

# Sedation and Analgesia for Pediatric Fracture Reduction in the Emergency Department

## A Systematic Review

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**Objective:** To assess the safety and efficacy of various forms of analgesia and sedation for fracture reduction in pediatric patients in the emergency department, as observed in randomized controlled trials in pediatric populations.

**Data Sources:** Cochrane Controlled Trials Register, CINAHL (Cumulative Index to Nursing & Allied Health Literature), and MEDLINE. The search terms “fractures,” “manipulation, orthopedic,” “an(a)esthetics,” “analgesics,” and “hypnotics and sedatives” were used.

**Study Selection:** Studies were included if they were randomized controlled trials studying sedative and/or analgesic regimens for fracture reductions in pediatric patients in the emergency department. The search yielded 915 references. From these, 8 studies including 1086 patients were selected.

**Data Extraction:** Interventions studied included intravenous regional blocks (Bier blocks), nitrous oxide,

and parenteral combinations. Data on measures of effectiveness and safety were extracted.

**Data Synthesis:** Ketamine hydrochloride–midazolam hydrochloride was associated with less distress during reduction than fentanyl citrate–midazolam or propofol–fentanyl. Patients receiving ketamine–midazolam required significantly fewer airway interventions than those in whom either fentanyl–midazolam or propofol–fentanyl were used. Data comparing Bier blocks with systemic forms of sedation or analgesia were limited.

**Conclusions:** Ketamine–midazolam seems to be more effective and have fewer adverse events than fentanyl–midazolam or propofol–fentanyl. Data on other forms of analgesia or sedation are too limited to make comparisons. More research is needed to define the regimen that maximizes safety, efficacy, and efficiency for fracture reduction in pediatric patients.

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**L**ONG-BONE FRACTURES ARE one of the most common injuries treated in the emergency department (ED) setting and are also one of the most common serious injuries of childhood. Published reports of fracture rates in children range between 160 and 360 per 10 000 children.<sup>1-3</sup> In Singapore, 6.8% of all children require hospitalization for fracture care by age 16 years.<sup>4</sup> In contrast, in the United States, reimbursement policies and patient preference have led to an increasing push toward providing definitive care to patients with fractures on an outpatient basis. This care is increasingly provided in the ED rather than in the operating room.

Fracture reduction is one of the most painful procedures commonly performed in the ED, but patients and families expect the ED to be a resource for relieving a large percentage of their pain.<sup>5</sup> Health care providers who care for chil-

dren with fractures are faced with the sometimes divergent tasks of providing effective analgesia and anxiolysis while ensuring timely, efficient, cost-effective, and safe care of the patient. The potential benefits of effective sedation during fracture reduction include diminished patient fear and discomfort; parental, provider, and patient satisfaction; decreased utilization of resources; improved outcome of the fracture reduction; and decreased reliance on general anesthesia.

Several studies have documented that children receive inadequate analgesia for fracture pain during their visit to the ED.<sup>6-10</sup> Furthermore, there has been a wide variation in sedation practice patterns,<sup>11</sup> in part because little consensus exists on the safest and most effective regimens.<sup>12</sup>

By systematically reviewing the literature, we hoped to answer the clinical question: What is the safest and most effective means of providing sedation and analgesia to children undergoing frac-

ture reduction in the ED setting? In addition, we hoped to identify areas that require further research.

## METHODS

We searched several bibliographic databases, including MEDLINE (January 1, 1966, through April 30, 2005), the Cochrane Collaboration and Clinical Trials Database (as of April 30, 2005), and CINAHL (Cumulative Index to Nursing & Allied Health Literature) (as of April 30, 2005). Searches for unpublished trials were limited to the Medical Editors' Trial Amnesty. The key word search terms "fractures" or "manipulation, orthopedic" were combined with the terms "an(a)esthetics," "analgesics," or "hypnotics and sedatives." Literature searches were further restricted to studies published in the English language. Abstracts from this initial search were examined and studies were excluded if they did not study sedation for fracture reduction. We also examined articles found when viewing the bibliographies of other clinical trials or review articles as well as articles from our personal files.

