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Paediatric procedural sedation based on nitrous oxide and ketamine: sedation registry data from Australia

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ABSTRACT

Objective Large, mainly North American, series has shown the safety of paediatric procedural sedation in the emergency department (ED). However, sedation practices elsewhere differ. This study set out to investigate the sedation practice and the associated adverse events profile at the largest Australian paediatric ED.

Method Review of a prospective single centre procedural sedation registry database at an urban tertiary children's hospital ED in Australia with an annual census of 67 000 patients over a 4-year period (2004–8). Sedation records were supplemented with medical record review. Patients 18 years and older were excluded. Demographics, agents used, adverse events and complications were analysed descriptively.

Results Over the 4-year period, 2002 patients underwent procedural sedation. The median age was 5.7 years. Nitrous oxide was used in 1625 (81%), ketamine in 335 (17%) and midazolam in 39 (2%). Propofol and chloral hydrate were used in two and one patient, respectively. Most sedations were for laceration repair (38%) and orthopaedic procedures (33%); 89% had no adverse events. Most adverse events were mild, mainly vomiting (8%). Serious adverse events were desaturation in 12 patients, seizures in two patients and chest pain in one patient. The maximum required airway support was bag mask ventilation. No patients aspirated or required intubation.

Conclusion In variation to reported practice elsewhere, almost all procedures in this Australian series were undertaken using nitrous oxide and ketamine. The serious adverse events rate was low.

Procedural sedation and analgesia (PSA) for painful and distressing interventions in children has become a standard tool for clinicians in the emergency setting.[1] Many national and international bodies have created policies, guidelines and other documents as a framework for effective and safe sedation.[2–9] However, the translation of these documents into actual clinical practice is left to individual hospitals and clinicians.[10 11]

Although larger prospective datasets of paediatric sedation outside the operating theatre or by non-anaesthetists have become available,[12–15] studies in paediatric sedation safety outside the operating theatre in general are still hampered by relatively small numbers to determine low frequency but high-risk events, inconsistent terminology and definitions[7] and a focus on North American practice.[1 8]

As part of a comprehensive sedation programme developed with the support of the hospital insurer,[10 16] we prospectively collated all emergency department (ED) sedations in a registry for ongoing quality assurance and observational sedation research.[17 18] We analysed 4 years of sedation registry data to determine the overall sedation practice and adverse events profile in a large paediatric ED.

METHODS

Design and setting

We conducted a prospective observational study in the ED of an urban children's hospital with an annual census of 67 000 patients. All children presenting to the ED since the commencement of the sedation programme in May 2004 were eligible for enrolment. We excluded patients 18 years of age and older and patients who received ketamine at analgesic doses via the pain management service. The hospital institutional review board approved this study as an audit and was exempted from informed consent.

Study protocol

PSA with any sedative agent was performed using a standardised pre-sedation assessment, monitoring during the procedure and post-sedation discharge criteria.[10 16] The sedation checklist became part of the medical record. As per ED guidelines nitrous oxide and oral benzodiazepine required a minimum fasting time of 2 h for solids and liquids, and parenteral agents required a 4 h fasting time for solids and milk and 2 h for clear fluids. Mandatory monitoring during procedural sedation included continuous oxygen saturation, heart rate, respiratory rate and sedation depth, with 5-minutely recording of these parameter by nursing staff on the observation chart until the child had returned to the pre-procedural state. There was an accredited senior nurse or physician to provide airway support and monitoring during the sedation in addition to the proceduralist. Ketamine or other parenteral agents required an additional senior member of staff to be available, and it was mandatory that the procedure was undertaken in the resuscitation rooms with full airway support equipment setup. Parenteral agents required additional monitoring including regular non-invasive blood pressure monitoring as well as a continuous cardiac monitoring. Nitrous oxide was administered by inhalation of a gas mixture with oxygen, with the nitrous oxide concentration varying between 30% and 70%.

Data collection

The sedation checklist functioned as the case report form and was used to record data before, during and after PSA. This form detailed the risk assessment, fasting status, procedures undertaken, adjunctive agents administered, deepest level of sedation and adverse events. Sedation forms were augmented by retrospective medical record review of all patients with incomplete information or any adverse events.

