1-day follow-up.

CONCLUSIONS. In children who had received oral oxycodone, both nitrous oxide/hematoma block and ketamine/midazolam resulted in minimal increases in distress during forearm fracture reduction at the doses studied. The nitrous oxide/hematoma block regimen had fewer adverse effects and significantly less recovery time.

Deep sedation of children for intensely painful fracture reduction is increasingly common in the emergency department (ED). Dedicated patient monitoring to assure effective cardiopulmonary and other vital functions is critical until the patient has recovered sufficiently to maintain these functions independently. Procedural sedation techniques for fracture reduction that result in prolonged recovery place a significant burden on health care resources in a busy ED.

Intravenous ketamine is increasingly used alone or with midazolam (K/M) for pediatric fracture reduction and has few serious adverse effects. However, recovery sufficient for discharge may take 1 to 2 hours. In addition, adverse effects, such as vomiting, and the need for intravenous access if a titration technique is used suggest the opportunity to investigate alternative methods for pediatric fracture reduction sedation/analgesia.

Inhaled nitrous oxide (N₂O) also has been reported to reduce pain and distress associated with fracture reduction in children. N₂O is more effective when augmented by injection of lidocaine into the hematoma (hematoma block [HB]) of fractures of the middle to distal forearm, the site of fractures for intravenous access if a titration technique is used suggest the opportunity to investigate alternative methods for pediatric fracture reduction sedation/analgesia.

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The purpose of this study was to compare the efficacy and adverse effects of intravenous K/M versus N₂O/HB for analgesia and anxiolysis during forearm fracture reduction in children, including differences in recovery times. We hypothesized that both regimens would effectively reduce procedural distress, but children who received K/M would have less increase in distress during fracture reduction compared with those who received N₂O/HB. In addition, we hypothesized that children who received N₂O/HB would have significantly shorter recovery time and fewer adverse effects.

METHODS
We conducted a prospective, randomized trial in American Society of Anesthesiologists (ASA) physical status class I or II children 5 to 17 years old presenting to the ED of St Louis Children’s Hospital for reduction of middle to distal forearm fractures. Children were excluded if there was an open fracture; a history of previous fracture reduction or adverse effect associated with previous ketamine, midazolam, N₂O, or lidocaine administration; a diagnosis of acute otitis media or psychiatric disease; or if they had food or liquid intake within 2 hours of the planned reduction. In accordance with our standard care for children with suspected fractures in the ED, all of the children received oral oxycodone 0.2 mg/kg (maximum: 15 mg) at triage before obtaining radiographs or study enrollment. The time between oxycodone administration and fracture reduction was not controlled and varied considerably, typically 1 to 3 hours, because of availability of personnel for fracture reduction.

After informed consent and, when appropriate, assent had been obtained, children were randomly assigned to receive intravenous K/M or inhaled N₂O/HB before fracture reduction. One of the authors (M.S.), who did not have any contact with patients or investigators during the study, generated the allocation procedure. The randomization code was developed using a computer random number generator to select random permuted blocks of varying length and maintained in sealed opaque envelopes until consent to participate was obtained. To minimize baseline distress associated with intravenous placement, patients randomly assigned to receive K/M had an intravenous catheter inserted using subcutaneously injected buffered lidocaine for skin and venous wall anesthesia. Midazolam 0.1 mg/kg with a maximum of 2 mg for anxiolysis and the antisialagogue glycopyrrolate 5 μg/kg with a maximum of 200 μg were administered ~2 minutes before fracture reduction. Ketamine 1 mg/kg was administered ~1 minute before fracture reduction.

Patients randomly assigned to the N₂O/HB group received a mixture of 50% N₂O/50% O₂ through a scented face mask for ~3 minutes before placement of the HB. N₂O was administered using a customized continuous circuit apparatus that allowed gradual increases in N₂O by a Washington University School of Medicine attending or fellow level pediatric emergency medicine physician. Before performing the fracture reduction, the resident physician in orthopedic surgery administered the HB. We steriley injected 2.5 mg/kg of 1% buffered lidocaine (0.25 mL/kg) with a maximum dose of 150 mg (15 mL) into the fracture hematoma using an 18-gauge needle. In subjects with fractures of both the radius and ulna, the buffered lidocaine dose was divided between.
fractures sites. Localization of the fracture site hematoma was achieved by manual palpation with secondary confirmation of needle position by fluoroscopy as needed. Proper location of the HB was confirmed by aspiration of the fracture hematoma immediately before injection of the lidocaine. Failure of either K/M or N₂O/HB was defined as patient distress either sufficient to interfere with fracture reduction or unacceptable in the opinion of the sedating physician. If failure occurred, supplemental ketamine was titrated to enable effective fraction reduction.

