Guideline for Pediatric Procedural Sedation and Analgesia in the Emergency Department

Introduction:

Pain is often an inherent part of a child's presenting complaint, and is frequently exacerbated by many of the routine procedures carried out in the investigative and management processes of the Emergency Department (ED). Sedation of the frightened or uncooperative child during painful procedures is a useful adjunct in reducing anxiety and optimizing procedural conditions. Indeed, effective management of pain and anxiety in the pediatric patient improves outcomes as well as patient cooperation and parental satisfaction. The ability to provide appropriate sedation and analgesia is now an expected skill of healthcare providers within the ED.

In the early nineties, the American Academy of Pediatrics (AAP) described three levels of sedation – conscious sedation, deep sedation and general anaesthesia. Unfortunately, the term "conscious sedation" created some confusion; however, the ensuing discussion helped refine standards to better define expectations for training, monitoring, documentation and selective pharmacologic strategies.

The American College of Emergency Physicians (ACEP) defines **Procedural Sedation/ Analgesia** (PSA) as "a technique of administering sedatives or dissociative agents with or without analgesics to induce a state that allows the patient to tolerate unpleasant procedures while maintaining cardiorespiratory function[1]." The goals of pediatric PSA are to:

1) Guard the patient's safety and welfare;
2) Minimize physical discomfort and pain;
3) Control anxiety, minimize psychological trauma, and maximize the potential for amnesia;
4) Control behaviour and/or movement to allow the safe completion of the procedure;
5) Return the patient to a state in which safe discharge from medical supervision is possible[2,3].

The intent is to achieve these goals while ensuring that the patient is able to independently maintain oxygenation, airway control, and cardiorespiratory function.

These guidelines will focus on three levels of sedation that are most often used to fulfil these goals in the ED. **Moderate sedation**, previously termed "conscious sedation," is defined as a drug-induced depression of consciousness during which patients respond purposefully. **Deep sedation** is defined as a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after repeated or painful stimulation. A separate

sedation category, **dissociative sedation**, is a trancelike cataleptic state characterized by profound analgesia and amnesia, with retention of protective airway reflexes, spontaneous respirations, and cardiopulmonary stability[1,3].

The ACEP has published several clinical policies pertaining to procedural sedation and analgesia in the pediatric population. During their review process, relevant articles were assigned a "strength of evidence" classification, which were subsequently utilized in establishing the following recommendation levels[1,4-6]:

Level A recommendations: Generally accepted principles for patient management that reflect a high degree of clinical certainty (i.e., based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all of the issues).
Level B recommendations: Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (i.e., based on strength of evidence Class II studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies).
Level C recommendations: Other strategies for patient management that are based on preliminary, inconclusive, or conflicting evidence, or in the absence of any published literature, based on panel consensus.

The following guidelines are derived from a variety of published policies from numerous professional organizations, including the AAP, ACEP, and the Canadian Association of Emergency Physicians (CAEP)[1-6]. The objective of these guidelines is to assist in appropriate patient/ procedure selection, ensure adequate preparation, and optimize patient monitoring so as to minimize the risk of adverse events. Where relevant, the ACEP levels of recommendation will be referenced with regards to various clinical policies and pharmacologic agents.

Indications:

In general, the indications for procedural sedation/analgesia can be classified into three categories:

1. Diagnostic Imaging (requiring sedation only)
2. Painful Diagnostic (requiring both sedation and analgesia), including:
    a. Lumbar puncture
    b. Sexual assault examination with forensic evidence collection
3. Painful Therapeutic (requiring both sedation and analgesia), including:
    a. Fracture/ dislocation reduction
    b. Complex laceration repair
    c. Foreign body removal
    d. Abscess incision and drainage

Procedures should be of reasonable duration and complexity to be undertaken in the often busy emergency department.

Patient Assessment:

The pre-sedation patient risk assessment should include a history and examination that highlights issues important to anaesthetic administration as well as the issues surrounding the chief presenting complaint.

