Procedural sedation and analgesia in the emergency department

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Purpose of review

Procedural sedation and analgesia is frequently administered outside of the operating room in emergency departments (EDs) and ICUs. Evidence was sought concerning patients' safety in the ED.

Recent findings

Procedural sedation, when administered in the ED by trained personnel, is safe. Extensive literature demonstrates that propofol, ketamine, midazalam, and fentanyl are appropriate medications with proper monitoring and the presence of appropriate personnel. Preprocedural fasting may not be necessary in many cases.

Summary

With appropriately trained personnel, proper equipment, and the studied drugs ED sedation and analgesia is safe and an appropriate procedure.

Keywords

emergency department, fasting, ketamine, monitoring, procedural sedation, propofol

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Introduction

Procedural sedation and analgesia (PSA) is a method of administering sedatives or dissociative agents to patients undergoing unpleasant procedures. For centuries, physicians administered PSA with medications ranging from morphine and whiskey to the chloroform and ether used in the civil war. More recently, anesthesiologists and intensivists have studied methods and medications that are increasingly applied in the less controlled emergency department (ED) setting prompting expressions of concern for patient safety. We reviewed the literature from 2010 related to ED PSA.

Credentialing

The safety of PSA is dependent upon the training and skill maintenance of those performing and assisting with sedation, adherence to accepted standards of practice, and the availability of necessary equipment and medications. Within the last decade there has been an expansion of privileges to perform deep sedation to nonanesthesiologists, the introduction of capnography, and the widespread use of propofol and other drugs previously restricted to the operating room. Three articles discussing PSA in children were reviewed; we feel that the conclusions are equally applicable to adults.

Shavit *et al.* [1] conducted a comprehensive survey of practice variation among pediatric emergency medicine practitioners in academic centers. They found a wide spectrum of strategies yet a low rate of adverse events. Differences between fellows and attendings according to years of practice showed no consistent theme. The use of supplemental oxygen (40%) and capnography (45%) was low. Practice variations in the community setting should be equally great but also not necessarily harmful. Babl *et al.* [2] evaluated a PSA training program administered to practitioners at an academic and community ED, and monitored sedation safety prospectively over 3 years. They demonstrated that the lessons learned persisted although more rapid deterioration occurred at the community facility perhaps because of fewer procedures and less continuing education.

Leroy *et al.* [3••] published a comprehensive review (104 references) of PSA in children and developed evidence-based recommendations related to many current issues in PSA. Level I data support the accepted perception that adverse events are more frequent in younger children, in those with underlying disease, and when more sedatives are employed. With level II certainty it is not the operators' specialty but that PSA is performed by 'specifically trained professionals working in dedicated teams. . .according to international guidelines' and that an appropriately trained team will have a 'significant decrease of procedural failure'. Level III evidence suggests that PSA 'with propofol, including deep sedation, is equally safe in the hands of anesthesiologists and nonanesthesiologists if the latter are well trained and part of a dedicated sedation team'. They conclude that having 'different levels of monitoring and competence for moderate and deep sedation is arbitrary and potentially dangerous'.

The three articles do not address who should be present during PSA. It is generally accepted that a separate professional administers sedation and another performs the procedure. In our ED, in addition to the professional performing the procedure, a respiratory therapist, a registered nurse, and a sedating provider are present. This latter person is an attending ED physician, senior resident, or assistant physician who has completed a course in PSA. In many community EDs this staffing or an anesthesiologist is not available. We recommend three professionals be present – one to perform the procedure, one to give medications, and one to watch the patient if feasible.

Key points

- Procedural sedation can be safely administered in the ED by properly trained and qualified personnel.
- Cardiac monitoring, blood pressure monitoring, and pulse oximetry are accepted standards, whereas the monitoring of end tidal carbon dioxide remains controversial. It should be performed when available in patients with significant comorbidities.
- Preprocedural fasting has not been proven to reduce aspiration in ED sedation.
- Propofol, ketamine, morphine, fentanyl, and midazalam have been shown to be safe and effective in appropriate patients. Newer medications such as dexmedetomidine and alfentanil have great potential but further study is needed.

