

## Paediatric sedation guidelines: where we came from, where we are now, and current drug controversies

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### Historical background

The American Academy of Pediatrics (AAP) became interested in sedation disasters in 1983 when three children died in a single dental office. The AAP asked the Section on Anesthesiology to help develop guidelines for monitoring children sedated by non-anaesthesiologists. I had the good fortune to co-author this first sedation guideline in 1985<sup>1</sup> Subsequently, the AAP recognised that the guideline was being ignored by general paediatric practitioners, particularly those in the emergency room, radiology, and other areas where sedation is widely used. Therefore, the guideline was revised in 1992 with a new title, and emphasis was placed on “systems issues”.<sup>2</sup> A major source of confusion was the definition of “conscious sedation”, which was defined as “a purposeful response to either a painful stimulus or a verbal command.” Some practitioners interpreted reflex withdrawal to pain as being consistent with “conscious sedation”, and this led to a number of accidents. This term is contradictory to what really happens to children, and is misleading.<sup>3</sup>

The 1992 guideline revision placed special emphasis on a “systems” approach modelled after anaesthesiology. Points of interest included:

- Informed consent: parents needed to know that sedative/analgesics have risk.
- A pre-sedation history was required: how would the child’s underlying medical conditions affect the safety of sedation?
- A focused airway examination: are there airway abnormalities or large tonsils that might affect airway management?
- Proper fasting prior to elective procedures and the need to balance the risk of sedation in children who required urgent or emergent procedures was described.
- Appropriate monitoring, particularly continuous pulse oximetry, during the procedure and into the recovery period was required for the first time.
- An independent observer, whose only responsibility was to “watch the patient”, was required during deep sedation.
- Appropriate staffing and monitoring were required during recovery.
- The children had to be returned to their pre-sedation level of consciousness.

The dental community published their own specialty-specific guideline which deviated significantly from that of the AAP.<sup>4-6</sup> Some

practitioners prescribed “light sedatives” at home prior to scheduled dental procedures.<sup>4</sup>

In 2002, a clarifying addendum to the AAP guideline was published so that the AAP, the American Society of Anesthesiologists (ASA) (<http://www.asahq.org/Standards/20.htm>) and the Joint Commission of Accreditation of Healthcare Organizations (JCAHO) all used the same terminology:

- The phrase “conscious sedation” was changed to “sedation/analgesia” and then to “moderate sedation”.<sup>7,8</sup>
- Children sedated in all venues, including private offices, were considered to fall under these guidelines;
- Children < 6 years were considered to be deeply sedated;
- It was emphasised that sedative medications were only to be administered under the safety net of medical supervision (no home prescriptions);
- Age- and size-appropriate equipment must be available;
- Sedation should only be administered by “individuals skilled in airway management and cardiopulmonary resuscitation”;
- The concept of “patient rescue” was introduced.

A task force was formed with the American Academy of Pediatric Dentistry (AAPD) to develop a joint AAP-AAPD Sedation Guideline, published in 2006.<sup>9</sup> The most recent iteration re-emphasised the principles defined in the previous documents, but went further in several areas:

- A statement that “*sedation of pediatric patients has serious associated risks, such as hypoventilation, apnea, airway obstruction, laryngospasm, and cardiopulmonary impairment*” was inserted;
- It clearly stated that “*reflex withdrawal*” to a painful stimulus is not consistent with moderate sedation, but consistent with deep sedation;
- There was recognition that the data regarding the need for dietary precautions in emergency situations are inadequate and further research is necessary;
- A need to inquire about herbal medications and their potential interactions with sedatives was described;
- An acronym (**SOAPME**) was introduced to underscore proper preparation (**S**uction, **O**xygen source, proper functioning **A**irway equipment, appropriate **P**harmaceuticals for rescue or reversal, **M**onitors, and special **E**quipment);

- Tables for calculation of local anaesthetics were added;
- The use of capnography was encouraged for the first time in non-operating room venues;
- Quality assurance techniques were emphasised;
- The desirability of training with patient simulation was encouraged;
- A clarification regarding nitrous oxide and its interaction with other sedating medications was added;
- A “time out” was added.