1. History:
    a. Concurrent medical illnesses – respiratory illness, volume depletion, fever
    b. Medications
    c. Allergies
    d. Prior adverse reactions to anaesthetic/ sedative agents (e.g. paradoxical reactions, nausea, vomiting, airway difficulties)
    e. History of sleep disordered breathing or snoring
    f. Major medical illnesses, physical abnormalities, and neurologic problems
    g. Last solid/ liquid intake (see further discussion)
2. Physical Examination:
    a. Cardiorespiratory status
    b. Airway anatomy/ function

Exclusion criteria:

- Difficult airway syndromes – abnormal face, mouth, dentition or neck
- Sleep apnea, stridor, airway obstruction, severe asthma
- Tracheal abnormalities
- Severe cardiorespiratory disease
- Severe gastroesophageal reflux
- Severe obesity
- Raised intracranial pressure
- Severe neurological impairment and/ or bulbar dysfunction
- Malignant hyperthermia
- Infants <6 months old

During the initial assessment, consideration should also be given to the psychosocial aspects of preparing patients and families for procedural sedation/ analgesia. Discussions should take into account the child's age/ developmental level, prior experience with painful procedures, the style of coping with stress, and the possible presence of care-givers during the procedure.

The American Society of Anesthesiologists (ASA) physical status classification is commonly used for preoperative risk stratification. The ASA classification is as follows[3]:

ASA Class	Description
I	Healthy, no underlying organic disease
II	Mild or moderate systemic disease that does not interfere with daily routines (e.g. well controlled asthma, essential hypertension)
III	Organic disease with definite functional impairment (e.g. severe steroid dependent asthma, IDDM, uncorrected congenital heart disease)
IV	Severe disease that is life threatening (e.g. head trauma with increased ICP)
V	Moribund patient, not expected to survive
E	Physical status classification appended with an "E" connotes a procedure undertaken as an emergency

Pediatric patients undergoing procedural sedation in the Emergency Department should be **ASA Class I (normal healthy) or II (mild systemic disease).** Patients with a higher ASA class should either undergo sedation by an anaesthesiologist or have the sedation postponed (if possible) until their clinical status is optimized.

Fasting Guidelines

ACEP has given the following **Level B recommendation** regarding fasting guidelines in pediatric PSA: **procedural sedation may be safely administered to pediatric patients in the ED who have had recent oral intake.** The risks and benefits of doing so must be evaluated individually on a case-by-case basis. Factors to bear in mind when making this decision include urgency of the procedure, the patient's baseline risk of aspiration, and the intended depth of sedation[7]. For example, a non-emergent abscess incision and drainage may prompt the physician to adhere more strictly to fasting guidelines, while it would be reasonable to sedate a child irrespective of fasting status in an emergent limb-threatening situation.

Traditionally, the AAP has recommended that the following fasting guidelines be followed for pediatric procedural sedation and analgesia[3]:

Clear liquids (e.g. water, clear fruit juices and carbonated beverages)	2 hours
Breast milk	4 hours
All other liquids and solids (including infant formula)	6 hours

These recommendations were developed by the ASA and extrapolated from patients undergoing general anaesthesia. In this population, the overall risk of aspiration is less than 1:3500 when both emergent and electives cases are taken into account[5,7]. There are, however, no established guidelines as to what constitutes an adequate fasting period for procedural sedation and analgesia. There are several differences between general anaesthesia and the level of sedation undertaken in the ED[5]. During general anaesthesia, the highest times of aspiration risk are during induction, introduction of the laryngoscope for intubation, and extubation; these actions are obviously not the goal in PSA. The level of sedation that one aims for during PSA is generally moderate to deep sedation; the majority of patients maintain respiratory effort and protection of airway reflexes at these depths of sedation. In addition, the agents used in general anesthesia (e.g. inhaled anesthestics) are inherently more emetogenic than the agents used for PSA.