Drugs

The agents used for PSA are associated with various risks that can be mitigated by careful patient selection, cautious selection of drugs, and appropriate monitoring and personnel. Leroy *et al.* [3••] find level I evidence that with ketamine the risk of airway compromise, including laryngospasm, 'necessitates specific skills and competence ... particularly with high intravenous doses, administration to children younger than 2 years or aged 13 years or older'. Level I evidence affirms the safety of propofol if the sedating physicians have 'the requisite competencies and skills'. Level II evidence indicates that nitrous oxide has an extremely good safety profile and that the combination of benzodiazepines and opiates is associated with a higher risk of respiratory complications than midazolam alone or ketamine with midazolam.

Ketamine is a commonly used dissociative agent in children that produces a trance-like state with both sedation and analgesia while maintaining airway reflexes and an intact respiratory drive. Ketamine can produce emergence phenomena and recovery agitation ranging from hallucinations and nightmares to violent outbursts, thought to be more common in adults, with incidences as high as 30% [4]. Coadministration of benzodiazepines is thought to reduce the incidence but few prospective randomized trials are available.

Ketamine is not extensively used in procedural sedation in adults due to concerns about recovery agitation. Its reduction would allow increased use of this inexpensive, safe, agent. Sener *et al.* [5•] published a well-designed double-blind, placebo-controlled study of 200 adults, randomized into four groups, comparing the incidence of recovery agitation occurring with intravenous (i.v.) or intramuscular ketamine with and without midazolam resulting in four treatment arms [5•]. Secondary objectives were to compare the effect of midazolam on patient and provider satisfaction and time to recovery from sedation. Recovery agitation was recorded as any perceived agitation, minor or major. Patients randomized to ketamine with midazolam had a lower overall incidence of recovery agitation. The i.v. ketamine with midazolam group had an incidence of recovery agitation of 7% compared with 22% in the group without midazolam. Results were comparable in the intramuscular groups, with an incidence of 9 and 28%, respectively. A patient satisfaction score of 4 or 5 on a 5-point Likert scale was considered 'satisfied' with 69% of patients receiving midazolam with ketamine rating the procedure as satisfactory compared with 48% of patients who did not receive midazolam. The results are very encouraging but the population was a relatively healthy 18–50 year old sample and the results may not extrapolate to the sedation of older patients and those with comorbidities. These warrant further investigation. We recommend midazolam as a safe and effective adjunct to ketamine in uncomplicated adults undergoing PSA.

In pediatric sedation, ketamine and propofol are commonly combined as 'ketofol' because of synergistic and complimentary effects. Propofol is thought to lessen some of the emetogenic effects of ketamine and ketamine, through its sympathomimetic effects, reduces the hypotension associated with propofol. Ketamine also has important analgesic properties not possessed by propofol.

Shah *et al.* [6] compared ketamine-propofol ('ketofol') to ketamine alone for PSA in children. In this double-blinded study, 140 children aged 2–17 with orthopedic injuries received either ketofol at 0.5 mg/kg each or ketamine alone at 1.0 mg/kg. Differences in time to sedation and recovery were not clinically significant. Notably, 12% of patients in the ketamine group experienced vomiting compared with only 2% in the ketofol group supporting the belief that propofol alleviates nausea associated with ketamine. However, antiemetics

such as odansetron have similar efficacy and avoid concern for adverse reactions from propofol. Adverse events were similar in the groups. None required intubation or suffered any permanent sequelae. Physicians and nurses had significantly higher sedation satisfaction scores with the combination. Ketofol, the combination of ketamine and propofol, is a viable alternative to ketamine or ketamine and midazalam.

Two studies worth noting explored the use of dexmedetomidine, extensively used in intensive care units, for ED PSA [7,8]. Preliminary evidence is favorable but further study is indicated. Also studied were alfentanyl and intranasal fentanyl also showing preliminary promise with possibly wider use if safety and efficacy are substantiated [9,10].