We next reviewed the full text of the remaining articles identified in the search. Studies were examined by 2 of us (E.J.K. and R.T.M.); neither reviewer was blinded to journal or authors. Each reviewer independently reviewed the "Methods" section of each article to determine whether it fulfilled criteria for inclusion in the final review. A third author (M.M.G.) resolved any disagreements. Our final analysis was restricted to studies that were identified as randomized controlled trials (RCTs), exclusively included children younger than 18 years, compared pharmacological methods of sedation or analgesia for fracture reduction in the ED setting, and included clinical outcomes and/or complications. Quality was assessed by all reviewers, and studies were included if they were RCTs with adequate randomization. Because of the unique properties of the various sedation modalities, blinding was considered but was not a criterion for inclusion in this analysis. Data were extracted independently by 2 of us (E.J.K. and R.T.M.) from all studies that met inclusion criteria. The primary outcome measure selected was pain scores of individuals undergoing fracture reduction. Secondary outcomes included surrogate measures of pain such as provider, patient, or parent satisfaction; patient memory of the event; procedural success; and the need for additional medication doses. Complications such as apnea, desaturation, hypotension, vomiting, and emergence reactions as well as length of stay were tabulated when data were available.

## RESULTS

The search yielded 915 references. From these, 119 were deemed eligible for more detailed review for potential inclusion. The most common reasons for exclusion of studies from the final analysis were adult subjects, medications studied that were not for procedural pain control in the ED, not patient research (review article, letters, opinion, survey), nonorthopedic procedures, and case series. A listing of articles that were excluded from the systematic review is available on request from the corresponding author.

The final analysis included 8 studies, with some studies evaluating more than one regimen (**Table**).<sup>13-20</sup> Three main forms of sedation-analgesia for fracture reduction were evaluated: (1) Bier blocks, (2) parenteral medications, and (3) nitrous oxide. Bier blocks and narcotic-

benzodiazepine combinations were each evaluated in 3 studies; propofol, ketamine hydrochloride, and nitrous oxide were each evaluated in 2 studies. The Bier block studies used either lidocaine hydrochloride or prilocaine hydrochloride.

## BIER BLOCKS

Three RCTs examined the effectiveness and safety of Bier block anesthesia in children undergoing fracture reduction. Bier blocks are regional nerve blocks in which an intravenous line is placed in the fractured extremity. A tourniquet is applied proximal to the injury and a local anesthetic is injected intravenously into the affected extremity. These studies compared regular-dose (3 mg/kg) and "mini-dose" (1.5 mg/kg) lidocaine hydrochloride,<sup>13</sup> regular-dose lidocaine with an equivalent dose of prilocaine,<sup>14</sup> and regular-dose lidocaine with nitrous oxide.<sup>20</sup>

### ARE BIER BLOCKS EFFECTIVE AT PROVIDING ANALGESIA FOR FRACTURE REDUCTION?

**Yes, but data are limited.** Only 1 RCT has compared Bier block analgesia with a systemic form of analgesia.<sup>20</sup> In this study, 28 children were randomized to receive either a Bier block with 3 mg/kg of lidocaine hydrochloride or self-administered 50% nitrous oxide. There were no significant differences between groups in pain scores by either child or treating physician report. However, given the small sample size, this study may be underpowered to detect a difference between the 2 regimens. Patients treated with nitrous oxide had a significantly shorter total procedure time than patients randomized to Bier block (41.1 minutes [range, 23-63 minutes] vs 61.5 minutes [range, 40-85 minutes];  $P < .001$ ).

### WHICH BIER BLOCK MEDICATION PROTOCOLS ARE MOST EFFECTIVE?

**Standard-dose (3-mg/kg) lidocaine hydrochloride Bier blocks seem to be more effective than either mini-dose or prilocaine Bier blocks.** Two studies have compared different drugs and doses for the Bier block. Bratt et al<sup>13</sup> compared standard-dose (3 mg/kg) lidocaine hydrochloride with a mini-dose Bier block (1.5 mg/kg) in a total of 283 patients. Those receiving standard-dose lidocaine reported significantly less pain than those receiving the low-dose Bier block (96% satisfactory anesthesia vs 87%;  $P < .01$ ). This difference was even more pronounced when the fracture was completely displaced (93% vs 67%;  $P < .01$ ). Davidson et al<sup>14</sup> compared 3-mg/kg doses of lidocaine hydrochloride vs prilocaine hydrochloride in a total of 249 children. In their study, children receiving lidocaine were significantly more likely to have minimal or no pain than those receiving prilocaine, per provider report (90.5% vs 78%;  $P = .01$ ).