There are very few cases of aspiration during PSA documented in the literature. In a series of over 30,000 children who underwent PSA, Cravero et al reported only 1 case of aspiration in a 5-year old girl who had adhered to the traditional ASA fasting guidelines[8]. Several studies have recently been conducted to examine the compliance of following fasting guidelines, and the risks associated with not doing so. A 2003 study by Agrawal et al looked at 1,014 children who underwent procedural sedation and analgesia[9]. Of the 905 patient for whom fasting status was documented, 509 patients (58%) did not meet the ASA/ AAP fasting guidelines. There were no documented episodes of aspiration in this study. The study also showed no difference in rate of adverse events between fasted and non-fasted patients. Fifteen patients experienced emesis; however, most of these patients vomited after the sedation was complete and prior to discharge home, while only one patient vomited during the procedure itself. There was no difference in the duration of fasting between the patients who vomited and those who did not.

A similar study was done by Roback et al in 2004[10]. Fasting status was documented on 1,555 adults and children patients receiving parenteral procedural sedation and analgesia. In these patients, there were no documented cases of aspiration and the rate of adverse events was statistically no different between patients who were fully fasted and those who were not. They found an overall higher risk of emesis compared to Agarwal et al (7.5% versus 1.5%); however, there was again no association found between the incidence of emesis and fasting times.

Personnel:

At least one physician should be immediately available who is knowledgeable in the diagnosis and treatment of adverse effects of sedation/ analgesia. Both the AAP and ACEP recognize that sedation is a continuum and it is often difficult to predict an individual's response to a specific sedative agent[1,3]. Although the goal of PSA is for the patient to maintain his/ her own respiratory drive and airway control, personnel trained in pediatric airway management must be present at all times.

1. Physicians should be competent in:
    a. Pediatric airway management and resuscitation
    b. Patient selection & preparation
    c. Patient monitoring
    d. Pharmacology of PSA
    e. Recognition and treatment of the complications of PSA

2. Nurses & ancillary personnel (i.e. respiratory technicians) should be:
    a. Comfortable with basic airway management and resuscitation
    b. Knowledgeable of patient preparation and monitoring procedures
    c. Familiar with proper documentation of PSA technique
    d. Able to prepare a "time-based record" of the treatment procedure

Patient Monitoring:

With the increasing use of sedative and anaesthetic drugs in the emergency and outpatient settings, it has been shown that the ability to recognize hypoxemia and impairment of protective reflexes is limited. Guidelines for the monitoring of patients undergoing sedation/ anaesthesia have been published by the AAP Work Group on Sedation[3]. Detailed documentation of the patient's status before, during and after the procedural sedation is of paramount importance (see Appendix 2: BCCH Sedation/ Analgesia Record).

Weight (kg) should be measured and documented for drug dosing. Prior to the procedure, baseline arousal score, respiratory rate, heart rate, blood pressure and oxygen saturation should be documented. These measurements should be repeated following completion of the procedure.

While multiple monitoring modalities are helpful, direct visualization of the patient during the procedure is essential. **Respiratory rate and depth should be observed continuously. All pediatric patients should be monitored with continuous pulse oximetry.** Cardiac monitoring is recommended but remains at the discretion of the physician.

Emergency resuscitation equipment appropriate for the pediatric patient should be immediately available. This includes oxygen and suction. A useful mnemonic that may be used to remember the necessary equipment is "SOAPME", as follows[3]:

S (suction) – size-appropriate suction catheters and a functioning suction apparatus (e.g., Yankauer-type suction)
O (oxygen) – adequate oxygen supply and functioning flow meters or other devices to allow its delivery
A (airway) – size-appropriate airway equipment: nasopharyngeal and oropharyngeal airways, laryngoscope blades (checked and functioning), endotracheal tubes, stylets, facemask, bag-valve-mask or equivalent device (functioning)
P (pharmacy) – all the resuscitation drugs needed to support life during an emergency, sedatives, and sedative antagonists
M (monitors) – functioning pulse oximeter with size-appropriate oximeter probes and other monitors as appropriate for the procedure (e.g., noninvasive blood pressure, end-tidal carbon dioxide, ECG, stethoscope)
E (extra equipment) – special equipment or drugs for a particular case (e.g., defibrillator)

Capnography

AAP currently recommends that capnography be considered for all pediatric patients undergoing PSA[3]. ACEP has given the following **Level B recommendation** regarding capnography in children and adults: **capnography may be used as an adjunct to pulse oximetry and clinical assessment to detect hypoventilation and apnea ealier than pulse oximetry and/or clinical assessment alone in patients undergoing PSA.**[6]