Monitoring

Monitoring during procedural sedation is intuitively important but the type and extent remains a subject of debate, study, and practice variance based on opinion and availability of resources. The consensus is that adults and probably children should have continuous cardiac, blood pressure, and pulse oximetric monitoring. Capnography, the continuous measurement of the patient's end tidal carbon dioxide ($ETCO_2$), continues to be controversial. Changes in the $ETCO_2$ reflect changes in the patient's arterial partial pressure of carbon dioxide and thus changes in ventilation and should provide advanced warning of hypoxia and in the presence of supplemental oxygen provide advance notice of respiratory depression.

An excellent trial by Deitch *et al.* [11••,12••,13,14]; an editorial; and a related letter to the editor along with a reply illuminated the potential benefits and the possible negative consequences of routine measurement of $ETCO_2$ in ED sedation. Deitch *et al.* [11••] attempted to answer the question in a study of 132 patients receiving sedation for orthopedic procedures or abscess drainage. Patients were randomized to either active capnographic monitoring by the treating physician or blinded recording of the values with the treating physicians unaware of the $ETCO_2$. All patients were sedated with propofol, received supplemental oxygen nasally at 3 l per minute, and had not received narcotics within 30 min of the start of sedation. In both groups the recorded interventions included stimulation, repositioning of airways, increased supplemental oxygen and potentially (though not done) intubation. Capnography was 100% sensitive for predicting hypoxia with an abnormal capnogram occurring 5–240 s before the onset of hypoxia. A conservative definition of a 10% change in $ETCO_2$ (vs. other studies 10 mmHg) was used. When the treating physician was aware of the $ETCO_2$ the incidence of hypoxia was reduced from 42 to 25% ($P = 0.35$). However, 32 patients (22 in the active capnography group of which 11 received some intervention and 10 in the blinded group of which one received an intervention) developed abnormal capnography without hypoxia, thus capnography was 64% specific. The continuous recording of oxygen saturation and $ETCO_2$ was suggested as the explanation for the unusually high incidence of hypoxia without adverse outcomes in these patients. The use of capnography in this group prevented the development of hypoxia in about 15% of patients; however, it did not prevent any serious adverse events.

In the same issue of the journal, Green and Pershad [12••] contribute an excellent Pro (Green) and Con (Pershad) editorial discussing 'should capnographic monitoring be standard practice during emergency department procedural sedation and analgesia?' They agreed that capnography foretells adverse airway and respiratory events regardless of supplemental oxygen use thus favoring capnography. Espousing the Pro argument, Green feels that 'hypoxemia should be minimized whenever possible. Transient hypoxemia may not be dangerous in and of itself; however, it is a harbinger of serious morbidity and even mortality'. Mentioning a pertinent 'con' argument, Green notes the potential for unnecessary positive pressure ventilation to cause gastric insufflation and aspiration. His feeling is that, overall, capnography 'improves the existing standard of care'. Pershad takes what is probably a more pragmatic approach. He accepts that capnography does reflect ventilatory response and that it is not harmful but notes that 'the safety benefit purported ... is decreased hypoxemia... lasting from 5 to 15 s (and the events are often) self-limiting or resolve with minimal interventions such as airway repositioning or supplemental oxygen'. In addition, he suggests there can be a downside with 'nuisance alarms' caused by patient movement, misplaced sensing cannulas, and so on. Pershad does not feel capnography should be routine but used with judgment.

In a follow-up letter to the editor, Sivilotti *et al.* [13] add to the con opinion stating that Deitch *et al.* 'fail to demonstrate that capnometry improved patient safety'. They suggest that in PSA performed without supplemental oxygen, pulse oximetry identifies respiratory depression before capnography and is a safe alternative considering the 'limited availability, cost, or false-positive results' of capnography. Deitch *et al.* [14], in reply, argue that $ETCO_2$ changes advocate for patient safety because 'the majority of patients who develop hypoxia have a preceding $ETCO_2$ change' and thus stand by their recommendation for the general use of $ETCO_2$ monitoring in ED PSA [14].