The primary outcome measure for efficacy was the change in subject distress from baseline to procedure as measured by the Procedure Behavior Checklist (PBCL), an observational measure that has been validated for children as young as 4 years old.¹⁵ The PBCL evaluates both the intensity and frequency of 10 defined behaviors that indicate distress (Table 1). Videotapes of subjects from baseline through recovery were scored using the PBCL by a single trained observer who was blinded to the study purpose. The observer rated each of the 10 PBCL behaviors from 1 to 5 during each of 3 intervals: baseline, procedure, and recovery. The baseline interval began immediately after study enrollment, included intravenous placement for K/M subjects, and ended after sedation medications were administered (K/M given or N₂O begun). The procedure interval included the HB (for N₂O/HB group), fracture reduction, and the painful cast molding. The recovery interval began after completion of cast molding, included the rest of the casting, and ended when a recovery Aldrete score of 10 was achieved.¹⁶ The 10 behavior ratings for each interval were assigned at the conclusion of the interval and reflected the behaviors throughout the entire interval. These were summed for each interval to give the PBCL score of the interval. PBCL scores range from 10 to 50, with higher scores indicating greater distress. Interobserver reliability between the observer and a psychologist experienced in PBCL scoring showed a mean weighted κ of 0.82 for 5 tapes. Recovery time was the duration in minutes of the recovery interval. Physicians, nurses, parents, and subjects were not blinded because of the obvious differences in sedation administration techniques.

We measured patient and parent rating of pain using a 10-point visual analog scale (VAS). These VAS ratings compared the secondary outcome measures of efficacy.

The orthopedic surgeon performing the reduction scored his/her satisfaction with the sedation technique at the conclusion of the procedure. Higher VAS scores indicated greater pain, anxiety, recall, and satisfaction. We also asked subjects and parents if they would choose the same sedation regimen for a future reduction as a global measure of satisfaction.

Primary outcome measures for adverse effects were abnormalities in cardiopulmonary function as measured by vital signs and pulse oximetry. An emergency nurse dedicated to patient monitoring and documentation during sedation and recovery recorded data on a standardized data collection form. Data were recorded every 5 minutes during the procedure and then during recovery until a level of moderate sedation occurred; thereafter, data were recorded every 15 minutes until full recovery. Hypoxia was defined as an oxygen saturation <93% while breathing room air or N₂O mixed with oxygen. Level of consciousness, vomiting, and any other adverse effects were also recorded.

We assessed other adverse effects that occurred during the ED visit or after discharge but within 1 day of the reduction procedure using questionnaires completed by the subjects. Subjects completed the questionnaire about adverse effects that occurred in the ED just before discharge, and the 1-day follow-up questionnaire was completed over the telephone. Adverse effects, including vomiting, headache, ataxia, difficulty breathing, nightmares, excessive crying, hallucinations, earache, and lethargy, were assessed.

Data Analysis

Data were analyzed using SAS 8.02 (SAS Institute, Cary, NC) and EpiCalc 2000, version 1.02 (available at: www.brixtonhealth.com). We used repeated-measures analysis of variance to test mean changes in PBCL score from baseline to procedure and to recovery between children who received K/M compared with those who received N₂O/HB for forearm reduction. We used t tests to statistically test differences in mean recovery time between the 2 groups. We used χ² to statistically test differences in the proportions of adverse effects and regimen acceptability by the children and their parents between both groups. We calculated 95% confidence intervals (CIs) to describe the variability in observed estimates.¹⁷ A P < .05 was considered to be statistically significant. We calculated sample size regarding efficacy using the PBCL as the critical measure. At the recommendation of a psychologist (E. Chen, PhD, written communication, 2003) experienced in using the PBCL, a change of 1 in the PBCL from baseline to reduction intervals was used as the effect size. Patients were analyzed according to the intention-to-treat method. To achieve statistical power of 0.80 and a significance level of 0.05, a sample size of 50 per group or a total of 100 patients was needed. No subgroup analyses were performed.

