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Title Page

Paediatric Procedural Sedation within the Emergency Department

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ABSTRACT

Procedural sedation and analgesia in children requires the use of non-pharmacological and pharmacological approaches to facilitate the management of painful procedures. The development of skills in such techniques has mirrored the development of paediatric emergency medicine as a sub-specialty. Governance, education and credentialing must facilitate safe sedation practice, using a structured approach, as sedating children in the busy environment of an emergency department is not without risk. Emergency clinicians, patients and caregivers all have a role to play in developing a safe, effective sedation plan.

INTRODUCTION

The development of procedural sedation and analgesia (PSA) parallels the development of paediatric emergency medicine (PEM) as a subspecialty. As clinicians developed confidence in managing the sedated child, procedures previously performed in the operating theatre have migrated to the ED.[1] ED performance of PSA allows more rapid discharge, reduces costs, and increases clinician skills and job satisfaction, while making unpleasant procedures more tolerable and less painful to children and their families.

Prior to performing PSA in the ED, there must be a practitioner competent in the necessary procedure (e.g. fracture manipulation). . If there is doubt, then ED sedation may not be appropriate. If necessary, referral to the appropriate proceduralist should be made and a collaborative plan for definitive care developed., At least one qualified clinician must be responsible for, and focus on, safe PSA and another performs the procedure.

Although serious adverse events are rare [2,3], PSA must be safe, and sedation providers should be prepared to intervene should complications occur. Cote[4] and Hoffman[5] demonstrated that patient selection, adherence to a prescribed process and minimisation of the number of sedating agents were important in reducing PSA risks. In Victoria, over the last decade, the development and dissemination of a PSA program[6-9] has provided a structure for teaching and providing practical experience. Hospital administrators and insurers support this program recognising the clinical risk reduction provided.

Three periods define a sedation event: pre-procedure, intra-procedure and post-procedure. Tasks for each period appear in Figure 1.

PRE-PROCEDURE

Patient Selection and Risk Assessment

The most important aspect is the identification of risk factors likely to affect PSA. Sedation risk is higher in younger children, with apnoea more likely in those under 6 months. Airway management is potentially more complicated and practitioner familiarity with younger infants may be lower. Risk factors for failed sedation outside an operating room include: upper respiratory tract infection (odds ratio[OR], 2.73 [range 1.58-4.73]), obstructive sleep apnoea (OR 2.06 [1.22-3.48]), American Society of Anaesthesiologists (ASA) class 3 (OR 2.31 [1.4-3.84]), obesity (OR 1.95 [1.01-3.75]) and older age (OR 1.15 [1.08-1.21]). [10]

Medical problems affecting airway, breathing, circulation and neurological function also influence the risk of PSA. Risk factors for sedation from a child's past medical history are contained in Table 1. Medication based side effects will be discussed later.

Registry data has assisted in the quantification of adverse events. The Pediatric Sedation Research

Consortium (http://www.pedsedation.org) in the USA is a multi-centre registry involving over 30 centres that perform PSA. Cravero[11] used this registry, with predetermined definitions, to report on the incidence of 26 complications associated with over 30 000 PSA events undertaken outside an operating room. In this cohort there were a total of 1020 adverse events with: no deaths, 1 cardiac arrest and 1 aspiration event. Vomiting occurred on 142 occasions yielding an incidence of 47.2 vomiting events per 10000 PSA events. Overall, unplanned treatments were needed in 336 PSA events (incidence 111.9 per 10000); intubation was required in 29 PSA events (incidence 9.7 per 10000) and bag-valve-mask ventilation in 192 PSA events (incidence 63.9 per 10000). The same consortium later reported data for over 49 836 PSA events using propofol from July 1, 2004 and September 1, 2007.[12] There were 2950 total adverse events with no deaths, 2 cardiac arrests and 4 aspiration events. The incidence of vomiting was 10.6 vomiting events per 10000 PSA events. Babl reported on a cohort of 2002 Australian children who received nitrous oxide and/or ketamine for PSA in a tertiary paediatric ED.[13] Vomiting occurred in 8%. There was no aspiration event. Such data are useful in identifying the skills, such as airway management, required to provide safe PSA.[11-14] There is little to support the association between fasting time, vomiting and aspiration, however pragmatic approaches are required[15] and will relate to the patient, the most recent oral intake and the perceived urgency of the procedure.

ED practitioners should recognise higher risk patients in planning PSA. For example, the 4-tier Malampati score has been used in anaesthesia to predict a difficult airway.[2] Higher scores (Class III and IV) predict difficult bag-valve-mask ventilation and risk of airway obstruction.[2] A degree of patient cooperation is required to use the Malampati score.