### ARE BIER BLOCKS SAFE?

**Probably.** The 3 RCTs that included Bier blocks observed no adverse effects among the 546 procedures.

**Table. Characteristics of Included RCTs**

Source	Age of Subjects, y	Treatment Arm A		Treatment Arm B		Outcome Measures
		Intervention	n	Intervention	n	
Bratt et al, <sup>13</sup> 1996	>3.5	Bier block with lidocaine hydrochloride, 3 mg/kg	140	Bier block with lidocaine hydrochloride, 1.5 mg/kg	143	Faces pain score
Davidson et al, <sup>14</sup> 2002	3-16	Bier block with prilocaine hydrochloride, 3 mg/kg	116	Bier block with lidocaine hydrochloride, 3 mg/kg	133	Subjective pain score; reduction success
Godambe et al, <sup>15</sup> 2003	3-16	Ketamine hydrochloride, 1-2 mg/kg IV; midazolam hydrochloride, 0.05 mg/kg IV	54	Propofol, 1 mg/kg IV; fentanyl citrate, 1-2 µg/kg IV	59	OSBD-r; nurse, parent, provider satisfaction; patient recall; reduction success; sedation and recovery time
Kennedy et al, <sup>16</sup> 1998	5-15	Ketamine hydrochloride, 0.5+ mg/kg IV; midazolam hydrochloride, 0.1+ mg/kg IV	130	Fentanyl citrate, 0.5+ µg/kg IV; midazolam hydrochloride, 0.1 mg/kg IV	130	OSBD-r; parent VAS; orthopedist VAS; patient recall; reduction success; recovery time
Havel et al, <sup>17</sup> 1999	2-18	Propofol, 1+ mg/kg IV; morphine sulfate, 0.05-0.1+ mg/kg IV	43	Midazolam hydrochloride, 0.1+ mg/kg IV; morphine sulfate, 0.05-0.1+ mg/kg IV	46	Ramsay sedation score; patient recall; recovery time; time to discharge
Pierce and Fuchs, <sup>18</sup> 1997	3-18	Ketorolac tromethamine, 1 mg/kg IV; fentanyl citrate, 1+ µg/kg IV; midazolam hydrochloride, 0.1 mg/kg IV	17	Fentanyl citrate, 1+ µg/kg IV; midazolam, 0.1 mg/kg IV	17	CHEOPS; VAS; dose required
Evans et al, <sup>19</sup> 1995	4-15	Meperidine hydrochloride, 2 mg/kg IM; promethazine hydrochloride, 1 mg/kg IM	15	50% Nitrous oxide	15	CHEOPS, reduction success
Gregory and Sullivan, <sup>20</sup> 1996	4-15	Bier block with lidocaine hydrochloride, 3 mg/kg	14	50% Nitrous oxide	14	Faces pain score, VAS, procedure time

Abbreviations: CHEOPS, Children's Hospital of Eastern Ontario Pain Score<sup>21</sup>; IM, intramuscular; IV, intravenous; OSBD-r, Observational Score of Behavioral Distress, Revised<sup>22,23</sup>; RCTs, randomized controlled trials; VAS, visual analog scale.

## NITROUS OXIDE TREATMENT

Two RCTs examined nitrous oxide. One compared nitrous oxide with meperidine hydrochloride and promethazine hydrochloride.<sup>19</sup> The other compared nitrous oxide with Bier block analgesia.<sup>20</sup> The regimens for nitrous oxide administration were generally similar to the protocol described by Wattenmaker et al,<sup>24</sup> with a scavenger system used to deliver a 50:50 nitrous oxide-oxygen mixture to the patient. The anesthetic is self-administered by the patient and requires the patient to generate negative pressure to open the supply valve. After the procedure is completed, patients are administered 100% oxygen for several minutes.