Definitions

Adverse events were defined a priori as serious or mild. Serious adverse events included oxygen desaturation less than 95%, apnoea, stridor, airway malalignment requiring repositioning, laryngospasm and cardiovascular instability. Complications were defined as adverse events with sequelae, including pulmonary aspiration, endotracheal intubation, unplanned additional tests or hospital admission (related to sedation event), permanent neurological injury or death. Inadequate sedation was not regarded as an adverse event. Oxygen administration, upper airway repositioning and tactile stimulation were regarded as minor interventions. Escalation of respiratory or circulatory support beyond this was considered a major intervention.

Analysis

All data were entered into an Access software sedation registry database (version 2003). Median values were reported as median with interquartile ranges. Statistical calculations were performed on STATA software (version 10.0).

RESULTS

Over the 4-year study period we assessed 2002 patients who had received a sedative agent for PSA in the ED. Patient demographics are listed in table 1. Sixty per cent of patients were male and the median age was 6 years. Eighty-one per cent of patients received nitrous oxide, 17% received ketamine, 1% midazolam administered with nitrous oxide and a further 1% midazolam alone. Propofol was administered only twice and chloral hydrate once. Sedative agents were most frequently administered for laceration repairs (38%), orthopaedic interventions (33%), foreign body removal (10%) and vascular access (4%). Twenty-two per cent of patients received an adjunctive agent, most frequently codeine was administered (12%) followed by morphine (4%).

Eighty-nine per cent of patients experienced no adverse events related to the PSA. Of the 11% who did experience an adverse event, vomiting was the most common (8%) followed by agitation (1%) as shown in table 2. Serious adverse events were experienced by a total of 15 patients. Twelve patients experienced oxygen desaturation, two patients experienced a seizure and another chest pain. These events will be discussed within the agent-specific sections.

Nitrous oxide

A total of 1625 patients received nitrous oxide for PSA in the ED, of which 59% were male and the median age was 7 years (table 1). The highest concentration was recorded in 1362 patients. Nitrous oxide 70% was used in 84.2% of patients. The most common procedures requiring nitrous oxide were orthopaedic intervention (38%), laceration repair (31%) and foreign body removal (10%). Twenty-one per cent of patients received an adjunctive agent, most commonly codeine (13%) followed by morphine (5%). Nine per cent of patients administered nitrous oxide experienced an adverse event. In 6% of cases vomiting was recorded, followed by 1% experiencing agitation (table 2).

Serious adverse events were reported in four patients (0.2%). Two patients experienced oxygen desaturation after the procedures. The first was a 12-year-old boy who underwent fracture reduction under intravenous regional anaesthesia (Bier's block). He had received 70% nitrous oxide during the procedure. He was recorded to desaturate to 73% after the procedure and vomit post-procedure. He was administered oxygen by face mask, admitted for observation and discharged without further interventions or sequelae. The other patient who experienced desaturation was a 3-year-old girl receiving an unknown concentration of nitrous oxide for a fracture reduction. Her oxygen saturations remained greater than 95% during the procedure, but dropped to 86% post-procedure. Oxygen was applied and saturations returned to 100%. She was discharged home without further complications.

An 11-year-old patient reported chest pain after receiving sedation with 70% nitrous oxide. His vital signs were recorded as within normal limits; an ECG and chest radiograph were obtained and were reported as normal. The pain subsided with the administration of an antacid and he was discharged home after a period of observation in the ED. A 16-year-old boy was recorded as having a 60 s seizure that self-resolved without further intervention. No patient sustained a clinically apparent pulmonary aspiration or required advanced airway manoeuvres.

Ketamine

A total of 335 patients received ketamine for PSA, administered intravenously (46.3%), intramuscularly (50.3%) or both intramuscularly and intravenously (3.6%) (table 1). Sixty-one per cent of patients were male and the median age was 3 years. Laceration repair accounted for 76% of procedures undertaken with ketamine sedation. Eighty-seven (27%) received an adjunctive agent, most commonly atropine in 12.3%. Adverse events were reported in 23% of patients most commonly vomiting (17%) (table 2).