<table>
<thead>
<tr>
<th>TABLE 1 PBCL Score</th>
<th>Anxiety verbalized</th>
<th>Verbal stalling</th>
<th>Physical resistance</th>
<th>Flinching</th>
<th>Groaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle tension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screaming</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crying</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restraint used</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain verbalized</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Intensity and frequency of each behavior is rated on a 1-to-5 scale: 1 = very mild, seldom; 5 = extremely intense, nearly constant.
RESULTS

Efficacy

We enrolled 102 children: 55 were randomly assigned to receive K/M and 47 to receive N2O/HB. The 2 groups were similar with regard to age, gender, race, ASA class, fracture location (Table 2), and baseline PBCL score (Table 3).

Both groups had very little increase in distress during the fracture reductions. The mean change in PBCL scores from baseline to procedure, the primary outcome measure, was statistically greater for K/M ($P_{H11005}=0.02$), indicating greater distress during reduction (Fig 1). The effect size for this change between groups was 1.6 (95% CI: 0.25 to 3.0). Consistent with this finding, although there were no significant differences in mean PBCL scores between sedation groups during baseline, procedure, and recovery intervals (Table 3), repeated-measures analysis of variance showed an interaction between the type of sedation and the time of PBCL measurement ($P_{H11005}=0.04$). The change from baseline to recovery was not statistically different between sedation groups ($P_{H11005}=0.57$). Subjects who received N2O/HB were rated by nurses to be more responsive than subjects who received K/M during the procedure (fracture reduction and molding; Fig 2). Mean recovery time was significantly shorter for children who received N2O/HB (16 minutes; median: 14 minutes) compared with K/M (83 minutes; median: 85 minutes; Fig 3).

There were protocol failures in both groups. One subject randomly assigned to receive N2O/HB was determined to be inadequately sedated for reduction and subsequently received intravenous ketamine. Five subjects randomly assigned to receive K/M required more ketamine than the study dose of 1 mg/kg. The range of ketamine doses in these 5 subjects was 2 to 4 mg/kg. These subjects were analyzed according to the intent-to-treat method. All of the fracture reductions were successfully completed.

Subjects randomly assigned to receive N2O/HB reported less memory of pain during reduction than those randomly assigned K/M, and their parents reported less observed pain during reduction (Table 3). There were no differences between groups in self-reported subject or parent anxiety or subject recall of the procedure. When asked if they would choose the same regimen if their

<table>
<thead>
<tr>
<th>Variable</th>
<th>K/M, Mean</th>
<th>N2O/HB, Mean</th>
<th>Difference in Mean Between K/M and N2O/HB, Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>10.5</td>
<td>11.3</td>
<td>0.8</td>
<td>(−0.5 to 2.1)</td>
</tr>
<tr>
<td>Procedure</td>
<td>12.6</td>
<td>11.6</td>
<td>0.9</td>
<td>(−0.4 to 2.2)</td>
</tr>
<tr>
<td>Recovery</td>
<td>10.8</td>
<td>11.2</td>
<td>0.4</td>
<td>(−0.6 to 1.5)</td>
</tr>
<tr>
<td>Subject reporting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>2.9</td>
<td>1.8</td>
<td>1.1</td>
<td>(0.0 to 2.1)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>3.2</td>
<td>3.1</td>
<td>0.2</td>
<td>(−1.1 to 1.5)</td>
</tr>
<tr>
<td>Recall</td>
<td>3.1</td>
<td>2.8</td>
<td>0.2</td>
<td>(−0.9 to 1.4)</td>
</tr>
<tr>
<td>Parental reporting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject’s pain during procedure</td>
<td>4.1</td>
<td>2.5</td>
<td>1.6</td>
<td>(0.6 to 2.6)</td>
</tr>
<tr>
<td>Subject’s anxiety during procedure</td>
<td>4.9</td>
<td>4.6</td>
<td>0.3</td>
<td>(−1.1 to 1.6)</td>
</tr>
<tr>
<td>Parent’s anxiety during procedure</td>
<td>6.5</td>
<td>6.3</td>
<td>0.3</td>
<td>(−1.1 to 1.6)</td>
</tr>
<tr>
<td>Regimen acceptability</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parents</td>
<td>84%</td>
<td>98%</td>
<td>0.1*</td>
<td>(0.0 to 0.9)</td>
</tr>
<tr>
<td>Subjects</td>
<td>86%</td>
<td>88%</td>
<td>0.6*</td>
<td>(0.2 to 2.3)</td>
</tr>
<tr>
<td>Orthopedic surgeon satisfaction (VAS)</td>
<td>8.8</td>
<td>8.4</td>
<td>0.7</td>
<td>(−0.3 to 1.61)</td>
</tr>
</tbody>
</table>

