The Lancaster experience of 2.0 to 2.5 mg/kg intramuscular ketamine for paediatric sedation: 501 cases and analysis

R G McGlone, M C Howes, M Joshi

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Ketamine is a unique drug giving complete anaesthesia and analgesia with preservation of vital brain stem functions. This “dissociative” state has been described as “a functional and neuro-physiological dissociation between the neocortical and limbic systems” [1]. Ketamine dissociation results in a clinical state of lack of response to pain or other noxious stimuli, with preservation of respiratory and cardiovascular functions despite profound amnesia and analgesia. The eyes often remain open, though nystagmus is commonly seen. Heart rate and blood pressure remain stable, and are often stimulated, possibly through sympathomimetic actions. Functional residual capacity and tidal volume are preserved, with bronchial smooth muscle relaxation and maintenance of airway patency and respiration [1-3].

There is a wealth of evidence reporting the suitability and safety of ketamine in the hands of non-anaesthetists in various settings: remote locations in countries in the developing world [4-5] “office” or outpatient surgeries and dental practices [6-10], battlefields [11], and diagnostic imaging [12]. Ketamine has been used by emergency physicians in the United States, Australia, and the UK for paediatric sedation with an excellent safety record, side effect profile, and staff and parent satisfaction [12]. Midazolam, still commonly used in the UK for paediatric sedation, has been shown to offer less suitable conditions, with child restraint being required, and staff and parent dissatisfaction [12-15]. Ketamine sedation/analgesia as used by emergency physicians may be considered as the technique of choice in the emergency department for short procedures when analgesia and distraction techniques have failed [2,15-16,18-19,21-23,28].

Our department—Lancaster Royal Infirmary, Lancaster, UK with an annual new patient attendance of 37 000—began using intramuscular (IM) ketamine as part of a defined protocol in a randomised comparison with intranasal midazolam [15]. The same protocol for ketamine administration was used in this study. Once these studies had been completed only IM ketamine was used for sedation. Children with wounds requiring formal surgical exploration and those with significant head injuries (knocked unconscious, vomiting, mentally obtunded) or other injuries requiring admission were excluded; a three hour fast before sedation was enforced. Those children presenting late at night were sometimes deferred until after 0900 the next day to comply with department senior staffing levels. A written parental advice sheet (appendix, available to view on the journal web site) was given and explained. If a delay in starting the procedure was anticipated topical local anaesthetic cream was applied to the child’s thigh. The sedation and procedure was performed in a dedicated theatre within the accident and emergency (A&E)

Objectives: To report the experience of using intramuscular ketamine 2.0 or 2.5 mg/kg for minor painful procedures in children in a medium sized district general hospital accident and emergency department. To demonstrate the safety and acceptability of ketamine and determine if the incidence of adverse effects is related to dose or other variables.

Methods: Prospective data collection and analysis using Statsdirect and SPSS software.

Results: 501 consecutive cases were collected from August 1996 to April 2002. A total of 310 children received 2.0 mg/kg and 191 received 2.5 mg/kg. Twenty six received a second dose. In seven cases oxygen saturation fell below 93%, three of these fell below 90%. There was one case of laryngospasm. Eight cases received airway suctioning, five of these were mouth or lip wounds. Seventeen per cent vomited in recovery or at home for which one child required admission. Muscle hypertonicity was observed in 6.8%, disturbed sleep or nightmares in 2%. The median time to discharge was 85 minutes. Ninety seven per cent of parents’ experiences were “the same as” or “better than” expected. No children suffered any lasting or troublesome complications.