In recent years, capnography has been increasingly studied in the context of PSA. Capnography has been used for decades in the operating room setting as a useful adjunct to monitor effectiveness of ventilation, but has not been the standard of care for sedation outside of the OR. Capnography is the noninvasive measurement of the partial pressure of carbon dioxide in exhaled breath[11]. The advantage of capnography is the ability to detect hypoventilation prior to the onset of hypoxemia. This has the potential to be quite useful, especially in the younger pediatric patient who may not have the same respiratory reserve as an adult and may deteriorate quite rapidly following apnea or bradypnea/ hypopnea.

A 2008 study by Keidan et al examined the ability of pediatricians to recognize the onset of apnea in a simulated pediatric sedation scenario, with and without the use of supplemental oxygen[12]. Irrespective of the use of oxygen, their findings showed that it took well over one minute for the study subjects to recognize the onset of apnea (173 seconds versus 83 seconds, with and without use of oxygen respectively). A 2009 study by Deitch et al looked specifically at the use of capnography in detection and intervention for hypoventilation[13]. Physicians were either able to access capnography results during propofol sedation, or were blinded to the results of ongoing capnography. The study's findings showed that there was a significant difference in the incidence of hypoxemia between the patients whose physicians could see the capnography tracing compared to the patients whose physicians could not (25% versus 42%). In addition, in the blinded group, all hypoxic events were preceded by hypoventilation on the capnography tracings.

These two studies demonstrate the challenges in detecting hypoventilation clinically, particularly with administration of oxygen or if direct visualization of the patient is compromised (e.g. patient positioning, draping, etc.). There is, however, uncertainty as to whether the use of capnography has a significant clinical benefit in the setting of short procedures in the ED: What is the clinical significance of a transient increase in $ETCO_2$ during procedural sedation and analgesia, especially without hypoxemia? Is a short episode of respiratory depression significant, especially if it does not lead to an adverse event? How do falsely elevated $ETCO_2$ readings affect patient care?[11] These questions remain to be answered.

Distraction Techniques for Procedural Pain in Children

Although the primary focus of this guideline is the pharmacologic basis for procedural sedation/analgesia, the timely use of distraction techniques may help optimize the therapeutic environment and ultimately, the patient's experience in the Emergency Department. Distraction stimuli can be employed right from the patient's presentation to triage, through the initial assessment phase and most importantly, during the induction and emergence phases of pharmacologic intervention.

The ability to access multiple modalities to engage numerous sensory pathways (sight, hearing & touch) may result in a more successful outcome. Breathing control, goal-directed tasks and the use of both visual and auditory distractions have all been shown to be helpful.

Although distraction techniques are known to be effective even with adults, it is of paramount importance that the stimuli used are age-appropriate. In addition, tailoring the techniques used to the specific coping style of each patient is key. Children should be engaged in the selection of distraction stimuli early in the evaluation process in order to minimize anticipatory anxiety.

The use of guided visual imagery may be of particular benefit to children as they are, in general, more accepting of the idea of fantasy and suggestion. The dissociative effects of Ketamine in particular make it an ideal agent for the adjunctive use of guided imagery.

Examples of age-specific distraction techniques:

Young children:
Favourite blanket/toys, bubbles, books, audiotapes, videos/movies.

Older children/teenagers:
Books, movies, virtual reality glasses, handheld video games, guided visual imagery.

Pharmacology:

Many pharmacologic agents exist for procedural sedation; however it is generally recommended that the physician become familiar with only a few different medication options and develop proficiency with the chosen agents. Optimal PSA depends on the physician's ability to titrate the level of sedation to a specific endpoint that will allow expeditious completion of the procedure. Ideally, the selected medication should be delivered intravenously in a controlled, incremental manner. The physician must be alert to the physiologic cues that suggest the desired level of sedation has been attained. The level of sedation required for most relatively short emergency procedures allows maintenance of protective reflexes, a patent airway and adequate respiratory effort throughout. These agents may induce any or all of: hypnosis, anxiolysis, amnesia or analgesia.

