Optimal dosing of intravenous ketamine for procedural sedation in children in the ED—a randomized controlled trial

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Objective: The objective of the study is to compare need for redosing, sedation efficacy, duration, and adverse events between 3 commonly administered doses of parenteral ketamine in the emergency department (ED).

Methods: We conducted a prospective, double-blind, randomized controlled trial on a convenience sample of children 3 to 18 years who received intravenous ketamine for procedural sedation. Children from each age group (3-6, 7-12, and 13-18 years) were assigned in equal numbers to 3 dosing groups (1, 1.5, and 2 mg/kg) using random permuted blocks. The primary outcome measure was need for ketamine redosing to ensure adequate sedation. Secondary outcome measures were sedation efficacy, sedation duration, and sedation-related adverse events.

Results: A total of 171 children were enrolled of whom 125 (1 mg/kg, 50; 1.5 mg/kg, 35; 2 mg/kg, 40) received the randomized dose and were analyzed. The need for ketamine redosing was higher in the 1 mg/kg group (8/50; 16.0% vs 1/35; 2.9% vs 2/40; 5.0%). There was no significant difference in the median Ramsay sedation scores (5.5 [interquartile range {IQR}, 4-6] vs 6 [IQR, 4-6] vs 6 [IQR, 5-6]), FACES-R score (0 [IQR, 0-4] vs 0 [IQR, 0-0] vs 0 [IQR, 0-0]), sedation duration in minutes (23 [IQR, 19-38] vs 24.5 [IQR, 17-34.5] vs 23 [IQR, 19-29]), and adverse events (10.0% vs 14.3% vs 10.0%) between the 3 dosing groups. Physician satisfaction was lower in the 1 mg/kg group (79.6% vs 94.1% vs 97.3%).

Conclusions: Adequate sedation was achieved with all 3 doses of ketamine. Higher doses did not increase the risk of adverse events or prolong sedation. Ketamine administered at 1.5 or 2.0 mg/kg intravenously required less redosing and resulted in greater physician satisfaction.

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1. Introduction

Ketamine has become one of the most commonly administered drugs for procedural sedation and analgesia for children in the emergency department (ED) due to its efficacy and favorable safety profile [1–7]. Two clinical practice guidelines for ED ketamine use state that the minimum dose of intravenous (IV) ketamine at which the dissociative state can be reliably achieved in children is 1.5 mg/kg IV, and common loading doses are 1.5 to 2 mg/kg [8,9]. Despite these recommendations, prospective, ED comparative trials have administered ketamine IV in 0.5-mg increments to a maximum of 2 mg [10], as 1 mg/kg [11–15], 1.5 mg/kg [16], 1 to 2 mg/kg [17], and 2 mg/kg [18]. Although previous studies using ketamine for procedural sedation and analgesia did not find a significant change in adverse event rates unless the initial IV dose exceeded 2.5 mg/kg or the total dose exceeded...
5.0 mg/kg, this wide practice variation of ketamine administration may impact sedation efficacy, duration of sedation, and, potentially, adverse events [5,6]. A retrospective report of sedation in the ED using ketamine and midazolam found that lower doses of IV ketamine (≤0.75 mg/kg) may provide adequate sedation; however, no differences in sedation duration were observed and adverse events were infrequent in all doses [19]. This study did not describe the infusion time of IV ketamine. Current recommendations suggest administration of IV ketamine over 30 to 60 seconds to prevent respiratory depression [9,20]. Recent studies have investigated the administration of lower doses of IV ketamine (<1 mg/kg) over much shorter time period (≤5 seconds) for brief procedures as well as lower initial doses of IV ketamine with subsequent “top-up” doses and have demonstrated adequate sedation with shorter sedation times [21,22]. Ketamine clearance has been shown to be higher in younger children, who might therefore potentially require a higher milligrams per kilogram dose of ketamine than older children to achieve similar sedation effects [23]. Despite this finding, current dosing recommendations for ketamine do not differ by age. Furthermore, ketamine pharmacokinetic studies have demonstrated that different initial doses of IV ketamine (1 mg/kg vs 1.5 mg/kg) are associated with different serum concentrations that lead to anesthetic and amnestic effects of varying duration with varying arousal times [23,24]. Lower doses of ketamine in older children have been evaluated. Street and Gerard [25] found that a fixed-dose ketamine protocol of 50 mg, followed by 25 mg IV, provided adequate sedation for 12- to 17-year-old normal weight and overweight/obese children in the ED. Although it is clear that a wide range of IV ketamine dosing has been reported, to our knowledge, no studies have directly compared the sedation efficacy, duration of sedation, and adverse events associated with the 3 most commonly administered initial IV doses of ketamine for children in the ED. A randomized controlled trial comparing 3 of the most commonly used ketamine dosing regimens would either support current recommendations or suggest modifications based on patient age and projected length of procedure. Most importantly, if differences in adverse events, sedation efficacy, and recovery times are found based on dose or age, it will help us develop strategies for providing safer, more effective ketamine sedation for children in the ED.