Equipment and Staff

Equipment and personnel to manage threats to airway, breathing and circulation should be available. Senior staff should be available within the ED and sedation practitioners should have airway management and basic life support (www.apls.org.au) skills. Real-time monitoring of oxygen saturation, ECG, respiratory rate and blood pressure is required for PSA. Equipment such as O2, suction, bag-valve-mask systems, oropharyngeal airways, endotracheal tubes, laryngeal mask airways, tapes, vascular access devices (intravenous [IV] and intraosseous cannulae) and resuscitation drugs should be available. Given the variation in size of children sedated, equipment should be prepared prior to commencing sedation, and drug dose calculations considered.

Rapport

Good rapport may reduce the amount of sedation required, and makes the procedure more positive for all involved. Caregivers should be given instruction in what to say, and what not to say;[16] avoiding bribery and statements suggesting that the procedure is “nearly finished” or “doesn’t hurt”. The use of distraction using: bubbles, books, screens (phones, tablets, televisions) and music (iPod, phones) can be useful [2,17]. Developmentally appropriate discussion about the procedure should occur with the patient. Play therapy [17],

guided imagery and meditation have also been used. Nitrous oxide delivery can be made more palatable by choosing a particular scent, via commercially available essences. This also provides a choice where the child has few choices, and another distracting discussion.

INTRA-PROCEDURE

Monitoring of airway, breathing and circulation are the priorities for the practitioner providing PSA. Continuous monitoring and observation of respiratory rate, work of breathing, pulse oximetry, heart rate and blood pressure are required for safe PSA. Blood pressure measurement may be more important when intravenous PSA agents (e.g. propofol) are used. Observations related to cardiovascular and respiratory status, as well as depth of sedation, must be recorded regularly. Non-invasive monitoring of exhaled CO2, as a marker of hypopnea, can alert clinicians earlier to hypopnea, than if desaturation or respiratory rate is used[5,18]. Such monitoring is not generally available at this time in Australia or New Zealand.

As the procedure concludes, sedation can be weaned. For example, reducing the concentration of nitrous oxide while increasing O2 concentration facilitates washout of nitrous oxide. The timing of additional doses when sedating with ketamine and/or propofol will be related to the duration of the procedure, the response of the child and their family. It can be difficult to judge when further doses are required. In these situations a balance between the need for further sedation and the duration of the procedure will be need to be found.

POST PROCEDURE

Monitoring of children following sedation is required. Vomiting may occur as children emerge from sedation. A return to pre-sedation vital signs and level of consciousness should be documented and nausea/vomiting, if it occurs, managed prior to discharge.[19]

Emergence dysphoria, particularly following ketamine can be managed by optimising the post PSA environment. The area can be darkened, familiar music and voices (e.g. parents, siblings) provided and medical handling minimised. Pre-procedure rapport building may also assist. Occasionally, more severe dysphoria may require benzodiazepine, although this is rare.[13].

Explicit discharge instructions, with hospital contacts, should be provided to families. Information provided should include: recommendations regarding levels of activity following PSA (e.g. avoid activities requiring high levels of coordination for 24 hours), dietary guidelines (e.g. avoid heavy meals immediately after sedation) and advice on when to return to hospital.

GOVERNANCE

PSA should be practiced by skilled and committed personnel, operating in a governance structure that supports them. EDs, hospitals and hospital networks all play a role in establishing, and then nurturing the

structure. Government health departments can affect change by supporting these processes. In Victoria, the State Department of Health has supported PSA education and developed a program (handbook, presentations for trainers, practical train-the-trainer sessions and testing materials) with the advice of a reference group.[9]

PHARMACOLOGICAL SEDATION

Nitrous Oxide (N2O)

Nitrous oxide is a gas, which provides mild to moderate levels of analgesia, sedation and amnesia. It is widely used in dental work and anaesthesia. In a survey of Australasian paediatric EDs it was found to be commonly used for PSA.[20] N2O can be inhaled in fixed concentration (Entonox [50% O2:50% N2O) or in a titratable mixture of up to 70% N2O using continuous flow systems. The low solubility of the gas in blood provides rapid onset and offset, allowing a quick return to baseline level of consciousness. N2O has been used either alone or in combination with other agents for: bladder catheterisation, IV access, fracture reduction, abscess drainage, foreign body removal and laceration repair.