See Appendix 1 for a table summarizing the more common drugs used in pediatric procedural sedation and analgesia.

Ketamine:

Ketamine is a dissociative anaesthetic with sedative, analgesic and amnestic properties[4,14]. It is a versatile drug with the ability to produce dose-dependent effects. Ketamine provides anxiolysis and analgesia at lower doses, while providing dissociative sedation, amnesia and analgesia at higher doses. This medication typically allows maintenance of respiratory drive and airway reflexes, and often causes increases in heart rate, blood pressure and cardiac output. The patient's eyes may remain open and nystagmus is frequently observed following sedative doses of ketamine. Prior to sedation, older children should be informed that they will dream during recovery. They should be encouraged to "plan" pleasant dream topics in advance. During both the induction and recovery phases, minimizing stimulation may alleviate the incidence of hallucinations or emergence reactions.

Ketamine was given a **Level A recommendation** in the ACEP policy statement for both safety and efficacy in providing PSA for children in the ED[4]. It is best suited for children 6 months to 15 years old.

Dose:	IV: 1 mg/kg, given over 1 minute; repeat dose (0.5 mg/kg) every 10 minutes as needed
	IM: 4 mg/kg; repeat dose (2 mg/kg) after 10 minutes as needed
Onset:	IV: 1 minute; IM: 3-5 minutes
Duration:	IV dissociation: 15 minutes; IM dissociation: 15-30 minutes
Recovery:	IV: 60 minutes; IM: 90-150 minutes

Adverse effects[15,16]:

- Emesis – 8.4%
- Hypersalivation
- Agitation/ emergence reactions – 7.6%
- Apnea – 0.8%
- Laryngospasm – 0.3%
- Other airway/ respiratory events (e.g. stridor, hypoventilation, desaturation) – 2.8%

Contraindications:

- Psychosis
- Intraocular trauma or glaucoma
- Systemic hypertension
- Thyrotoxicosis

Relative contraindications:

- Increased intracranial pressure
- Concurrent respiratory infection

A 2009 study by Green et al examined a series of over 8,000 children who had received ketamine sedation in the ED[15]. This study showed a very low overall rate of adverse airway events, including stridor, hypoventilation, oxygen desaturation, apnea and laryngospasm. On further analysis, predictors of adverse airway events included age under 2 years or over 13 years, high IV dosing of ketamine (≥2.5 mg/kg initial dose or ≥5 mg/kg total dose), and concurrent use of midazolam. Higher ASA class, IV vs. IM administration, and oropharyngeal procedures did not affect the incidence of adverse airway events. Low IM dosing (≤3 mg/kg) appeared to be the only protective factor.

Traditionally, anticholinergic medications have been administered along with ketamine to counteract observed hypersalivation, with the expectation to reduce the incidence of adverse airway events. Unexpectedly, Green et al's study showed that concurrent use of anticholinergic medications in fact increased the risk of adverse airway events, particularly the use of glycopyrrolate[15,17]. Another study done by Brown et al in 2008 found that, not only were most physicians not using concurrent anticholinergics with pediatric ketamine sedation, but also that the incidence of airway events felt to be secondary to hypersalivation was extremely low[18]. Thus, it would appear that coadministration of anticholinergic medications may be unnecessary during procedural sedation with ketamine; however, the treating physician may use his/ her discretion in cases where there is oropharyngeal manipulation or where the patient has an underlying upper respiratory illness.

Green et al also examined the incidence of emesis and agitation with the use of ketamine in the same cohort of 8,282 patients[16]. Predictors of emesis were high IV dosing (≥2.5 mg/kg initial dose or ≥5 mg/kg total dose), IM dosing vs. IV dosing, and increasing age (peak at 12 years). The use of anticholinergics and benzodiazepines were found to significantly decrease the incidence of emesis in this study. Another 2008 study by Langston et al also found IV ondansetron to be effective in reducing the incidence of emesis in pediatric ketamine sedation, particularly in children over 5 years of age (NNT = 7)[19]. Given the increased risk of adverse airway effects seen with anticholinergics and benzodiazepines, it appears ondansetron may be a reasonable adjunct to reduce the nausea and emesis seen with ketamine, especially in children at higher risk (e.g. older children).