The objective of our study was to compare the efficacy, duration of sedation, and adverse events between the 3 commonly administered doses of IV ketamine (1, 1.5, and 2 mg/kg) using the traditional administration method of 30- to 60-second infusion for procedural sedation in children in the ED. In addition, we sought to measure the effect of age on ketamine dosing.

2. Methods

2.1. Study design and setting

This was a prospective, double-blind, randomized controlled trial of a convenience sample of children aged 3 to 18 years who required IV ketamine for procedural sedation and analgesia for orthopedic procedures, incision and drainage of skin abscess, and laceration repair conducted in the ED. Written informed consent was obtained from the patient’s parents or guardians. In addition, an assent was obtained from all children older than 7 years. This study was approved by the human investigation committee of our institution. The human investigation committee requested the submission of the study protocol to the Food and Drug Administration (FDA) for review. The FDA required that we apply for an investigational new drug approval, which was granted (106,683). The study was registered at ClinicalTrials.gov (identifier: NCT02519595).

The study was conducted at a free-standing children’s hospital in a tertiary care pediatric ED and level 1 trauma center with 92,000 patient visits per year, of whom approximately 1,200 children receive procedural sedation and analgesia every year.

2.2. Selection of study participants

Children between the ages of 3 and 18 years with American Society of Anesthesiologists (ASA) classification I or II [26] who required IV ketamine for procedural sedation and analgesia for orthopedic procedures, incision and drainage of skin abscess, and laceration repair were eligible for participation in the study. We enrolled a convenience sample of eligible patients based on availability of the research assistants. Study participants were identified using the electronic medical tracking board which lists the presenting complaint and after need for procedural sedation and analgesia with IV ketamine was established with the treating physician.

The following patients were excluded from the study:

1. Children with hypertension, acute glaucoma or injury to the globe, increased intracranial pressure or intracranial mass lesion, acute porphyria, and major psychiatric disorder.
2. Children with a prior allergic reaction to ketamine.
3. Children who were pregnant.
4. If the parent or legal guardian was not available or declined to provide informed consent for the study or if the child declined to provide assent.
5. If the patient received intramuscular ketamine.
6. If the patient received benzodiazepines in addition to ketamine for sedation in the ED.
7. Children weighing more than 100 kg (study drug preparation was not possible using a 10-mL syringe and blinding could not be achieved).

Patients who received opioids or other pain medication before procedural sedation and analgesia were eligible for inclusion in the study.

2.3. Interventions

Random sequence allocation was performed using a computer-generated, random number table by a pharmacist from the investigational drugs section of the pharmacy department. The study subjects were grouped according to their age as follows: (1) 3 to 6 years, (2) 7 to 12 years, and (3) 13 to 18 years. Children from each age group were assigned in equal numbers to all 3 ketamine dosing groups (1, 1.5, and 2 mg/kg) using random permuted blocks stratified by the pharmacist. The randomized study drug was stored in a dedicated automated medication dispensing system in the ED. Once an eligible patient was identified and consent was obtained, a nurse who was not involved in the care or sedation of the patient determined the appropriate age strata of the patient. The same nurse then accessed the first sequentially labeled study drug appropriate for the age strata of the patient. Each study kit included a dose calculation and preparation instructions. Once the study drug was prepared, a second nurse, who was also not involved in the care or sedation of the patient, verified the accuracy of drug dosage and calculation. The study drug was administered as a slow IV push over 30 to 60 seconds by the ED physician who was in charge of the clinical care of the patient. Drug waste was documented in the medication dispensing system, and the used medication vial was saved for verification of drug administration and drug dosage by the study pharmacist.

All ED staff including the physician and the nurse in charge of sedation, the study research assistant, the parents/guardians, and the study subjects were blinded to the randomization and the group assignments. The dosage and administration of additional doses of ketamine were left to the discretion of the ED physician in charge of the care and sedation of the patient. The research team did not participate in the clinical care and
sedation of the patient. Children were monitored per ED policy for the entire duration of sedation.