There were 10 patients with desaturations. These patients were between 2 and 6 years of age. They desaturated to a low of 80%. Desaturations were due to upper airway obstruction (four patients) or hypersalivation (three patients). One patient had a mild laryngospasm. They were managed with the application of oxygen by face mask, suctioning and jaw thrust. Only one patient required a period of bag mask ventilation. No patients had clinically apparent pulmonary aspiration and no patients were intubated.

A 9-year-old boy without a history of epilepsy experienced a brief tonic/clonic seizure. The seizure self-resolved without further interventions. There was one case of severe emergence phenomenon. The 4-year-old patient had not received midazolam before the procedure. He recovered without further management and was discharged later that day.

There was only a single admission for ketamine sedation-related adverse events. A 4-year-old boy with persistent vomiting post-procedure was admitted to the short stay unit for intravenous fluid administration. This patient had previously failed nitrous oxide sedation.

Midazolam

A total of 18 patients received midazolam as a single sedative agent. Fifty-five per cent of patients were male, with a median age of 5 years. Midazolam was most commonly administered by mouth and most commonly for peripheral intravenous canula insertion (22%). Only one patient received an adjunctive agent (codeine).

Twenty-one patients received a combination of nitrous oxide and midazolam as sedative agents. Forty-eight per cent were

Table 1 Characteristics of patients who received a sedative agent for PSA in the ED

Characteristic	Overall agents n=2002 n (%)	Nitrous oxide n=1625 n (%)	Ketamine n=335 n (%)
Age, years			
Mean (range)	6.6 (1–18)	7.2 (1–18)	3.6 (1–16)
Median (IQR)	5.7 (3.3–9.6)	6.5 (4.0–10.2)	3.0 (1.9–4.5)
Male gender	1192 (59.5)	965 (59.4)	204 (60.9)
Sedative agents			
Nitrous oxide	1625 (81.1)		
Ketamine	335 (16.7)		
Midazolam	18 (0.9)		
Nitrous oxide and midazolam	21 (1.0)		
Propofol	2 (0.1)		
Chloral hydrate	1 (0.1)		
Procedures			
Laceration repair	767 (38.3)	508 (31.2)	255 (76.1)
Facial laceration repair	440 (22.0)	247 (15.2)	190 (56.7)
Sutures, unspecified	164 (8.2)	117 (7.2)	47 (14.0)
Non-facial	163 (8.1)	144 (8.9)	18 (5.4)
Orthopaedic	663 (33.1)	616 (37.9)	36 (10.7)
Reduction fracture	425 (21.2)	393 (24.2)	27 (8.0)
LAMP	94 (4.7)	81 (5.0)	8 (2.4)
Application of plaster	71 (3.6)	70 (4.3)	—
Reduction dislocation	73 (3.7)	72 (4.4)	1 (0.3)
Foreign body removal	198 (9.9)	161 (9.9)	34 (10.2)
Vascular access			
Peripheral IV line placement	74 (3.7)	68 (4.2)	–
Central venous line placement	3 (0.2)	3 (0.2)	–
Other procedure			
Abscess drainage	63 (3.2)	61 (3.8)	2 (0.6)
Urinary catheter	40 (2.0)	38 (2.3)	
Lumbar puncture	26 (1.3)	23 (1.4)	1 (0.3)
Wound debridement	25 (1.3)	23 (1.4)	1 (0.3)
Dressing application/removal	24 (1.2)	23 (1.4)	1 (0.3)
Dental procedure	13 (0.7)	9 (0.6)	4 (1.2)
Enema application	11 (0.6)	10 (0.6)	
Nasogastric or gastrostomy tube placement	11 (0.6)	10 (0.6)	
Pelvic examination	5 (0.3)	4 (0.3)	
Suprapubic aspirate	5 (0.3)	5 (0.3)	
Paraphimosis reduction	4 (0.2)	4 (0.3)	
Arthrocentesis	4 (0.2)	4 (0.3)	
Vaccination	3 (0.2)	3 (0.2)	
Hernia reduction	3 (0.2)	2 (0.1)	
'Other examination'	60 (3.0)	50 (3.1)	1 (0.3)

ED, emergency department; IQR, interquartile range; IV, intravenous; LAMP, local anaesthesia, manipulation and plaster; PSA, procedural sedation and analgesia.

male and the median age was 6 years. A third of patients underwent an orthopaedic procedure. Four patients received morphine as an adjunctive. There were no adverse events.