* An odds ratio of 0.1 suggests that parents were much less likely to choose the same regimen again in the future when their child received the K/M regimen.

Because the 95% CI included the null value, subjects were equally likely to choose the same regimen in the future.

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**Table 2: Subject Characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>K/M $(N = 55)$</th>
<th>N2O/HB $(N = 47)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>9.4 (8.5 to 10.2)</td>
<td>8.7 (7.9 to 9.4)</td>
</tr>
<tr>
<td>Male, %</td>
<td>58 (45 to 71)</td>
<td>62 (48 to 76)</td>
</tr>
<tr>
<td>Race, white, %</td>
<td>56 (43 to 70)</td>
<td>51 (37 to 66)</td>
</tr>
<tr>
<td>ASA class I, %</td>
<td>93 (86 to 100)</td>
<td>89 (81 to 98)</td>
</tr>
<tr>
<td>Fracture location, epiphyseal, physeal, metaphyseal, %</td>
<td>84 (74 to 93)</td>
<td>87 (78 to 97)</td>
</tr>
</tbody>
</table>

Data are mean (95% CI).
child required a future fracture reduction, a greater proportion of parents whose children received N\textsubscript{2}O/HB replied affirmatively (Table 3). There were no significant differences between groups when children answered the same question. Orthopedic surgeon satisfaction between groups was similar (Table 3).

**Adverse Effects**

Subjects randomly assigned to receive K/M were more likely to have an adverse effect while in the ED, and both groups reported adverse effects within the first day post-reduction (Table 4). During the procedure, vomiting occurred in 4% of subjects who received K/M and 6% of subjects who received N\textsubscript{2}O/HB; an additional 20% in each group vomited before discharge from the ED. Transient hypoxia occurred in 11% of subjects in the K/M group with 1 experiencing both vomiting and hypoxia; these incidents were managed with airway repositioning and oxygen administration by simple mask.

**Limitations**

This study was conducted by physicians and nurses experienced in deep sedation, the care of critically ill and injured children, and use of a “child-friendly” N\textsubscript{2}O delivery system custom built at our institution, but similar to commercially available dental/oral surgical devices. Because fracture HB use has been reported primarily for middle to distal forearm fractures, only fractures in these sites were studied. For these reasons and because only 5- to 17-year-old subjects were studied, caution in generalization of these results to other clinical settings, ages, fracture sites, and procedures is warranted.

Respiratory depression as an adverse event was indirectly approximated by detecting oxygen saturation of \textless 93\%. Subjects receiving 50\% N\textsubscript{2}O were actually receiving the N\textsubscript{2}O blended with 50\% oxygen; thus, oxygen desaturation was unlikely to occur unless severe respiratory depression occurred. It is possible that some subjects receiving N\textsubscript{2}O experienced mild respiratory depression, similar to that experienced by some who received K/M, yet no desaturation occurred because of the concurrent administration of oxygen. Further studies using end-tidal CO\textsubscript{2} monitoring may help clarify this issue.