The limited efficacy of N2O in very painful procedures (e.g fracture reduction) can be overcome. The options include: optimising the concentration of N2O (maximum 70%) and/or adding adjunctive agents such as intranasal fentanyl, to provide additional analgesia. Moderate or deep sedation, with up to 70% N2O, was achieved in only 3% of 762 children[21]. Zier et al found N2O provided inadequate sedation in 1.3%, minimal sedation in 94.3% and drowsiness in 4.3% of 1858 PSA events.[22]

While vomiting is relatively common, there has been no association found with pre-procedural fasting and rates of emesis.[23] The combination of N2O and IN fentanyl provides deeper PSA, however vomiting was more common.[24] Other side effects include: headache, dysphoria, and restlessness. In a large prospective study, adverse event rates for patients receiving more than 50% N2O were similar to those receiving up to 50% N2O.[21] N2O is contraindicated where there is a risk of gas diffusion into closed spaces where expansion is clinically important (i.e. pneumothorax, bowel obstruction, pneumocephalus, and middle ear disease), in children with impaired consciousness, and head injury. N2O inactivates vitamin B12 and should be avoided in B12 or folate deficiency and in immunocompromised children).[2,3]

Ketamine

Ketamine produces a trance-like cataleptic state, profound analgesia and amnesia, with retention of protective airway reflexes, spontaneous respirations, and cardiovascular stability. [18] Through separation of thalamo-cortical and limbic systems, it causes dissociation between external stimuli and the cerebral cortex. After ketamine administration, a threshold is crossed into the dissociated state. Dissociative anaesthesia/sedation does not neatly fit into the sedation continuum that progresses from sedation (light, moderate, deep) to anaesthesia.

Multiple guidelines exist for ketamine use in ED PSA. Within Australia and New Zealand, PREDICT reported 8 paediatric and mixed EDs had ketamine guidelines.[20] In the USA, ACEP clinical practice guidelines for ketamine were first published in 2004, and updated in 2011.[18]

Ketamine is appropriate for short, painful procedures, or where less potent PSA agents have failed. Absolute contraindications include: age under 3 months and known or suspected schizophrenia. Relative contraindications include active respiratory infections, previous airway surgery, porphyria, thyroid disorders and cardiovascular diseases.[18] Recent evidence[25-27] demonstrated that ketamine had a negligible effect on intracranial pressure, and maintained cerebral perfusion pressure, in both the traumatic and non-traumatic setting. Ketamine has historically been thought to increase intraoccular pressure, however Wadia et al [28] demonstrated minimal pressure increases in normal healthy eyes.

The dissociation threshold is typically reached at an IV dose of 1.0 to 1.5 mg/kg.[18] Lower doses, especially in patients over 70kg, may be used with subsequent titrated dose(s) given to maintain PSA. Once dissociation is achieved, further dosing does not provide deeper PSA, but smaller doses (e.g. 0.25 to 0.5 mg/kg) may be needed to maintain the dissociated state. Ketamine can be safely administered via the intramuscular (IM) route (dose 4mg/kg).[29] This route causes longer PSA and more vomiting than the IV route.[30] If administering IM ketamine, an IV cannula may not be needed.[29,31] However, maintaining the dissociated state is more convenient via IV titration. In addition, for the rare adverse event, having IV access may be important. Lower doses of ketamine (0.5 - 0.75mg/kg IV or IN) can provide analgesia, rather than dissociation.[32]

Current evidence does not suggest the use of prophylactic anticholinergics or benzodiazepines in children.[33] Prophylactic benzodiazepines in adolescents and adults may reduce unpleasant recovery reactions,[34] without increasing the risk of adverse events. Neither atropine nor glycopyrrolate have shown any efficacy in decreasing airway and respiratory adverse events.[35] Prophylactic ondansetron may reduce the incidence of vomiting with modest efficacy.[36] Other adverse events include: transient laryngospasm (0.3%), transient apnoea or respiratory depression (0.8%), hypersalivation (uncommon) and recovery agitation.[18] Muscular hypertonicity and random, purposeless movements are common in children.

Propofol

Propofol is an ultrashort acting, dose-dependent, deep sedative agent without analgesic properties. It can be used for short, painful procedures in combination with analgesia. Adverse events were rare in two paediatric series,[37,12] with reported complications of: hypotension (15.4%), desaturation (9.3%), apnoea (1.9%), assisted ventilation (1.4%), unplanned intubation (0.2%), emesis(0.14%), laryngospasm (0.1%), bradycardia (0.1%), and anaphylaxis in children with egg or soy allergies.[38].