Conclusions: 2.0 – 2.5 mg/kg intramuscular ketamine sedation is a safe and acceptable technique when used within a defined protocol. Lower dose ketamine (2 mg/kg) warrants further study in view of potentially less airway complications and quicker discharge times than previously reported.
department with oxygen, suction, and full paediatric resuscitation equipment available; a trained nurse and senior doctor with advanced airway and paediatric resuscitation skills (consultant, staff grade, or specialist registrar) were present to perform and supervise the sedation and perform the procedure. Written informed consent was gained after explanation of the procedure verbally and supplemented by the written parental advice sheet. Parents were encouraged to stay throughout. Monitoring consisted of oxygen saturation probe, and observation of the child. Supplemental oxygen was not routinely given. Ketamine (Ketalar, Parke-Davis; 100 mg/ml) was mixed with atropine 0.01 mg/kg in the same 1 or 2 ml syringe; during the initial trials ketamine was universally used in a dose of 2.5 mg/kg, thereafter 2.0 mg/kg was used by some—this choice of dose was operator dependent using their favoured dose and not randomised. A chart kept available in the theatre aided safe calculations of doses and drug volumes. The injection was given into the lateral thigh using a 25 gauge needle, with the child on the parent’s knee or lying on the trolley. Local anaesthesia of the wound with lignocaine (lidocaine) by local infiltration or nerve block where appropriate was performed once dissociation had occurred. If required, further ketamine IM doses of 1 mg/kg were given. After completion of the procedure, the child was observed and monitored in the theatre room for 30 minutes after injection time, and then moved to the dedicated children’s examination cubicle. Parents were encouraged to keep the child still and undisturbed, and background noise and light kept to a minimum. Once they were able to respond fully and weight bear unaided, they were discharged. The written information sheet included discharge advice regarding child care after sedation, and a vomit bowl was supplied. Parents were also given verbal and written advice regarding wound care. Reattendance was not arranged unless required for the purposes of wound monitoring.

Data collection
The following details were collected prospectively on a standardised form by the nurse caring for the child: patient and wound details; behaviour before procedure, during local anaesthesia, during suturing; occurrence of vomiting, dysphoria, muscular hypertonicity, clonus, lacrimation, salivation, rash; timing of completion of procedure, time to discharge; child behaviour during recovery. The degree of restraint of the child required was recorded as “number of limbs” with the head counted as a “fifth limb.” “Restraint” of a limb or head was recorded if any physical change of body posture was used.

Follow up was by written questionnaire given to parents at discharge with an addressed, prepaid envelope. This was supported by telephone inquiry within 72 hours, and the following were recorded: occurrence, frequency, and timing of vomiting; occurrence of nightmares; time needed for child supervision after discharge; length of time the child’s walking remained unsteady; child recollection of suturing; parental satisfaction with their experience in A&E.

Statistical methods
To investigate the association of dose levels with the complications being studied—e.g. any complications (defined as oxygen saturation below 93%), the need for restraint during anaesthesia or suturing, salivation, dysphoria, and vomiting—exact Fisher odds ratios were calculated before adjustment. Multiple logistic regression was used to yield odds ratios both with and without adjustment for the main confounding factors (age, weight, size of wound, site of wound). Cross tabulation was used in the case of oxygen saturation below 93% against dose category, as the figures were very low. The Statsdirect and SPSS packages were used for the analysis.

RESULTS
Altogether 504 cases of ketamine sedation were identified from the forms. These were checked against the log in the theatre room for discrepancies and none were found giving a consecutive series. Two cases entailed intravenous administration, and were excluded from this analysis; these were both head injured children for wound toilet and suturing who had returned to A&E from a ward after a period of observation with cannulas already sited. A child with cyanotic congenital heart disease with a normal oxygen saturation of 84% on air, who received ketamine for wound closure, was also excluded; this child’s oxygen saturation decreased to 78% despite supplemental oxygen, although the child recovered normally without incident. None of these three excluded cases suffered any long term sequelae.

Of the remaining 501 cases an initial dose of 2.0 mg/kg (n = 310) or 2.5 mg/kg (n = 190) IM ketamine was given, with one case receiving 3 mg/kg—a protocol violation. Twenty six received a second dose of 1 mg/kg IM (16 of these initially received 2 mg/kg). Two cases received second doses of 2 mg/kg—again, protocol violations. The mean age of the children was 3.6 years (median 3, mode 2, range 0–12). Injuries were located on the limb in 144, face 313, head 36, and trunk in 8. Excluding wounds, four were abscesses, eight were nail or fingertip injuries, and five were foreign bodies for removal. One case involved toilet and lavage of an eye contaminated with “Superglue.” Mean number of sutures required was 5.4 (median 5, mode 4), and the procedure was completed in a mean time from injection of 18 minutes (median 15, mode 15). Restraint of arms, legs, and head was required in only 2% of cases for local anaesthesia and suturing. None of these children remembered the events. Overall, adult reaction during the procedure was recorded as “upset” or “felt faint” in 19%.