Sivilotti *et al.* [15] enrolled 63 patients in a study of ED PSA with either fentanyl or low dose ketamine used as adjuncts to propofol sedation to determine if capnography added incremental benefit to pulse oximetry in healthy patients given supplemental oxygen only if desaturation occurred. More than half of their patients developed desaturation below 92% but 'in all cases, the oxygen desaturation was brief and uncomplicated and responded immediately to oxygen, decreased propofol or patient stimulation'. $ETCO_2$ values were inconsistent, not predictive of desaturation, and not helpful clinically and occurred nearly 2 min after pulse oximetry changes. In this setting 'although more information is generally regarded as being better for patient safety, redundant information, falsely reassuring information, false alarms and information overload can both distract and mislead clinicians'. They concede that 'capnometry has an important role in detecting more advanced respiratory depression masked by the use of supplemental oxygen'.

Eichhorn *et al.* [16•] reviewed PSA outside the operating room, not specifically in the ED, and express the opinion that 'end-tidal carbon dioxide monitoring aids in the detection of apnea ... (and) will detect clinically occult hypoventilation and is indispensable in patients undergoing deep sedation. .. (and should be monitored) in patients with pre-existing pulmonary or cardiac diseases ... even for light sedation'. This makes intuitive sense though not shown conclusively to be true in ED PSA.

Should capnometry be routine in ED PSA? Green notes that 'fortunately serious complications such as hypoxic brain injury, aspiration, or death (occur with) exceptional rarity in modern sedation practice (which) makes them virtually impossible to study' [12••]. In the authors' institution PSA is always performed with high-flow oxygen supplementation and capnography. Providers present are an ED respiratory therapist, registered nurse, and one physician for sedation and another provider performing the procedure. In a wide range of patients, many with significant comorbidities, with very close monitoring by experienced practitioners, the capnogram is rarely helpful. We conclude that capnography should be used if available but is not yet 'standard of care'. In a high personnel-resource environment it is less useful (though probably more available). With less personnel available capnography should be used if possible particularly in sicker patients as should high flow oxygen.

Fasting

Fasting prior to administering anesthesia was described by Mendelson in 1946 [17]. In a series of 44 016 obstetric patients undergoing general anesthesia, there were 45 reports of aspiration and two deaths. Subsequently, many studies have attempted to investigate those factors associated with increased risk of aspiration and pneumonitis during anesthesia. The American Society of Anesthesiologists (ASA) recommend fasting prior to general anesthesia [18]. These recommendations have been extrapolated to the performance of PSA for emergent patients; however, there is growing evidence that they may not be applicable.

Thorpe and Benger [19••] reviewed twenty-five articles for evidence related to fasting in both adult and pediatric patients undergoing emergency sedation. None specifically addressed the risk of aspiration. A total of 4657 adult patients had not been fasted according to ASA guidelines prior to PSA. Seventeen cases of vomiting during sedation were reported and none showed evidence of pulmonary aspiration. They note that 'with the exception of one case report, there are no reports of pulmonary aspiration associated with emergency procedural sedation in the literature' and conclude that 'there is no high-level evidence that specifically addresses the risk of pulmonary aspiration'. Thorpe and Benger also reference 44 articles on pediatric sedation of which three 'specifically investigated the relationship between preprocedural fasting and adverse effects'. Children have a higher incidence of vomiting and ketamine, used frequently, is more emetic but less likely to suppress protective airway reflexes. They found 'no reports of pulmonary aspiration in children ... the majority of whom were not fasted in line with ASA guidelines'. Patients undergoing PSA differ from those undergoing general anesthesia and aspiration may be less common with shallower depth of sedation allowing protective reflexes to be maintained. Airway manipulation (avoided in PSA) may increase the risk of aspiration during general anesthesia and PSA drugs may be less emetic than inhalational gases used during general anesthesia. Patients with pre-existing comorbidities have an increased risk of aspiration and alternatives to PSA should be considered.