Propofol use in PEM has been growing despite barriers, which include: restricted availability in some EDs and concerns regarding the deeper sedation achieved; with the potential for adverse respiratory events.[39] There is also a perception, in some centres that propofol should be reserved for anaesthetists, and this can cause tension between departments of anaesthesia and the ED.[1,39]

Initial propofol doses of between 0.5 to 1mg/kg, with subsequent titration doses, will achieve, and then maintain PSA. Younger children may require higher doses per kilogram than older children, with doses up to 3.5mg/kg sometimes used for induction. Administer propofol over 30-60 seconds to reduce discomfort and the risk of hypotension.

Ketofol (Combination of ketamine and propofol)

The effects of ketamine and propofol are theoretically synergistic. Ketamine's sympathomimetic effect may reduce the hypotensive and respiratory depressant effects of propofol and its analgesic effect adds to the pure sedation propofol provides. Propofol may reduce recovery agitation and vomiting associated with ketamine.[40]

A study of ketofol use in children found it highly effective[41], with a clinically insignificant shortening of the recovery time, but a reduction in vomiting.[42] While Cote et al[4] found that increasing the number of medications used in PSA increases the risk of adverse events, ketofol has not been found to have greater risk than either propofol[43] or ketamine alone.[42]

Intranasal (IN) Fentanyl

Fentanyl is a synthetic opioid with strong analgesic properties. It can be administered via IV or IN route for acute treatment of pain. The IN (transmucosal) route via a mucosal atomiser device (MAD) offers an option that is needle-free and effective within 5-10 minutes of administration[44],[45]. In a mixed ED, patients received IN fentanyl faster than IV morphine,[46] and required fewer IV cannulations[47]. IN fentanyl demonstrated similar efficacy to IN ketamine in children with limb injury.[48]

A summary of the pharmacological agents appears in Table 2.

CONCLUSION

PSA provides a safe and effective method of achieving positive outcomes for a variety of procedures in PEM that would be difficult to perform without causing unjustified levels of pain or distress. Prior to performing PSA, an environment that promotes learning and safe practice is essential. Families and children should participate in the development of a procedural sedation plan that will involve multiple modalities including: non-pharmacological, rapport building and pharmacological aspects of practice.

Over time, new medications, delivery devices and monitoring techniques will lead to new sedation practices. As these developments occur there will be an ongoing need to study them, to provide an evidence based foundation to what is one of the most clinically gratifying components of PEM.

TABLE 1

Factors to consider in assessing risk for procedural sedation

	Active Medical Problems	Past History
Airway	• croup • foreign body • head and facial trauma	• previous airway surgery • laryngomalacia • craniofacial abnormalities • risk of vomiting (e.g. bowel obstruction, gastro-oesophageal reflux)
Breathing	• respiratory tract infection (e.g. pneumonia, bronchiolitis) • asthma	• sleep apnoea
Circulation	• shock (e.g. hypovolaemia, sepsis) • arrhythmia	• congenital cardiac disease (e.g. cardiac failure, pulmonary hypertension)
Neurological	• altered level of consciousness (seizure; meningitis; trauma) • space occupying lesion	• unstable epilepsy • neuromuscular disease
Other	• unstable psychiatric disorder	• history of sedation failure • history of anaesthetic reaction • family history of anaesthetic reaction

Modified from Paediatric Procedural Sedation; ED Manual. Victorian Department of Health (ECIICN, Royal Children's Hospital, VMIA) 2013 and Daud YN, Carlson DW. Pediatric sedation. Pediatr Clin North Am. 2014 Aug;61(4):703–17.

Table 2: A summary of medications used in PSA

PSA Agent	Pros	Cons
Ketamine	1. Airway reflexes maintained 2. Cardiovascular stability 3. Provides excellent analgesia and sedation and thus can be used as a sole PSA agent 4. Can be used via both IM and IV route 5. Sub dissociative doses can provide analgesia and potentially reduce opioid use 6. Excellent safety profile	1. Contraindicated < 3 months of age 2. Animal studies have shown that it can cause neurotoxicity when used in high doses. No human data available 3. Side effects include recovery agitation and emesis and rarely can cause laryngospasm
Propofol	1. Ultrashort acting sedative anaesthetic agent 2. Ideal agent for non-painful procedures 3. Multiple large case series of safe use in Paediatric ED 4. Has antiemetic property, which helps reduce risk of vomiting and aspiration during sedation 5. Reduces ICP and can be used in haemodynamically stable head injured patients	1. Narrow therapeutic window 2. Contraindicated in patients with egg and soy anaphylaxis 3. Respiratory and cardiovascular depression 4. Lack of analgesic property 5. Can cause pain locally at injection site
Ketofol	1. Potential for decreased emesis, hypotension, emergence phenomena and airway events	1. Why combine 2 drugs when single drug could be used 2. Combining 2 drugs can potentially lead to drug dosing errors
Nitrous Oxide	1. Quick onset and offset 2. Reasonable anxiolysis and amnesia	1. Provides only mild analgesia - May need to combine with other agents for painful procedure 2. Adverse effects include vomiting and, rarely, respiratory depression, which is quickly reversible with cessation of gas

	3. Minimal cardiovascular effects 4. Evidence of good safety in children over 1 year of age	
Intranasal Fentanyl	1. Strong analgesic effect; synergistic with nitrous oxide and propofol 2. Reduces need for IV access 3. Use leads to faster time to analgesia	1. Need to use concentrated solution in older children due to limitation in volume that can be administered via this route 2. Provides analgesia rather than sedation, thus other agents are required.