Green et al found that recovery agitation was associated with both low IM and high IV dosing, but was not affected by the use of anticholinergics or benzodiazepines[16]. Although the incidence of recovery agitation increased with age, there was such borderline statistical significance that it questionable whether this was a clinically significant difference. Another study by Wathen et al

in 2000 examined the use of benzodiazepines in pediatric ketamine sedation. Their study of 266 pediatric patients randomized to receive either ketamine or ketamine + midazolam showed no difference in the occurrence of agitation or emergence phenomena.

ACEP has given a **Level A recommendation** that the addition of midazolam as an adjunct to ketamine for PSA in children *does not* decrease the incidence of emergent reactions. They have also given a **Level B recommendation** that the addition of midazolam as an adjunct to ketamine for PSA in children decreases the risk of emesis. However, given the risk of increased airway events with benzodiazepine use, ondansetron may prove to be a more favourable option.

Midazolam/ Fentanyl:

Midazolam is a short-acting benzodiazepine that provides sedation, amnesia and anxiolysis[4,14]. It is distinguishable from other benzodiazepines in that it is water soluble, less irritating when given intravenously, and has a short half-life and recovery time (especially compared to lorazepam). It is also a very versatile medication, in that it can be given many different routes and has effects that range from anxiolysis to moderate sedation. It has no analgesic properties; therefore it is generally administered in conjunction with an opiate for painful procedures. Midazolam can be given orally, rectally or intranasally in anxious children where an IV is not required (e.g., suture repair); however, the oral and rectal routes are limited by unreliable serum concentrations and variable onset of action, while the intranasal route is limited by mucosal irritation. In addition, midazolam has been associated with self-limited paradoxical reactions in 1-15% of children, characterized by crying, combativeness, disorientation, and restlessness.

Fentanyl is an opiate that is 100 times more potent that morphine[4,14]. It is a potent analgesic given on its own, with the ability to provide sedation and anxiolysis when used in combination with a benzodiapezine. It is preferable to morphine or meperidine in the ED setting, as it has a shorter onset of action, a faster recovery time, and tends to cause less nausea and vomiting.

In combination, midazolam and fentanyl provide moderate sedation for painful procedures; however, the risk of respiratory depression and apnea are increased in a dose-dependent manner. It is generally advisable to choose one drug for initial administration and titrate slowly to effect with the second drug.

The midazolam/ fentanyl combination was given a **Level B recommendation** in the ACEP policy statement for both safety and efficacy in providing PSA for children in the ED[4].

Midazolam:

Dose:	IV: 0.1-0.2 mg/kg, titrated in 0.05 mg/kg increments q 2 min (max 0.6 mg/kg) IM: 0.15 mg/kg PO: 0.5 mg/kg IN: 0.3-0.5 mg/kg PR: 0.5 mg/kg		
Onset:	IV: 2-3 minutes IM: 10-20 minutes PO: 15-30 minutes IN: 10-15 minutes PR 10-30 minutes	Duration:	IV: 45-60 minutes IM: 60-120 minutes PO: 60-90 minutes IN: 60 minutes PR 60-90 minutes

Fentanyl:

Dose: IV: 1 mcg/kg, given over 1 minute; repeat dose every 3 minutes as needed
Onset: IV: 3-5 minutes
Duration: IV: 30-60 minutes

Adverse effects:

- Hypoventilation and apnea
- Midazolam – paradoxical reactions, hypotension, mucosal irritation
- Fentanyl - nausea and vomiting, facial pruritis, bradycardia, chest wall rigidity (may be related to rapid administration and high doses >5 mcg/kg)

Reversal agents:

- Opiates – Naloxone 0.01 mg/kg/dose given q 2 minutes as needed (max 2 mg/dose)
- Benzodiazepines – Flumazenil 0.01 mg/kg/dose given q 1 minute as needed (max 1 mg)

Propofol

Propofol is an ultra-short acting sedative hypnotic which, due to its potency, has been used for both painful and painless procedures[4,14]. It has many desirable properties for sedation in the pediatric ED, such as its rapid onset, short recovery time, easy titratability, antiemetic properties, and its reliable potency to induce deep sedation. Because it has no inherent analgesic properties, it is generally given in combination with an opiate analgesic for painful procedures. The major drawbacks of propofol include respiratory depression and hypotension, though the decrease in blood pressure is often clinically insignificant and is tolerated well by healthy children. Propofol may be administered as sequential boluses for short procedures in the ED, or by infusion for longer procedures (e.g. MRI, prolonged laceration repair). Younger pediatric patients may require higher initial doses.