Molina, *et al.* reviewed the literature and found only two sources that met their criteria, one prospective cohort study and one guideline [20•]. The cohort study included 400 pediatric patients sedated with propofol. One fasted and one nonfasted patient vomited and there were no reports of aspiration. The guideline (from the American College of Emergency Physicians) found only a Level C recommendation that 'recent food intake is not a contraindication for administering PSA, but should be considered in choosing the timing and target level of sedation' [21]. Bhatt, *et al.* [22] published the results of a survey of Canadian emergency physicians to investigate their tolerance for risk when performing PSA on

children who have not met the ASA fasting guidelines. They found that 'a significant proportion of physicians indicated that they would administer PSA to children who had not met fasting guidelines', while 16.7% of physicians surveyed would not … regardless of the hypothetical risks.

Molina *et al.* [20•] suggest that recommendations to delay PSA to accommodate fasting guidelines may not account for detrimental effects of delays in treatment. We feel this is pertinent as the publications reviewed did not find evidence to support preprocedural fasting for patients undergoing PSA. The application of ASA fasting guidelines for PSA is in question and the risk in individual patients must be weighed against the risk of delaying an emergent procedure.

Conclusion

The 2010 literature discussing ED procedural sedation and analgesia was informative, has reinforced presumed tenets, and has introduced drugs and drug combinations some of which may become standards. The literature is moving us closer to consensus on some issues. Supplemental oxygen during PSA in adults coupled with monitoring of $ETCO_2$ is the 'gold standard'. However, monitoring the $ETCO_2$ is not yet 'standard of care' though we recommend its use in patients with significant comorbidities. In those less ill, with close monitoring by appropriate staff, it may not be necessary. Preprocedural fasting is encouraged but is not mandated for emergent procedures. It is recommended with deeper sedation, greater comorbidities, and less urgent procedural urgency when there is not a risk of delaying the procedures.

The most widely used sedation drugs (propofol, ketamine, and midazolam) were most studied and are safe for ED PSA in the carefully selected patients in the published series performed most commonly at teaching institutions where resources (particularly during studies) are plentiful. Newer medications, combinations, and medications by different routes including dexmedetomidine, nasal fentanyl, nitrous oxide, and alfentanil seem promising. Ketamine's use in adults will expand, particularly as recovery agitation can be ameliorated with midazam. Even with appropriate monitoring, complications can occur during PSA. Our review suggests that the risks can be mitigated by careful patient selection, cautious drug selection, appropriate cardiac and respiratory monitoring, and presence of trained personnel.

Acknowledgements

The authors have no conflicts of interest to declare.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 402).

1 Shavit I, Leder M, Cohen DM. Sedation provider practice variation: a survey analysis of pediatric emergency subspecialists and fellows. Pediatr Emerg Care 2010; 26:742–747.

2 Babl FE, Krieser D, Belousoff J, Theophilos T. Evaluation of a paediatric procedural sedation training and credentialing programme: sustainability of change. Emerg Med J 2010; 27:577–581.

3 •• Leroy PL, Schipper DM, Knape HJ. Professional skills and competence for safe and effective procedural sedation in children: recommendations based on a systematic review of the literature. Int J Pediatr 2010; 2010: 1–16.

The authors are Dutch with specialties of pediatric sedation, healthcare improvement, and anesthesia. Their outside view of ED PSA with extensive data, discussions, and recommendations make this a recommended read.

4 Corssen G, Reves JG, Stanley TH. Intravenous anesthesia and analgesia. Philadelphia, PA: Lea & Febiger; 1988. pp. 99–174.

5 • Sener S, Eken C, Schultz CH, *et al.* Ketamine with and without midazolam for emergency department sedation in adults: a randomized controlled trial. Ann Emerg Med 2011; 57:109–114.e2.

A well-done study answering a current huge question – should the use of ketamine be greatly expanded in adults? Ketamine is very safe but the concern has been recovery agitation. This suggests agitation can be reduced with the addition of benzodiazepines.

6 Shah A, Mossdossy G, McLeod S,*et al.*. A blinded, randomized controlled trial to evaluate ketamine-propofol versus ketamine alone for procedural sedation in children. Ann Emerg Med 2011; 57:425–433.e2.