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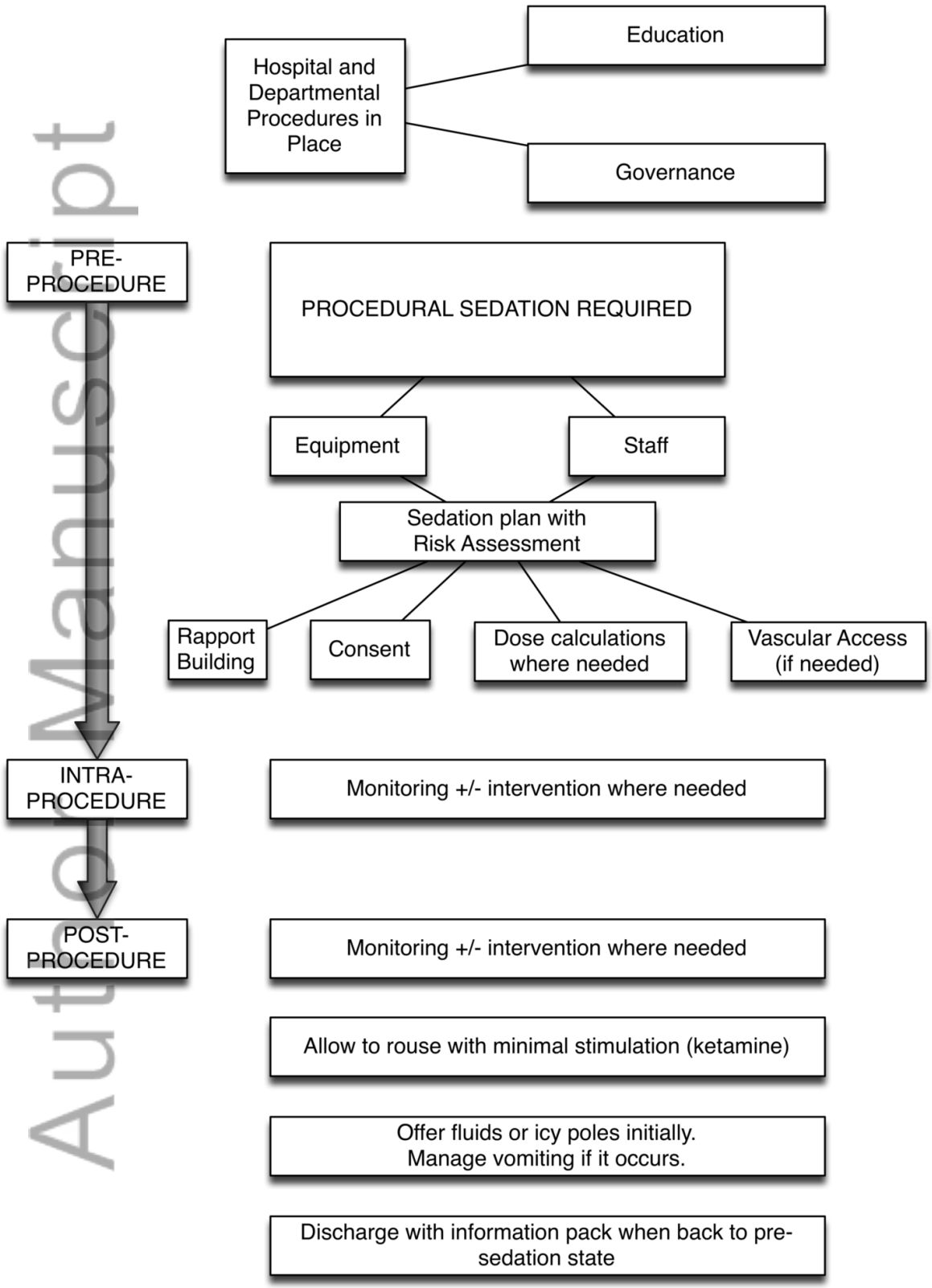

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