The study research assistant also performed a follow-up telephone call beginning 48 hours after discharge from the ED to obtain information on the child’s memory and recall of the procedure and any postdischarge adverse events. A total of 3 attempts were made to contact the child’s parent/guardian and, if unsuccessful, were considered as lost to follow-up.

2.4. Methods of measurements

The following variables were collected prospectively by trained research assistant: demographics, procedure type, time of last solid and liquid intake, ASA classification [26], pain medication administered before sedation (type, dosage, and timing), number and total doses of ketamine administered after the initial study dose, sedation efficacy and duration, length of procedure, adverse events related to sedation including interventions performed to address the adverse events and patient disposition.

Patient distress was documented by the trained research assistant at the following intervals: presedation (3 minutes before study drug administration), during the procedure (after ketamine administration and before and after any redosing), and postsedation (before discharge) using the Ramsay Sedation Scale [27]. Assessment of severity of pain on a scale of 0 (no pain) to 10 (most pain) was performed on children 5 years or older during the above 3 intervals using the FACES Pain Scale-Revised [28]. Pain severity was determined by the research assistant during sedation (using facial expression of patient or if the patient did not respond, pain was scored as 0) and by self-assessment by the

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Fig. 1. Study flow diagram.
study participants for presedation and postsedation. In addition, sedation efficacy was assessed by the physician performing the procedure using a 3-point Likert scale (not satisfied, satisfied, or very satisfied with the sedation).

2.5. Outcome measures

The primary outcome measure for this study was the number of additional doses of ketamine administered after the study drug to achieve adequate sedation. The secondary outcome measures were (1) sedation efficacy as measured by Ramsay Sedation Scale, FACES-R scale, and satisfaction scores of the physician performing the procedure; (2) sedation duration; and (3) sedation-related adverse events along with interventions performed to manage the adverse events.

2.6. Definitions

Length and efficacy of sedation and all adverse events were defined using the standardized definitions provided by the Quebec Guidelines for ED sedation terminology and reporting of adverse events in children [29].

Procedure duration was defined as the time duration from start to completion of the procedure. Length of sedation was defined as the time from the administration of study medication until the patient was ready for discharge. Readiness for discharge was assessed using standardized discharge criteria (Aldrete scoring ≥9) [30] by the physician providing sedation or the nurse taking care of the patient.

The following adverse events were recorded for the study: oxygen desaturation (pulse oximetry reading ≤90%), apnea, laryngospasm, emesis, unpleasant recovery reactions, or any others that were deemed by the physician taking care of the patient as an adverse event related to sedation. Interventions performed in response to adverse events such as airway maneuvers (chin lift, jaw thrust), supplemental oxygen, and bag-mask ventilation were also identified and documented using standardized criteria [29]. Adverse events and interventions performed were recorded by the study research assistant and the nurse providing patient care using a standardized sedation monitoring sheet for every sedation performed in the ED.

2.7. Statistical analysis

A database was created using Excel to host all data collected for this study. Study variables were systematically coded for analysis. The research assistant performed double data entry to verify accuracy. Descriptive statistics (proportion, median ± IQR) were calculated for patient demographic variables, ketamine dosing, and adverse events. The difference in variables among the 3 dosing groups (ie, 1, 1.5, and 2 mg/kg) and among the 3 age groups (ie, 3-6, 7-12, and 13-18 years) was examined using a χ2 test for categorical variables and Kruskal-Wallis test for continuous variables. Effect sizes with a 95% confidence interval (CI) were calculated to compare the difference between the dosing groups (1 vs 1.5 mg/kg) and (1 vs 2 mg/kg). Logistic regression analysis was performed to evaluate predictors associated with need for redosing with ketamine. Significance level was set at 0.05. All statistical analyses were performed using the SAS 9.3 statistical software package (SAS Institute, Inc, Cary, NC).