7 Jewett J, Phillips WJ. Dexmedetomidine for procedural sedation in the emergency department. Eur J Emerg Med 2010; 17:60–61.

8 Shukry M, Miller JA. Update on dexmedetomidine: use in nontintubated patients requiring sedation for surgical procedures. Ther Clin Risk Manag 2010; 6:111–121.

9 Miner JR, Gray R, Delavari P, *et al.* Alfentanil for procedural sedation in the emergency department. Ann Emerg Med 2011; 57:117–121.

10 Saunders M, Adelgais K, Nelson D. Use of Intranasal fentanyl for the relief of pediatric orthopedic trauma pain. Acad Emerg Med 2010; 17:1155–1161.

11 •• Deitch K, Miner J, Chudnofsky CR, *et al.* Does end tidal CO_2 monitoring during emergency department procedural sedation and analgesia with propofol decrease the incidence of hypoxic events? a randomized, controlled trial. Ann Emerg Med 2010; 55:258–266.

A very well-done study, the best we are aware of, that shows capnography to be an excellent predictor of respiratory depression in the group of patients they studied (healthy, sedated with propofol, given supplemental oxygen) at the expense of many 'false alarms'.

12 •• Green SM, Pershad J. Should capnographic monitoring be standard practice during emergency department procedural sedation and analgesia? Pro and Con Ann Emerg Med 2010; 55:265–267.

Excellent pro vs. con style editorial that gives the consensus and then discusses some pros and cons of routine capnography during sedation. This and Deitch above do not give 'the answer' but allow the sedating provider to help decide how to best achieve patient safety in a lot of circumstances.

13 Sivilotti ML, Murray HE, Messenger DW. Does end-tidal CO2 monitoring during emergency department procedural sedation and analgesia with propofol decrease the incidence of hypoxic events? Ann Emerg Med; 56:702–703.

14 Deitch K, Chudnofsky CR, Miner J. Does end tidal CO2 monitoring during emergency department procedural sedation and analgesia with propofol decrease the incidence of hypoxic events? (Letter) Ann Emerg Med 2010; 56:703–704.

15 Sivilotti MLA, Messenger DW, van Vlymen J, *et al.* A comparative evaluation of capnometry versus pulse oximetry during procedural sedation and analgesia on room air. Can J Emerg Med 2010; 12:397–404.

16 • Eichhorn V, Henzler D, Murphy MF. Standardizing care and monitoring for anesthesia or procedural sedation delivered outside the operating room. Curr Opin Anaesthesiol 2010; 23:494–499.

Referenced review that discusses most aspects of sedation pointing out how appropriate concern for details allows sedation outside the OR to be safe and effective.

17 Mendelson CL. The aspiration of stomach contents into the lungs during obstetric anaestesia. Am J Obstet Gynecol 1946; 52:191–204.

18 American Society of Anesthesiologists. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures. Antesthesiology 1999; 90:896–905.

19 Thorpe RJ, Benger J. Preprocedural fasting in emergency sedation. Emerg •• Med J 2010; 27:254–261.
An excellent discussion of the subject presenting the emergency medicine view and experience that these procedures have to be done, should be done humanely, and there is no one else to do them but fortunately are safely done.

20 Molina JA, Lobo CA, Goh HK, *et al.* Review of studies and guidelines on • fasting and procedural sedation in the emergency department. Int J Evid Based Healthc 2010; 8:75–78.
An evidence-based search used and little data found but a well-written discussion of fasting (or not).

21 Godwin SA, Caro DA, Solf SJ *et al.* Clinical policy: procedural sedation and analgesia in the emergency department. Ann Emerg Med 2005; 45:177–196.

22 Bhatt M, Currie GR, Auld C, Johnson DW. Current practice and tolerance for risk in performing procedural sedation and analgesia on children who have not met fasting guidelines: a canadian survey using stated preference discrete choice experiment. Acad Emerg Med 2010; 17:1207–1215.