During sedation, there were eight instances of oxygen desaturation below 93% (table 1). These all occurred in children given more than 2.0 mg/kg. One case of laryngospasm occurred in a 2 year old having a lip wound sutured. There was a brief dip in SpO2 to 90%, returning to 100% with oxygen supplementation and airway repositioning. No secretions in the oropharynx or hypopharynx were noted and suctioning was not performed. The other episodes of desaturation were attributed to hypoventilation alone; no interventions were made and all recovered within 1–3 minutes. Two children were reported to cough during sedation; their lowest oxygen saturations were 94% and 96% respectively. One child breath held (during recovery while micturating) but did not desaturate below 98%. There were no episodes of apnoea and no episodes of vomiting during the procedure.

A transient rash, consisting of facial and/or truncal flushing or blotchy erythema, was observed in 56 cases (11%). Hypersalivation occurred in 59 (12%) despite the administration of atropine 0.01 mg/kg in all cases. Muscle hypertonus or clonus was observed in 34 cases (6.8%).

During recovery the main problem was vomiting, which occurred in 52 cases (10%), eight of who had received a second dose of ketamine. The behaviour of the children during recovery was uneventful in 406 cases (81%), mild agitation in 74 (15%), moderate agitation in 16 (3%), and pronounced agitation in 4 (0.8%). Median time to discharge was 85 minutes (mean 89, mode 90, range 40–185).

Follow up was completed in 469 cases, the rest not responding with the prepaid questionnaire and not contactable either through lack of a telephone in the household, or moving out of the area (Lancaster and surrounds attract holidaymakers and tourists). Parents reported the following
adverse events after discharge: vomiting 53 cases (11%); unsteady gait 62% (no falls or other accidents occurred, and most children went to bed on arrival home due to the late hour). Nightmares or disturbed sleep were reported in 2%, none of which persisted longer than the first night. The overall incidence of vomiting, either in the department or at home, was 17%; this incidence fell to 15% if children given a second dose are excluded. One child was admitted for observation because of vomiting—the only child requiring admission in our study. He was discharged well the next day. Four children said they remembered the suturing, but were cooperative during the suturing, with no form of restraint required. Altogether 380 (81%) of parents described their experience in A&E as “better than expected,” 74 (16%) as “the same as expected,” and 15 (3%) as “worse than expected”—only four of these related their dissatisfaction to the sedation, commenting respectively “not expecting sedation, but otherwise happy,” “upset because monitor kept alarming” (the nurse reported difficulties obtaining a satisfactory pressure wave), “vacant expression of child was concerning,” and “disturbed by child’s eyes being open.” The other 11 complaints were attributable to waiting times and attempts at wound treatment in an uncooperative child before sedation was offered.

**Association of adverse events with confounding variables**

As the number of people receiving a total dose over 2.5 mg/kg of ketamine was only 5% of the sample, the dose was categorised into 2 mg/kg and 2.5 mg/kg or over, for the purpose of analysis. As a measure of airway complications, oxygen saturation below 93% was used, as the number of people who would have fitted the US reporting of 90% was too low for any useful analysis. Again, the number of people with all five body appendages restrained were too few to be useful, and it was decided by the clinicians that the restraint of three or more limbs would be a useful restraint variable. The variables examined were dose given, age, weight, size, and site of wound. The complications examined were airway problems including desaturation, vomiting, emergence dysphoria, salivation, and restraint.

Table 2 shows the unadjusted odds ratios and those resulting from logistic regression. For airway complications, because of the small numbers, confidence intervals for the difference in proportions were calculated instead; the difference in proportions is 3.4%, with 95% confidence intervals of (1.6% to 6.8%). There is evidence that a lower dose of ketamine is associated with a lower rate of airway obstruction. When other factors are adjusted for in logistic regression, the small figures create a large standard error for the estimated odds ratio; this also happens for dysphoria.

Table 2 also shows that a lower dose of ketamine is associated with a lower rate of salivation, and the pattern persists when confounding factors are adjusted for. An association of a lower dose of ketamine with a lower rate of dysphoria emerges after confounding factors are adjusted for.

There is no evidence of any association of a lower dose of ketamine with restraint required during either suturing or local anaesthesia, or with vomiting.