A previous ketamine sedation study found that approximately 25% of children who received 1 mg/kg IV ketamine for orthopedic fracture reduction received at least 1 additional dose of ketamine [13]. Based on a previous study using 2 mg/kg IV of ketamine, we postulated that a previous study using 2 mg/kg IV of ketamine, we postulated that

Table 2

Primary and secondary study outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>1 mg/kg, n = 50</th>
<th>1.5 mg/kg, n = 35</th>
<th>2 mg/kg, n = 40</th>
<th>Effect size (95% CI), 1 mg/kg vs 1.5 mg/kg</th>
<th>Effect size (95% CI), 1.5 mg/kg vs 2 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Need for redosing</td>
<td>8 (16%)</td>
<td>1 (2.9%)</td>
<td>2 (5%)</td>
<td>13.14% (0.15%-26.43%)</td>
<td>11.00% (1.20%-23.20%)</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ramsay Sedation Scale score, median (IQR)</td>
<td>5.5 (4-6)</td>
<td>6 (4-6)</td>
<td>6 (5-6)</td>
<td>0 (0-0)</td>
<td>0 (0-1)</td>
</tr>
<tr>
<td>FACES-P score, median (IQR)</td>
<td>0 (0-4)</td>
<td>0 (0-0)</td>
<td>0 (0-0)</td>
<td>0 (0-0)</td>
<td>0 (0-3)</td>
</tr>
<tr>
<td>Sedation duration in minutes, median (IQR)</td>
<td>23 (19-38)</td>
<td>24.5 (17-34.5)</td>
<td>23 (19-29)</td>
<td>0.00 (−0.70 to 6.00)</td>
<td>0.00 (−5.00 to 4.00)</td>
</tr>
<tr>
<td>Overall adverse events (%)</td>
<td>5 (10.0%)</td>
<td>5 (14.3%)</td>
<td>4 (10.0%)</td>
<td>−4.29 (−18.55 to −9.98)</td>
<td>0.00 (−12.47 to 12.47)</td>
</tr>
</tbody>
</table>
patients who received 2 mg/kg will have a 5% chance of requiring additional doses of ketamine [18]. Using a 2-sided Fisher exact test to determine a significant difference in proportions, we estimated that 55 patients would be needed in both the 1 mg/kg group (25% chance of redosing) and the 2 mg/kg group (5% chance of redosing) to achieve an \( \alpha = .05 \) and power of 0.80 resulting in a total sample size of 165 patients (55 in each of the 3 dosing groups).

Based on the study mentioned above [13], 25% of children of median age of 7.5 years received an additional dose of ketamine after an initial 1 mg/kg IV dose. Herd's pharmacokinetic study of ketamine in children [25] found an inverse relationship between age and ketamine dosing. A conservative estimate of redosing in the younger age group would be 5% more than that experienced in the group with a median age of 7.5 years. We calculated sample size for the secondary outcome using a 2-sided Fisher exact test to determine a significant difference in proportions to be 132 patients in both the younger group 3 to 6 years (30% chance of redosing) and the older group 13 years and older (15% chance of redosing) to achieve an \( \alpha = .05 \) and power of 0.80. We used the sample size for the 2 extreme groups as the sample size for children aged 7 to 12 years resulting in a total sample size of 396 patients.

During the study, it became apparent that the ED physicians did not administer the entire randomized dose to some study subjects for whom they felt that adequate sedation was achieved with less than the randomized dose. We report “per-protocol” results for those study subjects who received the randomized dose of ketamine.

### 3. Results

A total of 1347 patients received ketamine in the ED during the study period. Of these, 1176 patients were excluded from the study (Fig. 1); 171 patients were consented and enrolled in the study from August 1, 2010, to August 31, 2012, and randomized as follows: 1 mg/kg, \( n = 58 \); 1.5 mg/kg, \( n = 57 \); 2 mg/kg, \( n = 56 \). Because of lower than expected enrollment rate, the study ended before achieving the targeted 396 subjects as funding for the study was no longer available.

Forty-six (26.9%) of patients did not receive the ketamine dose to which they were randomized (Fig. 1). In 2 patients, the child’s weight was incorrectly recorded which resulted in calculated dose that was below the randomized dose. Forty-four patients received less than the randomized dose (protocol violation) as the physicians discontinued the administration of ketamine when the patient achieved dissociation and did not appear to require further drug administration for sedation. These 46 study patients who did not receive the randomized dose of IV ketamine were excluded leaving 125 patients for analysis (1 mg/kg, 50%; 1.5 mg/kg, 35%; 2 mg/kg, 40%).

Patient demographics, procedure type, ASA classification, and premedication pain medications for the study patients are shown in Table 1.

Eleven children (8.8%) received an additional dose of ketamine in the study cohort. The need for ketamine re-dosing was higher in the 1 mg/kg group (8/50; 16.0% vs 1/35; 2.9% vs 2/40; 5.0%) (Table 2).