Other agents

Two patients, a 13 and a 16-year-old, received propofol for fracture reductions. No adjunctive agents were administered and no adverse events occurred. A 3-month-old boy received chloral hydrate for an echocardiogram. No adjunctive agents were administered and there were no adverse events.

DISCUSSION

This dataset represents the largest sedation dataset in Australasia and the largest worldwide of a setting that includes nitrous oxide as a standard sedation agent. In our setting nitrous oxide was used in 81% of sedations. In the USA two multicentre sedation registries have been established, the Paediatric Sedation Research Consortium[13] and the Procedural Sedation in the Community Emergency Department registry.[12] The Paediatric Sedation Research Consortium is collecting data from 26 paediatric US institutions on paediatric sedation and anaesthesia outside the operating theatre in a web-based de-identified database. In an initial publication,[13] epidemiological and safety data from 30 000 sedations were presented. Although a large list of agents were used no patient received nitrous oxide for procedural use. The Procedural Sedation in the Community Emergency Department registry[12] examines sedations in patients of all ages in community EDs in the USA in an observational on-line

Table 2 Adverse events of ED patients who received a sedative agent for PSA

	Overall		Nitrous oxide		Ketamine	
Parameter	**n***	**(%)**	**n†**	**(%)**	**n‡**	**(%)**
Nil adverse event	1774	(88.9)	1474	(90.8)	266	(79.9)
Adverse event	222	(11.1)	148	(9.1)	67	(22.5)
Vomiting	162	(8.1)	104	(6.4)	58	(17.4)
After	84	(4.2)	37	(2.3)	47	(14.1)
During	43	(2.1)	36	(2.2)	7	(2.1)
Unknown time	36	(1.8)	31	(1.9)	5	(1.2)
Agitation	26	(1.3)	23	(1.4)	3	(0.9)
Nausea	18	(0.9)	18	(1.1)	—	—
Hypersalivation	14	(0.7)	—	—	14	(4.2)
Desaturation	12	(0.6)	2	(0.1)	10	(3.0)
Airway malalignment	4	(0.2)	—	—	4	(1.2)
Rash	4	(0.2)	—	—	4	(1.2)
Light-headed	4	(0.2)	4	(0.2)	—	—
Hallucinations	3	(0.2)	3	(0.2)	—	—
Admission related to adverse event	2	(0.1)	1	(0.1)	1	(0.3)
Abdominal pain	2	(0.1)	2	(0.1)	—	—
Seizure	2	(0.1)	1	(0.1)	1	(0.3)
Tachycardia	2	(0.1)	1	(0.1)	1	(0.3)
Hypertension	1	(0.1)	—	—	1	(0.3)
Trembling	1	(0.1)	—	—	1	(0.3)
Hiccups	1	(0.1)	1	(0.1)	—	—
Pallor	1	(0.1)	1	(0.1)	—	—
Hyperventilation and carpoped spasm	1	(0.1)	1	(0.1)	—	—
Chest pain	1	(0.1)	1	(0.1)	—	—

*Six missing values.
†Three missing values.
‡Two missing values.
ED, emergency department; PSA, procedural sedation and analgesia.

database. Based on the analysis of 1028 patients, a wide variety of agents were used; nitrous oxide, however, was not listed or discussed. There was an 'other' category of sedation agents (4.7%) but these agents were not specified further. Both registries indicate that sedation practice in the USA is quite different from the practice in other countries. UK data on actual sedation practices in EDs are limited.[19–21] A national survey in UK EDs[21] found that midazolam was the most widely used agent for procedural sedation followed by ketamine. Nitrous oxide was not reported as an agent used; as the actual survey was not included it is not clear if nitrous oxide was not used in EDs or questions about nitrous oxide had not been included in the survey. In a Scottish ED report[20] entonox use was reported as a procedural agent but most sedations were in adults and sedation agents were not reported by patient age. In Australia and New Zealand, data from two surveys of sedation practice in paediatric EDs[22 23] indicated that nitrous oxide was the most frequently used procedural agent; the most recent survey indicated that all departments surveyed used nitrous oxide and ketamine.[22] Therefore, our sedation registry data will to some degree reflect Australasian practice.