### IS NITROUS OXIDE EFFECTIVE?

Data are too limited to support this intervention's effectiveness. The 2 RCTs that included nitrous oxide studied a total of 58 patients. Evans et al<sup>19</sup> compared self-administered 50% nitrous oxide vs intramuscular meperidine and promethazine. Children's Hospital of Eastern Ontario Pain Scores were not significantly different between the 2 groups (9.6 for nitrous oxide, 9.3 for meperidine-promethazine;  $P > .05$ ). There were also no significant differences between the groups on memory or patient's reported subjective experience. Patients who were

randomized to receive nitrous oxide had a significantly shorter total treatment time (30 minutes vs 83 minutes;  $P < .01$ ).

As already described, Gregory and Sullivan<sup>20</sup> compared nitrous oxide vs a Bier block using lidocaine hydrochloride at 3 mg/kg. There were no significant differences between the 2 groups on either child- or provider-reported pain scales, and patients treated with nitrous oxide had a significantly shorter total procedure time than patients randomized to Bier block.

### IS NITROUS OXIDE SAFE?

Data are too limited to make conclusions on this intervention's safety. Drawing firm conclusions about the safety of this intervention is difficult given the few patients studied. The literature on nitrous oxide included in the study observed no adverse events.

## NARCOTIC-BENZODIAZEPINE COMBINATIONS

Three RCTs included narcotic-benzodiazepine combinations.<sup>16-18</sup> In addition, 1 RCT studied meperidine and promethazine, a nonselective histamine 1 antagonist with sedative and antiemetic properties.<sup>19</sup>

## ARE NARCOTIC-BENZODIAZEPINE COMBINATIONS EFFECTIVE?

The evidence indicates that there are more effective drug combinations. Kennedy et al<sup>16</sup> randomized a total of 260 subjects to either fentanyl citrate–midazolam hydrochloride or ketamine-midazolam. Patients randomized to receive fentanyl-midazolam had more pain and anxiety by every measure: Observational Score of Behavioral Distress, Revised (OSBD-r)<sup>22,23</sup> (mean±SD, 2.7±2.16 vs 1.08±1.12;  $P<.001$ ), parental reporting of pain (5.55±3.33 vs 4.21±3.30;  $P=.05$ ), parental reporting of anxiety (5.49±3.26 vs 4.48±3.26;  $P=.05$ ), and orthopedists' satisfaction (8.71±2.21 vs 9.61±0.78;  $P<.001$ ). Amnesia and depth of sedation were similar between the 2 groups. The group that received fentanyl-midazolam had shorter recovery times than the ketamine-midazolam group (113.7±36.9 minutes vs 127.6±56.2, respectively;  $P=.05$ ).

Havel et al<sup>17</sup> compared midazolam–morphine sulfate with propofol-morphine. A total of 89 patients were randomized to receive either propofol-morphine or midazolam-morphine. The depth of sedation was measured by the Ramsay sedation scale at 5-minute intervals after medication administration. No pain or sedation scores were reported at the time of fracture reduction. Sedation scores at each time point and total morphine dose administered did not differ between the 2 groups. Nine (21%) of 43 patients receiving propofol-morphine had some memory of the reduction, with 1 of those patients relating detailed recall of the pain; 4 (9%) of 46 patients receiving midazolam-morphine recalled their procedure, with none recalling significant pain. Recovery time (midazolam-morphine, 48.2±45.3 minutes; propofol-morphine, 13.6±11.3 minutes) and time to discharge (midazolam-morphine, 71.9±41.9 minutes; propofol-morphine, 43.1±28.2 minutes) favored propofol-morphine.

Pierce and Fuchs<sup>18</sup> evaluated ketorolac tromethamine as an adjunct to fentanyl-midazolam therapy. They administered fentanyl-midazolam to all 34 patients in their study. Patients were randomized to receive ketorolac or saline placebo before fracture reduction. Patients who received ketorolac tended to receive lower doses of fentanyl citrate than those who received the saline placebo, although the difference was not statistically significant (2.26 µg/kg vs 2.85 µg/kg;  $P=.07$ ). Pain scores were not significantly different between the 2 groups.