There was no difference in the median Ramsay sedation score (5.5 [IQR, 4-6] vs 6 [IQR, 4-6] vs 6 [IQR, 5-6]), median FACES-R score (0 [IQR, 0-4] vs 0 [IQR, 0-0]) and median sedation duration in minutes (23 [IQR, 19-38] vs 24.5 [IQR, 17.5-34.5] vs 23 [IQR, 19-29]) between the 3 dosing groups. There was no difference in the frequency of adverse events between the 3 dosing groups (1 mg/kg, 10.0%; 1.5 mg/kg, 14.3%; 2 mg/kg, 10.0%) (Table 2). None of the patients experienced apnea or laryngospasm, and none required positive pressure ventilation. The distribution of the types of adverse events among the 3 dosing groups is shown in Table 3.

Physician satisfaction data were available in 119 patients (95.2%). Of these, physicians reported that they were either “satisfied” or “very satisfied” in 89.1% (106/119) of the sedation. Consultant physicians were less likely to be satisfied or very satisfied with sedation in the 1 mg/kg dosing group vs the 1.5 mg/kg and 2 mg/kg dosing group (79.6% vs 94.1% vs 97.3%) (Table 4). Telephone follow-up was completed in 101 (80.8%) of the study patients. Approximately 13.9% of patients experienced vomiting at home (10.5% in the 1 mg/kg group, 12.5% in the 1.5 mg/kg group, and 20.0% in the 2 mg/kg group). The majority of children (82.2%) reached for follow-up reported having no memory of the painful procedure (80.6% in the 1 mg/kg group, 92.9% in the 1.5 mg/kg group, and 93.3% in the 2 mg/kg group). (Table 4).

There were no significant differences in the mean dose of ketamine administered, need for redosing, or frequency of adverse events among the 3 age groups studied (Table 5).

Logistic regression analysis showed only the initial IV ketamine dose (1 mg/kg) to be a significant predictor for need of redosing (Table 6).

### 4. Discussion

To our knowledge, this is the first prospective, double-blind, randomized control trial comparing sedation efficacy, duration, and adverse events of the 3 most commonly administered dosing regimens of IV ketamine sedation for children in the ED. Our study demonstrates that all 3 dosing regimens (1, 1.5, and 2 mg/kg) of IV ketamine were effective in achieving acceptable levels of sedation and analgesia. However, children in the 1 mg/kg group required redosing with ketamine more frequently than in the other 2 groups, and physicians were less likely to be satisfied with the level of sedation achieved with the lower dose. Children in the 2 mg/kg group were significantly less likely to recall the procedure. The frequency of adverse events was low, and there was no difference in frequency of adverse events detected between

### Table 3

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>1 mg/kg IV, ( n = 50 )</th>
<th>1.5 mg/kg IV, ( n = 35 )</th>
<th>2 mg/kg IV, ( n = 40 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen desaturation</td>
<td>1 (2.0%)</td>
<td>2 (5.7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Emesis</td>
<td>1 (2.0%)</td>
<td>3 (8.6%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Unpleasant recovery reaction</td>
<td>3 (6.0%)</td>
<td>0 (0%)</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>Others</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>Any</td>
<td>5 (10.0%)</td>
<td>5 (14.3%)</td>
<td>4 (10.0%)</td>
</tr>
</tbody>
</table>

* Other adverse reaction include maculopapular rash.

### Table 4

| Consultant satisfaction, telephone follow-up for ketamine sedation* |
|--------------------------|--------------------------|
|                          | 1 mg/kg | 1.5 mg/kg | 2 mg/kg | Effect size (95% CI) 1 mg/kg vs 1.5 mg/kg | Effect size (95% CI) 1 mg/kg vs 2 mg/kg |
| Consultant satisfaction, \( n = 119 \) |          |          |        |                                      |                                      |
| Not satisfied             | 10 (20.4%) | 2 (5.9%) | 1 (2.7%) | 14.53 (0.75-28.31) | 17.63 (5.13-30.13) |
| Satisfied                 | 12 (24.5%) | 3 (8.8%) | 6 (16.7%) | 15.67 (0.31-31.02) | 7.82 (9.30-24.95) |
| Very Satisfied            | 27 (55.1%) | 29 (85.3%) | 29 (80.6%) | -30.19 (-48.51 to -11.87) | -25.45 (-44.46 to -6.45) |
| Telephone follow-up, \( n = 101 \) |          |          |        |                                      |                                      |
| Emesis                   | 4 (10.5%) | 4 (12.5%) | 6 (20.0%) | -1.97 (-17.02 to -13.08) | -9.47 (-26.80 to -7.85) |
| No recall of painful procedure | 29 (80.6%) | 26 (72.9%) | 28 (93.3%) | -4.98 (-24.06 to -14.19) | -17.02 (-33.22 to -0.82) |