Propofol, in combination with opiates, was given a **Level B recommendation** in the ACEP policy statement for efficacy in *painful* therapeutic or diagnostic procedures[4]. Propofol alone was given a **Level C recommendation** for efficacy in *painless* diagnostic studies in ED patients[4]. With regards to safety, ACEP provided a **Level A recommendation** that propofol can be safely administered to children and adults for PSA.[6]

Dose:	IV: 1-2 mg/kg; repeat 0.5 mg/kg doses as needed *(Note: Children younger than the age of 6 years may require the higher end of this dose range.)* Infusion rate: 100-150 mcg/kg/min
Onset:	IV: Within 1 minute
Duration:	IV: 5-15 minutes

Adverse effects[20,21]:

- Pain at the injection site
- Respiratory depression and apnea (2.8-4.6%)
- Hypotension (31%)

Contraindications:

- Allergy to soybean oil, egg lecithin (yolk), glycerol and EDTA

Given the incidence of airway depression with the use of propofol, there has been some concern by anesthesiology groups regarding the use of propofol for procedural sedation outside the operating room. Cravero et al recently published the largest known series of pediatric propofol sedations in 2009[20]. Of their 49,836 reported sedations, the majority were carried out by pediatric emergency physicians and pediatric intensivists. In their series, the overall complication rate was found to be 5.92%, with the majority of complications being airway obstruction and desaturation. Most of these patients required simple head repositioning, jaw thrust or blow-by

oxygen. Only 103 patients in total required either endotracheal intubation or laryngeal mask airway placement (0.21%). This study would suggest that propofol is a safe medication to use for PSA in the pediatric ED. The limitation of this study, however, is that many instances of brief desaturation or hypopnea were likely not recorded, i.e. because they were known and expected effects of propofol sedation, they were not recorded to be unexpected adverse events. This only further emphasizes the fact that propofol in the ED should be limited to health care providers who are adept at managing pediatric airways.

The other major drawback to the use of propofol is that it is lipophillic; thus, it may cause pain on IV injection. One way of alleviating this pain is to coadminister a dose of IV lidocaine. A meta-analysis done by Picard and Tramer in 2000 examined the most effective way of alleviating the pain with propofol injection[22]. Of the 6,264 adult patients in their study, up to 70% reported pain on injection. The most effective method of analgesia was found to be IV lidocaine (0.5-1 mg/kg) injected in the tourniqued limb 30-120 seconds prior to the administration of propofol; this method was found to reduce injection pain in 60% of patients. This method was found to be more effective than lidocaine mixed in with propofol, pre-administration of opiates or pre-administration of metocloperamide. Neither altering the temperature of the propofol nor site of injection appeared to have any effect on injection pain.

Ketamine/Propofol or **"Ketofol"**

In recent years, the combination of propofol and ketamine (nicknamed "ketofol") has been increasingly used and reported in the literature. Given the analgesic properties of ketamine, this combination is ideal for painful procedures in the ED (e.g. fracture reduction, abscess drainage). The advantage of such a combination over ketamine alone is a shorter recovery time, decreased incidence of nausea and vomiting, and lower incidence of emergence reactions[23,24]. In addition, combining propofol and ketamine appears to result in smaller doses of each medication needed than either alone; with propofol in particular, smaller drug doses may mean fewer adverse respiratory events. Multiple regimens have been described in the literature, with no one method being described as favourable over others.