**COMMENT**

It is possible that some instances of ketamine sedation were not recorded, although this is unlikely, as administration required the use of the observation form included in the form. In addition, all instances of ketamine sedation were recorded in a separate log in the theatre room. There were missing data on several forms, and it is possible that some instances of harmful, or potentially harmful, side effects went unrecorded. However, this is unlikely as the lowest oxygen saturation obtained was recorded in every case save one, and follow up was completed in most cases (94%). Accuracy of data recording may vary between the nurses particularly when recording subjective data such as agitation, child behaviour, and restraint. The requirement for any restraint of the child during local anaesthesia, or during suturing, may seem to show our technique was ineffective. Previous randomised trials have shown ketamine to be

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Airway complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age/injury</td>
<td>Dose (mg/kg)</td>
</tr>
<tr>
<td>1</td>
<td>2/lip</td>
</tr>
<tr>
<td>2</td>
<td>6/facial wound</td>
</tr>
<tr>
<td>3</td>
<td>1/cheek wound</td>
</tr>
<tr>
<td>4</td>
<td>5/facial wound</td>
</tr>
<tr>
<td>5</td>
<td>6/lip wound</td>
</tr>
<tr>
<td>6</td>
<td>4/facial wound</td>
</tr>
<tr>
<td>7</td>
<td>1/facial wound</td>
</tr>
</tbody>
</table>

* SpO₂ fell after second dose.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Association of complications with confounding factors</th>
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<tbody>
<tr>
<td>Outcome complication</td>
<td>Low dose 2.0 mg/kg fraction (%)</td>
</tr>
<tr>
<td>Oxy sat &lt;93</td>
<td>0/294(0.0)</td>
</tr>
<tr>
<td>Restraint (sitting)</td>
<td>28/294(9.7)</td>
</tr>
<tr>
<td>Restraint (LA)</td>
<td>12/294(4.1)</td>
</tr>
<tr>
<td>Salivation</td>
<td>23/294(7.8)</td>
</tr>
<tr>
<td>Dysphoria</td>
<td>2/294(0.7)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>47/289(16.3)</td>
</tr>
</tbody>
</table>

*Five missing; †one missing. One other association that may be of interest is that vomiting is associated with ages 3 to 7, and the odds ratio persists even when other confounders are adjusted for: The adjusted odds ratio is 3.18; the CI being (1.79 to 5.66). LA, local anaesthesia.
Low dose ketamine sedation

superior to midazolam with less distress shown by the children and less restraint required.\textsuperscript{15–18} It is felt by the authors that “restraint” was over-reported by our nursing staff, who admitted that any limb or head repositioning or support was recorded as “restraint”. Random, uncoordinated movements often occur during ketamine dissociation and can interfere with wound treatment. True restraint (immobilisation of all limbs and head) was recorded in 12 cases (2%) during local anaesthesia, and 9 (1.8%) during suturing. The lower dose used may, in some instances, mean children are not always fully dissociated, but our data collection did not specifically report this. We found our median discharge time to be 85 minutes, somewhat lower than the reported US time of 110 minutes, which may be relevant to a busy emergency department.

The wide confidence intervals quoted mean any lower rates of complications for the various variables should be interpreted with caution. The study was not powered to detect any significant differences in adverse events between the confounding variables, as the primary objective was to report our experience using IM ketamine.

During the initial studies strict adherence to protocol ensured 2.5 mg/kg was universally adopted; after recruitment had ceased, selection of the dose occurred by personal choice of operators. Both doses are 50% lower than those cited in other reports on paediatric sedation with ketamine. Follow up data collection by telephone risks biased answers, but it is difficult to perform any other form of follow up in the emergency department setting.

DISCUSSION

This report is the largest case series published on ketamine sedation of children in the UK. Controversy surrounds the issue of ketamine sedation in the UK, where the technique is still little used. The experience in the USA and Australia is somewhat greater, where doses of 4–5 mg/kg IM are commonly used, but many departments still use other drugs when sedation is indicated. Green recommended in his review of 1999\textsuperscript{32} that 4 mg/kg is the minimum IM dose required to achieve consistent dissociation. The painful stimulus of local anaesthesia is less than that of, say, fracture reduction (a common indication for ketamine sedation in the US)\textsuperscript{14–17, 20, 22–24} and so a lower dose can be justified, particularly as the primary aim of sedation in our study was to facilitate local anaesthesia in an otherwise uncooperative child. Dissociation may not be consistently occurring at this lower dose level but conditions were adequate for the procedure, with overall staff and parent satisfaction; a quicker discharge time may also be beneficial. Our lower incidence of airway complications in children given 2.0 mg/kg deserves further investigation. However, Green \textit{et al}\textsuperscript{32} calculated 7216 subjects would be required to detect a 50% relative difference in airway complications from a 1.4% baseline incidence in the context of a randomised controlled trial.