## ARE NARCOTIC-BENZODIAZEPINE COMBINATIONS SAFE?

The evidence indicates that there are safer treatment regimens available. The largest study of this combination was by Kennedy et al.<sup>16</sup> They found that patients receiving fentanyl-midazolam were more likely to have hypoxia (25% vs 6%;  $P<.001$ ), need breathing cues (12% vs 1%;  $P<.01$ ), and require oxygen (20% vs 10%;  $P<.05$ ) than those receiving ketamine-midazolam. Vomiting was more common in the ketamine group ( $P=.05$ ). In the study by Havel et al,<sup>17</sup> no difference was found in the incidence of complications when midazolam-morphine was compared with propofol-morphine therapy. Propofol-

morphine therapy was associated with hypoxemia requiring supplemental oxygen, stimulation, and/or airway positioning 11.6% of the time (95% confidence interval [CI], 4.3%-26.0%) compared with 10.9% of the time (95% CI, 4.1%-24.6%) for midazolam-morphine therapy (odds ratio [OR], 1.08; 95% CI for OR, 0.24-4.76). Oversedation was noted in 32.6% of those given propofol-morphine therapy compared with 34.8% of those given midazolam-morphine therapy (OR, 0.91; 95% CI, 0.52-1.68); agitation in 4.7% vs 6.5%, respectively (OR, 0.70; 95% CI, 0.08-5.53); and injection pain in 7.0% vs 4.3%, respectively (OR, 1.65; 95% CI, 0.21-15.02). The other 2 RCTs<sup>18,19</sup> had small numbers (total  $n=64$ ) of patients and reported that there were no adverse reactions.

## KETAMINE THERAPY

Ketamine was studied in 2 RCTs. Both of these studies combined ketamine with midazolam. One RCT compared ketamine-midazolam therapy with fentanyl-midazolam therapy,<sup>16</sup> while the other compared ketamine-midazolam therapy with propofol-fentanyl therapy.<sup>15</sup>

## IS KETAMINE-MIDAZOLAM THERAPY EFFECTIVE?

**Yes.** Kennedy et al<sup>16</sup> randomized 260 subjects to either fentanyl-midazolam therapy or ketamine-midazolam therapy. Observers were blinded to study purpose and design and scored the patients' distress by watching a videotape of the procedure. Compared with those who received fentanyl-midazolam, patients randomized to receive ketamine-midazolam had less pain and anxiety, less parental reporting of pain, less parental reporting of anxiety, and greater orthopedists' satisfaction. Amnesia and depth of sedation were similar between the 2 groups. The group that received ketamine-midazolam therapy had longer recovery times.

Godambe et al<sup>15</sup> compared ketamine-midazolam therapy with propofol-fentanyl therapy in 113 children undergoing orthopedic procedures. The primary outcome measures were behavioral distress, as measured by the OSBD-r, and recovery time. The OSBD-r was scored by independent blinded reviewers who watched videotapes of the procedures. An attempt was made to blind the observers further by placing sunglasses on the patients to hide the characteristic faces associated with ketamine and by performing mock jaw thrusts on the patients in anticipation of the greater frequency of airway positioning that would be required with propofol therapy. The OSBD-r scores during fracture reduction favored ketamine-midazolam therapy (0.084 for ketamine-midazolam vs 0.278 for propofol-fentanyl; 95% CI for the mean difference, -0.34 to -0.048). Parent visual analog scale scores, nurse satisfaction, and orthopedists' satisfaction did not differ between the 2 groups. Total sedation time (62.1 minutes vs 38.9 minutes; 95% CI for mean difference, 15.4-30.4 minutes) and recovery time (54.2 minutes vs 20.8 minutes; 95% CI for mean difference, 26.1-40.8 minutes) were significantly longer for ketamine-midazolam than for propofol-fentanyl.