In 2010, Andolfatto and Willman published a series of 219 pediatric patients who received a 1:1 mixture of 10 mg/mL ketamine and 10 mg/mL propofol in a single syringe[23]. Their study found that the median dose needed for adequate PSA was 0.8 mg/kg of each medication. The overall incidence of adverse effects was low and the median recovery time of 14 minutes was shorter than that observed with ketamine alone. Adequate sedation was achieved in all patients and both families and staff were very satisfied with performance of the drug mixture.

Another 2007 study by Sharieff et al described a slightly different method of "ketofol" administration, where subjects were first given ketamine 0.5 mg/kg followed 1 minute later by propofol 1 mg/kg[24]. Additional doses of ketamine 0.25 mg/kg and/ or propofol 0.5 mg/kg were given as deemed necessary by the ED physician. The sedation was satisfactory in all patients with a low incidence of adverse effects, similar to the Andolfatto study. Only one child required additional doses of ketamine or propofol, again demonstrating the need for smaller doses of ketamine and propofol when given together.

A series of three Turkish studies from 2007 to 2009 compared the combination of propofol and ketamine to the combination of propofol and fentanyl in patients undergoing upper gastrointestinal endoscopy, burn dressings, and interventional radiologic procedures[25-27]. All three studies found that the ketamine/ propofol combination resulted in a higher number of adequate sedations and fewer adverse effects than the fentanyl/ propofol combination. Overall, the more propofol was required in the fentanyl groups to achieve adequate sedation compared to the ketamine groups. The time to recovery and discharge did not appear to differ between patients given ketamine and those who were not.

Two double-blinded randomized controlled trials comparing "ketofol" to a single agent were published in 2011. In the study by David and Shipp[28], which included both children and adults, ketamine 0.5 mg/kg or placebo was administered prior to propofol 1 mg/kg. Additional propofol doses of 0.5 mg/kg were given as necessary. All patients received fentanyl 0.5-1 mcg/kg. There was no difference in the incidence of respiratory depression or adverse events; however the physician and nurse satisfaction scores were higher and the total propofol dose was lower in the ketamine group. In the pediatric study by Shah et al[29], ketamine 1 mg/kg was compared to ketamine 0.5 mg/kg with propofol 0.5 mg/kg. Additional ketamine doses of 0.25 mg/kg were given as necessary in both groups. In the "ketofol" group, total sedation time was shorter (13 vs. 16 mins) and recovery time was faster (10 vs. 12 mins). There was also less vomiting (2 vs. 12%) and the total ketamine dose was lower in the "ketofol" group.

The above studies suggest that the "ketofol" combination is both a safe and effective drug regimen for pediatric PSA in the ED. However, as stated previously, it should only be considered for use by personnel familiar with the complications of propofol and proficient in management of the pediatric airway. **ACEP has provided a Level B recommendation** that propofol and ketamine can be safely administered to children and adults for PSA.[6]

Recovery:

Patients should be monitored closely until return to pre-treatment level of awareness, verbalization and motor activity. Discharge criteria should include the following:

1) Airway patency, ventilation, cardiovascular function, and hydration are satisfactory;
2) The patient's level of consciousness has returned to baseline (as expected for age or developmental level);
3) The patient can sit unassisted (if age appropriate);
4) The patient can take oral fluids without vomiting;
5) The patient, or a responsible person who will be with the patient, can understand the discharge instructions[2].

Particular attention should be paid to children receiving multiple drug combinations, as this may prolong recovery time and increase the risk of adverse effects. As well, any patient requiring antagonists must be monitored carefully until the risk of re-sedation has passed (i.e., a patient receiving flumazenil should be observed for at least 2 hours after flumazenil administration)[2].

Sedation Discharge Instruction handouts are of particular benefit to families who will be asked to continue careful observation of their child following hospital discharge (see Appendix 3: Discharge Information after Sedation Medication). Ensure that children and infants requiring car seats are fully recovered, as they are at greater risk for airway obstruction after sedation when placed in these restraints.

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Appendix 1:
Summary of Drugs used for Pediatric Procedural Sedation and Analgesia (Table)

Appendix 2:
BCCH Sedation/ Analgesia Record

Appendix 3:
Discharge Information after Sedation Medication