Because of the obvious differences in sedation techniques between groups, full blinding was not possible. However, when the PBCL scorer of the videotapes (our primary outcome measure) was asked after scoring all of the tapes what she thought was the study purpose, she responded, “to evaluate different orthopedic techniques (maneuvers) for reducing fractures.” For all of the other outcome measures, blinding did not occur. Finally, plasma lidocaine levels were not measured to assure that rapid absorption of lidocaine from the HB did not contribute to depth of sedation and adverse effects.

**DISCUSSION**

**Efficacy**

Contrary to our hypothesis, at the doses studied, subjects who received N\textsubscript{2}O/O\textsubscript{2} plus lidocaine HB had statistically less increase in distress and less memory of pain during orthopedic reduction of acute middle to distal forearm fractures compared with subjects who received K/M. Although the increase in distress from baseline was statistically less for the N\textsubscript{2}O/HB group (\(P = .02\)), it should be noted that both groups had very low PBCL scores

<table>
<thead>
<tr>
<th>Variable</th>
<th>In ED</th>
<th>First Day Postdischarge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting, %</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>Headache, %</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Ataxia, %</td>
<td>24</td>
<td>9</td>
</tr>
<tr>
<td>Difficulty breathing, %</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Nightmares, %</td>
<td>20</td>
<td>7</td>
</tr>
<tr>
<td>Excessive crying, %</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>Hallucinations, %</td>
<td>29</td>
<td>4</td>
</tr>
<tr>
<td>Earache, %</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Lethargy, %a</td>
<td>47</td>
<td>44</td>
</tr>
</tbody>
</table>

\(a\) Only measured on first day postdischarge questionnaire.
both at baseline and during fracture reduction indicating low levels of distress; mean increases in PBCL scores were 0.3 for N₂O/HB and 2.1 for K/M of a possible 40. Whether the difference in PBCL scores of 1.8 is clinically significant is unclear. To our knowledge, careful validation of how much change in PBCL is considered clinically significant has not been performed (L. Zeltzer, written communication, 2005). Both groups had high success rates of fracture reduction.

Ketamine-based sedation/analgesia has been shown to be very effective in reducing pain and distress associated with extremely painful orthopedic forearm fracture reductions. Although less extensively studied, N₂O-based sedation/analgesia and lidocaine HB analgesia have also been shown to provide effective reduction of pain and distress during forearm fracture reductions, especially in combination. However, the 2 had not been compared previously.

The dose of ketamine chosen for the current study was based on our previous work in which a mean dose of 1.05 ± 0.52 mg/kg of ketamine (along with 0.11 mg/kg of midazolam) was determined by titration to be effective for fracture reduction. This ketamine dose is consistent with that used by some authors but less than that recommended by others. In the current study, each patient also received an oral oxycodone dose of 0.2 mg/kg administered in triage. The analgesic effectiveness of this regimen was supported by the very small increase in PBCL scores from baseline during the fracture reduction. Larger doses of ketamine would likely induce deeper sedation, even less distress, and less recall but would also likely result in even longer recovery.

Midazolam was administered intravenously in a fixed dose of 2 mg to reduce patient anxiety before ketamine sedation and may have deepened sedation. Whether midazolam reduces ketamine-induced dysphoria during recovery has been questioned. The similar PBCL scores during recovery in both groups suggest that this dose of midazolam did not noticeably impact subject recovery.

Other researchers have shown that 50% N₂O facilitates forearm fracture reductions in children. The apparatus used in these studies and most commonly available for delivery of N₂O in the emergency setting (Nitronox) requires patient generation of a sufficient negative pressure to open a demand valve to deliver a fixed 50% N₂O/50%O₂. The N₂O/O₂ delivery device in the current study was a locally constructed valveless, continuous circuit apparatus that allowed variable delivery of N₂O from 0% to 50% as the patient breathed normally. Our compact design is less intrusive in the room space but is functionally similar to commercially available devices used by oral surgeons and dentists. This device allows the N₂O percentage to be gradually increased (usually over 2–5 minutes) to 50% to avoid the sometimes frightening sudden onset of the floating, tingling effects of the gas that may occur if the patient initially receives 50% N₂O. To further enhance acceptance of the N₂O, children were also encouraged to choose a lip balm flavor such as bubble-gum or watermelon to scent the mask and to hold the mask, if desired, during delivery.