Our overall incidence of vomiting (15%) may seem unacceptably high for a technique designed to alleviate suffering in children. This incidence is somewhat higher than that reported by Green \textit{et al}\textsuperscript{32} but his case series did not report on adverse events after discharge. Holloway\textsuperscript{19} reported an incidence of 19%, with follow up being completed up to 14 months after discharge. The alternatives to sedation are no sedation (physical restraint) or general anaesthesia. The incidence of postoperative nausea and vomiting (PONV) in surgical paediatric patients varies from 0% to 70%. Incidences of PONV are reported to be higher in emergency procedures and those where the patient may be anxious or distressed, and where the patient is mobilised early after the procedure.\textsuperscript{33} Motion sickness (in the car going home), and concurrent

head injury may be confounding factors contributing the reported incidence of vomiting after discharge in our study. The overall parent satisfaction of 97% for ketamine sedation of their children shows the side effects appear acceptable to them, at least.

An anti-sialogogue is often used to help reduce the incidence of hypersalivation seen with ketamine and many authors recommend this. We found an incidence of hypersalivation of 12% despite all patients receiving atropine; the trend towards a lower incidence of salivation in the lower dose group (2 mg/kg) warrants further comment, particularly as many authors suggest excess secretions and suctioning may precipitate laryngospasm. The incidence of hypersalivation reported by Green \textit{et al}\textsuperscript{32} was only 1.7% despite co-administration of atropine with a larger dose of ketamine, though these data were collected retrospectively by review of medical records. Fourteen children in this study did not receive atropine and hypersalivation was observed in none of these cases.

We report a quicker median time to discharge compared with that reported by Green \textit{et al}\textsuperscript{32} although both the ranges are wide. The times quoted by both are times from injection of ketamine to actual departure from the emergency department. Green’s original study\textsuperscript{22} and that of Dachs and Innes\textsuperscript{25} recorded time to “ready for discharge,” a better measure of sedation recovery time as it would exclude department management issues such as completion of paperwork and organisation of transport. The comparisons of subjective events such as hypersalivation, agitation, and dysphoria are difficult without rigid standardised definitions and complete prospective data.

IM administration does have drawbacks not least the pain of an injection. We used topical anaesthetic cream ("Ametop") to help alleviate this where possible. Haematoma formation and inadvertent intravascular or
intraural injection are known complications, but were not observed in our study. We postulate that some instances of sedation failure requiring second doses may be attributable to accidental injection into fat or other tissue planes where absorption of the drug may be slower. IM injection was tolerated well. Intravenous administration would obviously require cumulative of an uncooperative child, a procedure possibly more stressful and painful than an IM injection.

Our case series is not unique in reporting potentially life threatening complications, and it must be emphasised that the procedure is only safe if the environment, monitoring, staffing, and training are all skilled at identifying and treating the rare adverse events quickly and effectively.

In conclusion, IM ketamine sedation in the A&E department is a safe and acceptable technique when used within a defined protocol by trained and experienced staff, with appropriate monitoring and equipment available. Low dose (2–2.5 mg/kg) is sufficient for most procedures likely to be undertaken in UK emergency departments and may offer quicker discharge times. There seems to be little difference in clinical effect between these two doses, although 2.0 mg/kg may offer a lower incidence of airway problems and salivation.

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Contributors
RGMcG conceived the study, collated data and performed the follow up. MCH collected data, performed a further literature search and wrote the paper. MJ performed the statistical analysis. RGMcG acts as guarantor for the paper.

The parental advice sheet is available to view on the journal web site (http://www.emjonline.com supplemental).

Authors’ affiliations
R G McGlone, M C Howes, Accident and Emergency Department, Royal Lancaster Infirmary, Lancaster, UK
M Joshi, Research Support Statistician, Medical Statistics Unit, Lancaster University, UK

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Conflict of interest: none declared.

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REFERENCES
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