In 2005, the American College of Emergency Physicians updated their policy. There was a stronger statement regarding the skills of the individuals providing sedation. However, the use of pulse oximetry was not required if “*verbal communication could be maintained*”; this seems to invite the potential for delayed recognition of a developing event, since it is easy to become engrossed in the task at hand, become distracted, and forget to keep talking to the patient. This might also be a problem with preverbal children. This policy was updated in 2007.<sup>10</sup> Much discussion focuses on fasting and aspiration risk. They concluded that there was no evidence linking the period of fasting and pulmonary aspiration in children.

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has their own set of rules. It should be noted that their “Standards for Additional Special Procedures” which include moderate and deep sedation apply “in any setting”. and practitioners who provide sedation must have the following skills:

- a) *Moderate sedation - are qualified to rescue from deep and able to manage a compromised airway and to provide adequate oxygenation and ventilation, and*
- b) *Deep sedation – are qualified to rescue patients from general anesthesia and are competent to manage an unstable cardiovascular system as well as a compromised airway and inadequate oxygenation and ventilation.”*

A “time out” process and documentation of care and monitoring of outcomes is also required.

The Scottish Intercollegiate Guidelines Network (SIGN)<sup>11</sup> takes a slightly different approach than the AAP-AAPD document.<sup>9</sup> In SIGN, the “grades of recommendation” are more evidence-based and more detail is provided regarding sedation administered by nurses, sedation for painful vs non-painful procedures, and specific issues regarding subspecialties. The governing principles of safe sedation and the definitions of the levels of sedation are identical to those of the AAP-AAPD document.

### **How did the guidelines develop, and how did we get to the current status?**

I wanted to see if there were any data to support our recommendations in the first AAP Sedation Guideline.<sup>1</sup> I obtained adverse drug reports from the FDA through the Freedom of Information Act. In addition, I conducted a survey of paediatric anesthesiologists, intensive care specialists, and emergency medicine physicians (all members of

the AAP). Over 600 reports were reviewed from the FDA, the United States Pharmacopoeia, the survey, and anonymous reports sent to me. With the support of Roche Pharmaceuticals (then the patent holder for Versed®; midazolam), two paediatric anesthesiologists, one paediatric emergency medicine specialist, and one paediatric critical care specialist examined the data independently and we debated each case. We formulated 17 categories of potential system failure, and more than one event could be contributory for each patient. We narrowed the enormous database to 95 cases where all four reviewers agreed to the contributory causes.

As anticipated ~ 80% of cases presented with some form of respiratory depression. However, nearly three times as many children sedated in non-hospital based-venues suffered cardiac arrest, despite the fact that they were older and healthier (lower ASA physical status), indicating that efforts at ventilation and oxygenation were not effective.<sup>12</sup> In addition, there was no relationship between adverse outcomes (death or neurologic injury) and route of drug administration (IV, nasal, rectal, IM, PO, inhalational i.e. nitrous oxide plus other sedatives) or drug class (opioids, benzodiazepines, barbiturates, sedatives, chloral hydrate).<sup>13</sup> “Failure to rescue” and inadequate CPR skills were the major contributory factors. Other contributory causes included drug overdose, drug-drug interactions, inadequate monitoring, inadequate recovery, prescription/transcription errors, drug administration without medical supervision, drug administration by a technician, inadequate equipment, and premature discharge from recovery or inadequate recovery procedures. These “systems” issues are basically the same as peri-operative misadventures.<sup>14-18</sup>

A concern for any procedure performed in a non-hospital venue is the immediate availability of additional skilled help when an adverse event occurs. In an office, it may take 3 - 10 minutes or longer for the emergency medical technicians to arrive, whereas, in a hospital, help literally comes from throughout the institution immediately. In our database, it was clear that monitoring with pulse oximetry was an important safety feature. All 15 in-hospital patients monitored with pulse oximetry who suffered an adverse sedation event were rescued, whereas four out of five non-hospital based patients who suffered an event and were monitored with pulse oximetry were not rescued. This observation emphasises the importance of airway and CPR skills, and the ability to recognise that an event is occurring, and then successfully intervening.<sup>19</sup> The concept of rescue is important, because any patient can get in trouble at any time. A drug will have the same effects regardless of who administers the drug or in what venue the drug is administered, anyone can make a drug administration error, and there is enormous patient-to-patient variability in responses to medications. However, as long as the problem is recognised and timely intervention initiated, the outcome should be that the patient is rescued. If, however, there is delayed recognition, or intervention is delayed, or the practitioner lacks the skills to intervene successfully, then a disaster will result.