## IS KETAMINE-MIDAZOLAM THERAPY SAFE?

Ketamine-midazolam therapy is associated with fewer adverse events than other parenteral drug combinations. Kennedy et al<sup>16</sup> found that ketamine-midazolam therapy was associated with fewer respiratory events, decreased need for breathing cues, and less need for supplemental oxygen than fentanyl-midazolam therapy. Vomiting was more common in the ketamine-treated group both during the ED stay (9% vs 2%;  $P=.05$ ) and during the 7 days after the procedure (4% vs 0%;  $P<.05$ ). Although ketamine has frequently been described as causing emergence agitation, there was no significant difference between the 2 groups in its incidence (5% vs 2%;  $P=.33$ ). Godambe et al<sup>15</sup> found that patients receiving ketamine-midazolam had significantly fewer desaturation events (7% vs 31%;  $P<.01$ ) and required fewer airway maneuvers (2% vs 25%;  $P=.01$ ) than those who received propofol-fentanyl therapy.

## PROPOFOL THERAPY

Propofol, in combination with a narcotic analgesic, was studied in 2 RCTs. Propofol is generally combined with an analgesic, as it has no intrinsic analgesic properties. One study compared propofol-fentanyl therapy with ketamine-midazolam therapy,<sup>15</sup> while the other compared propofol-morphine therapy with midazolam-morphine therapy.<sup>17</sup>

## IS PROPOFOL THERAPY EFFECTIVE?

Propofol therapy is not as effective as ketamine therapy. Recovery time and total sedation time are shorter with propofol than with other parenteral agents. In the study by Godambe et al,<sup>15</sup> children receiving propofol-fentanyl therapy had higher OSBD-r scores (indicating greater observed distress during fracture reduction) than those receiving ketamine-midazolam therapy. Parent visual analog scale scores, nurse satisfaction, and orthopedists' satisfaction did not differ between the 2 groups. Total sedation time and recovery time were significantly shorter for propofol-fentanyl than for ketamine-midazolam.

Havel et al<sup>17</sup> found no differences in Ramsay sedation scores between propofol-morphine and midazolam-morphine in 89 patients. However, they did not specifically report sedation or pain scores at the time of fracture reduction. There was less recall of the event in the patients receiving midazolam-morphine therapy (9%) than in patients in the propofol-morphine group (21%). Recovery time and time to discharge favored propofol.

## IS PROPOFOL THERAPY SAFE?

Propofol therapy is associated with more adverse events, particularly respiratory events and hypotension, than other parenteral agents. Godambe et al<sup>15</sup> found that patients receiving propofol-fentanyl therapy had significantly more desaturation events (31% vs 7%;  $P=.002$ ) and required more airway maneuvers (25% vs 2%;  $P=.003$ ) than those who received ketamine-midazolam therapy.

There was no significant difference between the 2 groups in the frequency of emergence agitation or emesis. In the study by Havel et al,<sup>17</sup> no difference was found in the incidence of complications when propofol-morphine therapy was compared with midazolam-morphine therapy, although the study may not have had enough power to detect a clinically important difference.

## COMMENT

There is no clear consensus on which pharmacological regimen is most effective for fracture reduction in the pediatric population.<sup>12</sup> In part, this is because there have been very few studies that have made direct comparisons between agents. Drawing conclusions from these studies is difficult, as many studies used different objective pain measures.

Bier blocks have been studied by many investigators and have the advantage of being associated with little risk of respiratory depression. Therefore, Bier blocks may be appropriate in centers that have less experience in managing a pediatric airway. However, Bier blocks require specialized equipment to prevent the transient neurologic sequelae associated with premature tourniquet release and do not provide anxiety relief. To date, to our knowledge, there have been no comparative studies of Bier block analgesia and parenteral sedation. The studies suggest that the most effective agent is lidocaine at a dose of 3 mg/kg.

Nitrous oxide provides the advantage of significantly shorter treatment times than other modalities. However, it is difficult to draw conclusions about the effectiveness of nitrous oxide given the very small number of patients studied in RCTs. Luhmann et al<sup>25</sup> recently reported results in abstract form of an RCT comparing ketamine-midazolam therapy with nitrous oxide-hematoma block. They found that patients in the nitrous oxide group had significantly less pain than those receiving ketamine, suggesting that nitrous oxide may be an excellent sedative option if combined with adequate analgesia.