Overall, our data show sedations to be performed with a low rate of serious adverse events when embedded in a comprehensive sedation education and credentialling programme. In particular, no patient had clinically apparent pulmonary aspiration, required intubation or other invasive interventions and only two patient required admission due to sedation-related adverse events. Many agents have been used or proposed for procedural sedation in children.[1] The ideal agent would have quick onset and off-set, be highly efficacious with a favourable adverse events profile and be administered in a non-parenteral fashion. One such potential agent is nitrous oxide.[24] Our analysis confirms other studies to show that high-concentration nitrous oxide (70%) has a favourable safety profile with a low rate of serious adverse events.[18 25 26]

Ketamine was the second most frequently used agent. Ketamine has been shown in a number of large-scale ED studies to provide safe sedation.[14 15] Our registry data show that ketamine has an adverse events rate similar to published data. The major drawback of ketamine is the prolonged recovery time, irrespective of its use via the intramuscular or intravenous route.[17 28] Although no patient required endotracheal intubation or experienced any long-term sequelae, the number of desaturations encountered during ketamine sedation supports the focus of the education and credentialling programme on removing high-risk patients from consideration, requiring senior ED staff to participate in all ketamine sedations and with staff being very familiar with the agent and its adverse events profile. ED staff should only use the agent if they are able to rescue paediatric patients who develop airway or breathing compromise with appropriate interventions.

Few patients (1%) received midazolam as a single agent for procedural sedation. This is in contrast to reported UK practice in which midazolam was reported as the most frequently used agent.[21] Although a useful sedative, anxiolytic and amnestic agent,[1] midazolam in the ED setting is hampered by a lack of analgesic properties. In addition, a portion of children will become paradoxically agitated. Most procedures in our registry were painful, such as wound repairs and orthopaedic procedures. In addition, in terms of patient flow in the ED midazolam compares poorly with nitrous oxide, which has almost immediate discharge readiness upon completion of the procedure. Reduced midazolam use may reflect emerging evidence and departmental observations suggesting a number of issues such as

unpredictable sedation,[29 30] paradoxical reactions with restlessness[29 31] and poor palatability.[32] In addition, midazolam does not reduce the incidence of emergence dysphoria associated with ketamine.[33] Twenty-one patients received a combination of nitrous oxide and midazolam. There is no data on patient safety and depth of sedation when combining high-concentration nitrous oxide and midazolam. As a result of the low use and utility of midazolam we have since removed the agent from the departmental sedation teaching programme.

Only three patients received sedative agents beyond this, propofol (two) and chloral hydrate (one). Propofol is a general anaesthetic used widely in adult EDs for PSA and has also been used in paediatric EDs. It is hampered by a high rate of respiratory depression and also hypotension, and its application outside of the operating theatre by non-anaesthesiologists has provoked more controversy than any other sedation agent.[34–36] Chloral hydrate has been used as a sedative agent for many years. In the ED setting it is hampered by its inconsistent depth of sedation, the long recovery time and the lack of analgesic properties.[1]

The use of the sedation checklist, which formed the basis for the data collected in the sedation registry, was not mandated in a small number of patients who required immediate PSA. An example would be a displaced ankle fracture with vascular compromise, which requires immediate reduction. It is possible that these patients constitute a particularly high-risk group, in terms of fasting status, exclusion due to pre-existing conditions etc, which were not included in the registry. There were also a number of patients who underwent non-emergent sedations and did not have a checklist completed. The authors are not aware of any significant adverse events occurring after these emergent or non-emergent procedures. A review of the hospital adverse events system (Riskman) and the adverse drug reaction reporting system did not identify further ED sedation-related adverse events. Finally, this registry was set up before a consensus article standardising the terminology and the reporting of adverse events in ED PSA.[7]

CONCLUSION

In this large single centre sedation database almost all procedures were undertaken using nitrous oxide and ketamine. The serious adverse events rate was low and did not require invasive interventions. The data indicate that the sedation education and credentialling programme provided an appropriate framework for ED procedural sedation.

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Contributors FEB conceived of the study, supervised it and wrote the draft of the paper, and takes ultimate responsibility.CD, JB, SH and TT contributed data, analysed data and assisted in revisions of the paper.

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