However, many children exhibit significant distress during fracture reduction when 50% N₂O is the sole analgesic administered. Hennrikus et al found that addition of a lidocaine fracture HB significantly augmented the effectiveness of the N₂O sedation. HBs have been shown to be a safe and effective method to anesthetize a forearm fracture site before manipulation and not to affect fracture healing or increase the rate of infection when placed with sterile technique. We believe placement of an HB and subsequent fracture reduction without anxiolysis would frighten many children and would incompletely block procedural pain. Consistent with the work of Hennrikus et al, the current study found that the combination of 50% N₂O with the HB, augmented by oral oxycodone, provided effective analgesia, including those with completely displaced and overriding fractures. This may be because displaced fractures likely have large hematomas, which may enable a more effective HB in comparison with greenstick fractures with little or no hematoma. Most of the patients in this study had distal forearm fractures and diaphyseal sites or between displaced and nondisplaced fractures.

A maximum dose of 2.5 mg/kg of lidocaine for the HB, chosen for the current study, has been shown to be safe in adults undergoing HB for forearm fracture reduction. Meining et al found that this dose resulted in maximum plasma lidocaine levels of 1100 ng/mL, well below the thresholds of ~5 to 10 000 ng/mL for neurologic and cardiac toxicity. Although no overt signs of lidocaine toxicity, such as seizures or dysrhythmias, occurred in any subject in the current study, significant systemic absorption of lidocaine through an intraosseous mechanism may have resulted in central nervous system depression and enhanced N₂O sedation; this issue warrants further study.

Recovery Time

Recovery was remarkably shorter with N₂O/HB compared with K/M with means of 16 vs 83 minutes, respectively. Indeed, many subjects were near full recovery by completion of casting, because the N₂O was turned off after the painful molding of the cast around the fracture site had been performed. This allowed the subjects to recover while the nonpainful proximal portion of the cast was completed. Recovery from the ketamine sedation may have been slightly longer because of
the addition of midazolam, but recovery from this combination has been shown not to be significantly longer than with ketamine alone.²¹,²²

The poor solubility of N₂O in plasma results in rapid onset of effect and rapid recovery.²⁶ It is this rapid recovery that makes this agent of special interest in the busy ED. Patients should be observed by parents for 5 to 10 minutes after discontinuation of N₂O, because they may be ataxic or have emesis during this period, but bedside monitoring by a health care provider usually is not required.

Safety
The frequency of adverse events while in the ED, especially ataxia, nightmares, and hallucinations, was greater in subjects who received K/M. However, these symptoms occurred in some within the N₂O/HB group as well, and some within both groups had vomiting, headache, and crying postsedation before discharge. Both groups also reported numerous but similar adverse effects within 1 day postsedation with nightmares, more frequently reported in the K/M group. The higher frequency of nightmares found in this study compared with previous work by ourselves and others²⁴ may partly be because of difficulty in defining adverse psychotomimetic effects. For this study, nightmares were defined as frightening dreams, and subjects drew their own conclusions. The long-term clinical significance of psychotomimetic effects on children needs further investigation.

Oxygen saturations <93% transiently occurred in 11% of subjects in the K/M and in none of the N₂O/HB group; all were resolved with airway opening maneuvers and/or supplemental oxygen administration without use of positive pressure. The addition of K/M may have been responsible for some of the transient hypoxemia. Wathen et al²¹ noted desaturation <90% in 7% of patients with K/M and in 2% with ketamine alone. Ad hoc analysis in our previous study found, despite using larger doses of midazolam, no clear relationship between the dose of midazolam and desaturation <90% with K/M. Another contributor to respiratory depression may have been the oxycodone administered in triage. As noted in the “Limitations” section above, the N₂O/HB group was receiving 50% O₂ blended with the N₂O, and, thus, respiratory depression as indirectly suggested by oxygen desaturation may have been obscured; however, these subjects were also less deeply sedated. Diffusional hypoxia after cessation of N₂O has been described²⁸ but was not noted in any subject in this study.