Among the parenteral medications studied, the available evidence suggests that ketamine is the most effective and safest parenteral agent. However, ketamine is consistently associated with longer recovery times than other agents. Both of the RCTs in this review combined ketamine with midazolam. Other studies that have included nonorthopedic procedures in children have found that the addition of midazolam to ketamine does not reduce recovery agitation or alter the clinical effects of ketamine.<sup>26,27</sup> In addition, a recent practice guideline has recommended avoiding the use of coadministered benzodiazepines in most children because of the risk of additive respiratory depression.<sup>28</sup>

This study has several limitations. We included only studies that were written in the English language. In addition, there have been relatively few well-designed RCTs studying children who require sedation and analgesia for orthopedic procedures, including no RCTs evaluating etomidate for pediatric fracture reduction. The studies used different criteria for establishing the degree to which

analgesia was achieved. Few studies used validated pain scores, and many that did were not adequately blinded. This makes it difficult to establish the relative efficacy of various interventions. It is also difficult to make firm statements about the relative safety of the different methods. Many studies reported no adverse events and did not go into detail about the mechanisms used for ascertainment of adverse events. In addition, many studies had a small enrollment. Therefore, it is difficult to make definitive statements about the safety of some of the treatment regimens. We deliberately chose to limit the reviewed studies to those that included children who required fracture reduction. Many other studies have examined the effectiveness and safety of various agents for other minor procedures; however, fracture reduction is the most painful routinely performed procedure in the pediatric population, and results gleaned from populations who were undergoing less painful procedures such as laceration repair may not be applicable to patients undergoing fracture reduction.

This systematic review identifies significant gaps in our knowledge about comparable efficacies of different sedative and analgesic modalities. Few high-quality RCTs have compared different agents, and even fewer provide validated, objective measures of pain. We were unable to perform a meta-analysis of the relative efficacies of the different treatment modalities. Future research should use a validated pain scoring system such as the Children's Hospital of Eastern Ontario Pain Score,<sup>21</sup> OSBD-r,<sup>22,23</sup> or Procedure Behavior Checklist<sup>29</sup> so that comparisons can be more readily made between studies. An ideal therapeutic regimen would be noninvasive, have short recovery times, and have minimal adverse effects. Although it appears from the current literature that ketamine is the superior agent for fracture reduction to date, ketamine, etomidate, propofol, and nitrous oxide all warrant further comparative study. Nitrous oxide may provide an excellent combination of attributes if combined with adequate local or regional analgesia.