* \( P = .011 \).
the 3 dosing regimens. The distribution of adverse events with all 3 dosing regimens is similar to that reported in previous studies with ketamine [5,6]. Because of its dissociative effects, ketamine does not exhibit a dose-dependent sedation continuum like other sedatives which has been stated as one of the reasons for the favorable safety profile of ketamine [9]. A recent meta-analysis of predictors of airway and respiratory adverse events with ketamine determined that a single intravenous dose of greater than or equal to 2.5 mg/kg to be an independent predictor for adverse events. This dose is higher than any of the dosing regimens used in our study [5]. Previous studies have also shown no relationship between ketamine dose and incidence of laryngospasm [31]. In addition, there was no significant difference in length of sedation or time to discharge between groups. Given these reasons, there would appear to be no benefit to starting with a lower (1 mg/kg) dose of ketamine. We did not demonstrate significant differences in the total duration of sedation and recovery times between the 3 dosing regimens. In an attempt to decrease total time of sedation with ketamine, a recent study investigated the use of rapidly administered IV ketamine for sedation in children with forearm fractures. The authors found a dose of 0.7 to 0.8 mg/kg IV to be effective for healthy children in 3 different age groups [21]. However, the median length of procedure in these groups was 2.5 to 4 minutes. Previous studies of ketamine sedation for orthopedic reductions have found length of procedures to be 13 and more than 19 minutes, respectively [13,18]. Although rapid administration of ketamine in lower doses may result in shorter length of sedation and ultimately shorter ED lengths of stay, the majority of orthopedic reductions (the most common painful sedation-requiring ED procedure for children) require a longer duration of sedation and analgesia making this rapid-administration regimen amenable to a limited number of, very brief, procedures. Future studies comparing low-dose, rapid-administration ketamine to traditional ketamine administration would clarify the impact of this administration technique on procedural sedation in the ED for children. On telephone follow-up, more children in the 2 mg/kg group (93.3%) reported no memory of the painful procedure. This difference in amnesia of the painful procedure may be especially important for children with ED visits for recurrent sedation for painful procedures. The true clinical significance and impact on patient care of this finding require further investigation of the long-term effects of ketamine sedation.

5. Limitations

Enrollment of patients in our study was limited by the availability of research assistants and thus represents a convenience sample of eligible patients. However, we collected information from the automated medication dispenser list weekly to determine the dose and adverse events for those patients who received IV ketamine but who were not enrolled in the study, and the findings are similar to those of our study patients. One-fourth of the study subjects did not receive the dose of ketamine to which they were randomized. Emergency department physicians reported, after the fact, that once they determined that patients were adequately sedated, they stopped administering ketamine. This practice precluded patients from receiving the entire dose to which they had been randomized and resulted in exclusion from analysis.

Patient enrollment took longer than was anticipated. Funding was exhausted and the study closed before we were able to enroll an adequate sample size to definitively compare sedation efficacy and dose-related adverse events by age stratification. Although no differences were detected between age groups, patient numbers were inadequate to achieve statistical significance. The need for redosing was based on sedation physician discretion and not on objective sedation scoring; however, this is consistent with everyday clinical practice. Because of FDA direction, children younger than 3 years were excluded from the study. Younger children have been shown to require a higher milligrams per kilogram ketamine dosing and to be at higher risk for airway and respiratory adverse events when compared to older children [5,24]. Finally, we did not randomly by type of procedure performed which could have confounded length of sedation and total dose administered by group; however, more than 60% of the enrolled patients in all 3 dosing groups received sedation for orthopedic reduction. In addition, logistic regression analysis showed only initial IV ketamine dose to be predictive for need for redosing.

6. Conclusions

Adequate sedation was achieved with all 3 doses of IV ketamine (1, 1.5, and 2 mg/kg), and higher doses did not increase the risk of adverse events or prolong the duration of sedation. Because children assigned to the 1 mg/kg IV ketamine group required more frequent redosing and resulted in less physician satisfaction with sedation, we conclude that our study supports the current recommendation to use 1.5 or 2.0 mg/kg IV ketamine as an initial dose for procedural sedation of children in the ED. The apparent benefit of greater amnesia of the painful procedure with 2.0 mg/kg over 1.5 mg/kg requires further study.

Acknowledgment

The authors acknowledge the work of research assistants Mariam Hussain and Birgete Webb for enrollment of study participants and the data collection.

References