It should be noted that some children who received the combination of oxycodone and N₂O/HB experienced deep sedation, thus patients receiving this regimen should be monitored as for deep sedation.¹⁻¹¹ In the current study, the physician administering the N₂O was also responsible for monitoring the subject’s cardiopulmonary status and was empowered to intervene immediately, if necessary, for subject safety, for example, to help clear the airway during vomiting. Administration of the N₂O and monitoring of the patient could be performed by other health care workers trained in its use, as permitted by local regulation. Because of the use of lidocaine for the HB, providers responsible for the sedation should be prepared for management of seizures or cardiac dysrhythmias because of unlikely but potential lidocaine toxicity.³⁰

Vomiting is an adverse effect of both ketamine⁴⁻⁹ and N₂O.¹⁴,²⁶,³²⁻³⁴ Furthermore, a greater frequency of postoperative nausea and vomiting has been reported in pediatric patients than in adults.³⁵ The incidence rates have been estimated at 34% in children 6 to 10 years old and 32% in children >11 years.³⁶ N₂O may cause nausea and vomiting through stimulation of the sympathetic nervous system with catecholamine release, changes in middle ear pressure with stimulation of the vestibular system, and increased distension of the gastrointestinal tract.³⁸⁻³⁹ Protective laryngeal reflexes are believed to remain intact with 50% N₂O alone³⁸ but may be blunted in patients more deeply sedated with the combination of N₂O and oxycodone. Laryngeal reflexes are also believed to remain largely intact with ketamine,⁹,³⁹⁻⁴¹ but it is unclear whether the addition of relatively low doses of midazolam impacts these reflexes. Vomiting occurred during the deepest sedation in 4% of subjects who received K/M and 6% of subjects who received N₂O/HB, yet no clinical signs of pulmonary aspiration were noted in any subject. The lack of symptoms of aspiration after emesis suggests that protective airway reflexes remained at least partially intact in both groups. However, the sample size of this study is not large enough to accurately access aspiration risk.

The frequency of vomiting with both regimens is approximately double that of our previous studies¹⁴,²² but consistent with that of recovery from general anesthesia.⁴³ Because the addition of an opioid to anesthetic regimens has been shown to increase postoperative vomiting, it is likely that the increase in emesis in the current study is attributable in part to the coadministration of oxycodone, which was not part of the earlier studies. However, the advantages of increased patient comfort during manipulations for radiographs and while awaiting reduction seem clinically significant. Whether the frequency of emesis can be reduced by coadministration of antiemetic agents, such as ondansetron, remains to be determined.

Significance
This first direct comparison of a commonly used regimen (K/M) to a regimen based on N₂O and local anesthesia (lidocaine HB), with both regimens augmented by systemic analgesia (oxycodone), has demonstrated that the N₂O-based regimen is an effective alternative to deep
sedation induced by ketamine for forearm fracture reduction. The primary advantages of the N₂O/HB regimen are its remarkably short recovery time and lack of need for venous access; as noted above, many subjects were fully responsive and interactive by the time casting was completed. Ketamine administered intramuscularly also avoids the need for venous access but results in a median recovery time of ~2 hours.44 Rapid recovery may make this N₂O/HB regimen especially attractive in a busy ED with limited resources.

Another advantage of the combination of local anesthesia with N₂O sedation is that effective analgesia is provided with less sedation. Anecdotally, several children who received the N₂O/HB regimen indicated that they preferred not being “put to sleep.” The linking of local anesthesia with N₂O anxiolysis, moderate analgesia, and amnesia also has been used to reduce distress during the suturing of facial lacerations in young children,45,46 and decades of dental procedures. This strategy may enable health care workers to tailor sedation strategies to patients’ preferences for procedures in which local anesthesia can be achieved, for example, abscess drainage.

CONCLUSIONS
In children who had received oral oxycodone, both the combination of inhaled N₂O with lidocaine fracture HB and the combination of intravenous ketamine and midazolam resulted in minimal increases in distress during forearm fracture reduction. However, the N₂O/HB regimen had significantly less recovery time than the K/M regimen. Orthopedic surgeons were similarly satisfied with both regimens. Although adverse effects occurred in both groups, they were fewer for children who received N₂O plus fracture HB.

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A Randomized Comparison of Nitrous Oxide Plus Hematoma Block Versus Ketamine Plus Midazolam for Emergency Department Forearm Fracture Reduction in Children

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