There were two cases in which children who got into trouble on the way to a facility after receiving sedating medications at home. Both were administered drug doses considered safe (chloral hydrate 60 mg/kg, or midazolam 0,5 mg/kg). What is most likely is that the children were placed in a car seat, fell asleep, and were unable

to unobstruct their airways when their heads fell forward. Eight children suffered adverse events after discharge. All had received long-acting drugs such as chloral hydrate (half-life ~ 10 hours), intramuscular pentobarbital (half-life ~ 25 hours), intramuscular Demerol/Phenergan/Thorazine (DPT) (half-life 7 - 12 hours).<sup>20</sup> Our data were used to help in the development and evolution of the sedation guidelines of the AAP, ASA, JCAHO, and now the joint AAP-AAPD sedation guideline.

### Areas of controversy

- Should use of propofol be restricted to anaesthesiologists? How do we accredit people for its use?<sup>21-23</sup>
- Should all sedated children be monitored with capnography?<sup>24</sup>
- Is sedation with ketamine deep sedation, or something else entirely?<sup>25-27</sup>
- Is ketamine totally safe?<sup>28-30</sup> There is a low, but consistent, ~ 1 - 2% incidence of apnoea, airway obstruction and laryngospasm that may occur with ketamine sedation.<sup>31-33</sup> Just as with propofol, the provider must have the skills to manage a non-breathing child and a child with an obstructed airway, and the skills to effectively relieve laryngospasm.<sup>31,32,34-39</sup> Is atropine useful?<sup>40,41</sup> Since secretions may promote the development of laryngospasm and atropine is virtually harmless in children, I see no reason not to use atropine.
- Is fasting necessary in the emergency room patient? The literature is quite unclear; all published series lack sufficient power to answer this question. These papers imply that there is no difference in complications between those who have properly fasted compared with those who have not but, when examined closely, most patients were not deeply sedated, so the risk for aspiration was minimal.<sup>42-48</sup>
- Is dexmedetomidine the answer? Its alpha 2-adrenoceptor agonist activity, if injected rapidly, will produce hypertension (hence the need to administer as an infusion over 10 minutes) while, at higher doses, produces bradycardia and hypotension.<sup>49-52</sup> Several papers have reported its utility for sedating children.<sup>53-57</sup> The doses administered were several-fold greater than those approved by the FDA and, although the success rate was high, a careful analysis of the data revealed a large proportion of children with severe bradycardia.<sup>58-60</sup> A report of severe hypertension in children who developed bradycardia (heart rates 38, 37, and 41 beats per minute, in children aged 12, 3, and 12 years, respectively) following high dose dexmedetomidine (3 µg/kg over 10 minutes followed by 2 µg g/kg/hour infusion), that required treatment with glycopyrrolate, is very worrisome. These cases strongly suggest that high dose dexmedetomidine is likely not safe and that lower doses combined, when needed, with other sedating medications may be safer.<sup>61</sup>

### Conclusion

This meeting is a good example of the current heightened awareness of adverse sedation events and how to prevent them. It is only through

large scale studies (The Sedation Consortium) that we can determine the areas of concern and then develop methods to avoid or prevent these.<sup>62,63</sup> Similarly to the airline industry, there is a constant need to keep track of what we do, determine what went wrong and why it went wrong, and then fix it so that it will not happen again. That is the value of discussion, analysis, climate change, and removing ego from the health care process.

### Definitions

**Minimal sedation (anxiolysis)** is a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilatory and cardiovascular functions are unaffected.

**Moderate sedation/analgesia (“conscious sedation”)** is a drug-induced depression of consciousness, during which patients respond purposefully to verbal commands,\* either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.

**Deep sedation/analgesia** is a drug-induced depression of consciousness, during which patients cannot be easily aroused but respond purposefully following repeated or painful stimulation.\* The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.

\*Reflex withdrawal from a painful stimulus is NOT considered a purposeful response.

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