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## REFERENCES

- Landin LA. Epidemiology of children's fractures. *J Pediatr Orthop B*. 1997;6:79-83.
- Lyons RA, Sellstrom E, Delahunty AM, Loeb M, Varilo S. Incidence and cause of fractures in European districts. *Arch Dis Child*. 2000;82:452-455.
- Stark AD, Bennet GC, Stone DH, Chishti P. Association between childhood fractures and poverty: population based study. *BMJ*. 2002;324:457.
- Cheng JC, Ng BK, Sing SY, Lam PK. A 10-year study of the changes in the pattern and treatment of 6,493 fractures. *J Pediatr Orthop*. 1999;19:344-350.
- Fosnocht DE, Heaps ND, Swanson ER. Patient expectations for pain relief in the ED. *Am J Emerg Med*. 2004;22:286-288.
- Brown JC, Klein EJ, Lewis CW, Johnston BD, Cummings P. Emergency department analgesia for fracture pain. *Ann Emerg Med*. 2003;42:197-205.
- Cimpello LB, Khine H, Avner JR. Practice patterns of pediatric versus general emergency physicians for pain management of fractures in pediatric patients. *Pediatr Emerg Care*. 2004;20:228-232.
- Friedland LR, Kulick RM. Emergency department analgesic use in pediatric trauma victims with fractures. *Ann Emerg Med*. 1994;23:203-207.
- Petrack EM, Christopher NC, Kriwinsky J. Pain management in the emergency department: patterns of analgesic utilization. *Pediatrics*. 1997;99:711-714.
- Wilson JE. Oligoanalgesia in the emergency department. *Am J Emerg Med*. 1989;7:620-623.
- Krauss B, Zurakowski D. Sedation patterns in pediatric and general community hospital emergency departments. *Pediatr Emerg Care*. 1998;14:99-103.
- Kennedy RM, Luhmann JD, Luhmann SJ. Emergency department management of pain and anxiety related to orthopedic fracture care: a guide to analgesic techniques and procedural sedation in children. *Paediatr Drugs*. 2004;6:11-31.
- Bratt HD, Eyres RL, Cole WG. Randomized double-blind trial of low- and moderate-dose lidocaine regional anesthesia for forearm fractures in childhood. *J Pediatr Orthop*. 1996;16:660-663.
- Davidson AJ, Eyres RL, Cole WG. A comparison of prilocaine and lidocaine for intravenous regional anaesthesia for forearm fracture reduction in children. *Paediatr Anaesth*. 2002;12:146-150.
- Godambe SA, Elliot V, Matheny D, Pershad J. Comparison of propofol/fentanyl versus ketamine/midazolam for brief orthopedic procedural sedation in a pediatric emergency department. *Pediatrics*. 2003;112:116-123.
- Kennedy RM, Porter FL, Miller JP, Jaffe DM. Comparison of fentanyl/midazolam with ketamine/midazolam for pediatric orthopedic emergencies. *Pediatrics*. 1998;102:956-963.
- Havel CJ, Strait RT, Hennes H. A clinical trial of propofol vs midazolam for procedural sedation in a pediatric emergency department. *Acad Emerg Med*. 1999;6:989-997.
- Pierce MC, Fuchs S. Evaluation of ketorolac in children with forearm fractures. *Acad Emerg Med*. 1997;4:22-26.
- Evans JK, Buckley SL, Alexander AH, Gilpin AT. Analgesia for the reduction of fractures in children: a comparison of nitrous oxide with intramuscular sedation. *J Pediatr Orthop*. 1995;15:73-77.
- Gregory PR, Sullivan JA. Nitrous oxide compared with intravenous regional anesthesia in pediatric forearm fracture manipulation. *J Pediatr Orthop*. 1996;16:187-191.
- McGrath PJ, Johnson G, Goodman JT, Schillinger J, Dunn J, Chapman JA. CHEOPS: a behavioral scale for rating postoperative pain in children. *Adv Pain Res Ther*. 1985;9:395-402.
- Jay SM, Elliott C. Behavioral observation scales for measuring children's distress: the effects of increased methodological rigor. *J Consult Clin Psychol*. 1984;52:1106-1107.
- Jay SM, Ozolins M, Elliott CH, Caldwell S. Assessment of children's distress during painful medical procedures. *Health Psychol*. 1983;2:133-147.
- Wattenmaker I, Kasser JR, McGravey A. Self-administered nitrous oxide for fracture reduction in children in an emergency room setting. *J Orthop Trauma*. 1990;4:35-38.
- Luhmann JD, Schootman M, Voytas L, Luhmann SJ, Kennedy RM. A comparison of ketamine/midazolam and nitrous oxide/hematoma block for forearm fracture reduction in children. Abstract presented at: Pediatric Academic Societies' Annual Meeting; May 1, 2004; San Francisco, Calif.
- Sherwin TS, Green SM, Khan A, Chapman DS, Dannenberg B. Does adjunctive midazolam reduce recovery agitation after ketamine sedation for pediatric procedures? a randomized, double-blind, placebo-controlled trial. *Ann Emerg Med*. 2000;35:229-238.
- Wathen JE, Roback MG, Mackenzie T, Bothner JP. Does midazolam alter the clinical effects of intravenous ketamine sedation in children? a double-blind, randomized, controlled emergency department trial. *Ann Emerg Med*. 2000;36:579-588.
- Green SM, Krauss B. Clinical practice guideline for emergency department ketamine dissociative sedation in children. *Ann Emerg Med*. 2004;44:460-471.
- LeBaron S, Zeltzer L. Assessment of acute pain and anxiety in children and adolescents by self-reports, observer reports, and a behavior checklist. *J Consult Clin Psychol*. 1984;52:729-738.