



Procedural Sedation for Orthopedic Fracture Reductions in the Pediatric Emergency Department

Çocuk Acil Serviste Ortopedik Redüksiyonlarda Girişimsel Sedasyon

Alkan Bal¹, Halim Hennes²

¹İzmir Tepecik Training and Research Hospital, Clinic of Child Health and Diseases, İzmir, Turkey

²Texas Southwestern University Faculty of Medicine, Department of Pediatric Emergency Medicine, Dallas, Texas, USA

Abstract

To provide an updated literature review on pediatric procedural sedation in the emergency department. Discuss patient evaluation, monitoring, indications, and contraindications of common pharmacologic agents used for procedural sedation during orthopedic fracture reductions in the pediatric emergency department. Literature search from 1995 to 2015 was conducted using MEDLINE (PubMed), CINAHL, Cochrane and EMBASE databases. Terms included; procedural sedation, fracture reduction, orthopedic reduction, fasting, monitoring, capnometry, Bispectral index and pediatric procedural sedation. We identified a total of 1268 publications covering the literature search criteria listed above. Twenty-two studies evaluated procedural sedation for reduction of closed skeletal injuries in the pediatric emergency department (eight retrospective case series, five prospective case series and nine randomized controlled clinical trials). The published literature utilized different pain assessment scales, pharmacologic agents, and satisfaction evaluation methodology. Ketamine alone or in combination with midazolam was the most common sedation agent used in the published literature. The use of procedural sedation for performing painful procedures in the pediatric emergency department is common. Ketamine and nitrous oxide are the most commonly used pharmacologic agents. Both agents have an excellent safety profile when published sedation guidelines are followed. Patient monitoring is the single most critical element for providing safe sedation in the emergency department. There are several adjuncts for providing safe and effective sedation in the emergency department including capnography, Ramsay sedation scale, Bispectral index, and Aldrete score.

Keywords: Sedation, childhood, pediatric emergency department, orthopedic reduction, capnometry, Bispectral index

Öz

Çocuk acil servisinde sık olarak uygulanan ortopedik redüksiyonlar süresince girişimsel sedasyon uygulaması ile ilgili literatürün gözden geçirilmesi ve girişimsel sedasyonda hasta seçimi, monitorizasyon ve sık kullanılan ilaçların tartışılması amaçlandı.

MEDLINE (PubMed), CINAHL, Cochrane ve EMBASE veritabanları kullanılarak 1995 ve 2015 yılları arasındaki yayınlar tarandı. Çocuk acil serviste girişimsel sedasyon uygulaması sırasında hastanın açık durumu, monitorizasyonu, kapnometri ve Bispectral indeks kullanımı ile ilgili ulaşılabilen 1268 makale incelendi. Literatürde çocukluk dönemindeki ortopedik redüksiyon uygulamaları ile ilgili ulaşılabilen yirmi iki makale incelendi (sekiz retrospektif olgu, beş prospektif olgu ve dokuz klinik randomize çalışma). Ketamin ve/veya midazolam kombinasyonu incelenen çalışmalarda en sık kullanılan ilaçlardı. Girişimsel sedasyon çocuk acil servislerinde sıklıkla uygulanmaktadır. Ketamin ve azot oksit girişimsel sedasyonda en yaygın kullanılan ve mevcut sedasyon rehberlerine uyularak kullanıldığında oldukça güvenli iki ilaçtır. Acil servislerde güvenli sedasyonu sağlamanın en kritik öğelerinden biri hasta monitorizasyonudur. Güvenli ve etkin sedasyonun sağlanmasında kapnografi, Ramsay sedasyon skorlaması, Bispectral indeks ve Aldrete skorlamasında içeren birçok etmen vardır. Çocuk acil servislerde sedasyon ile ilgili iyi planlanmış, geniş serili çalışmalara gereksinim vardır.

Anahtar Kelimeler: Sedasyon, çocukluk çağı, çocuk acil servisi, ortopedik redüksiyonlar, kapnometri, Bispectral indeks

Introduction

Procedural sedation and analgesia (PSA) is an essential element of care for children requiring painful procedures in the pediatric emergency department (PED). While several medications are available for PSA, the ideal agent should have rapid onset of action, short recovery time, provide adequate analgesia and sedation, and have no or minimal adverse effects. To date, there is no single agent having all these properties.

Medication selection for PSA is guided by the patient's underlying medical conditions, age, anticipated degree of pain, and required procedure. To ensure patient safety during PSA, pre-sedation evaluation, American Society of Anesthesiologists (ASA) status, type of procedure, length of procedure, and monitoring equipment are important adjunct to ensure patient safety during the procedure and selecting appropriate sedation agent.¹ The safety and efficacy of PSA in the PED are well described in the literature.^{2,3} The objective of this review was to discuss patient evaluation and monitoring, as well as indications and contraindications of common procedural sedation (PS) pharmacologic agents properties, dose, indications, contraindications, and adverse effects during orthopedic fracture reductions in the PED.

Preparing the Patient for Procedural Sedation and Analgesia

The first step in preparing for PSA in the PED is to have dedicated staff appropriately trained in airway management, monitoring equipments, medications, and a sedation plan based on the required procedure. Requirements for safe PS are well documented in the guidelines.⁴⁻⁶ In addition to monitoring equipment, oxygen, bag-mask system, suction catheters, resuscitation medications, laryngoscope with appropriate size blades, endotracheal tubes and the other rescue airway devices should be readily available in the PSA room.^{4,5}

The number of personnel required to provide safe PSA is not clear.⁶ However, the minimal requirement is one physician skilled in airway management to administer medication and one qualified nurse for monitoring.⁴ The physician responsible for sedation should not be responsible for performing the procedure.

Pre-sedation Patient Evaluation

A review of the patient allergies, medical and surgical history, and family history relevant to anesthesia is important to identify contraindication to sedation. Physical examination should include a thorough evaluation of the upper airway, including degree of mouth opening (Mallampati classification),

respiratory, cardiovascular, and neurologic systems. The goal in evaluating the airway is to identify a potentially difficult airway prior to sedation (facial abnormalities, neck masses, neck mobility, obesity, etc.). The Mallampati classification is a simple scoring system to assess mouth opening and visualization of the posterior oropharynx.⁷ Mallampati class 3 and 4 predict a potentially difficult airway.⁸ The ASA classifications categorize the health status of candidates into one of 5 classes. Patients with ASA class 1 and 2 are generally considered appropriate candidates for PSA.⁴

Patient's last oral intake [nil per os (NPO) status] for PS in the emergency department (ED) remains controversial. The American Academy of Pediatrics and ASA guidelines recommendations for elective procedures are: 2 hours for clear liquids, 4 hours after breast-feeding, and 6 hours after solid and non-clear fluids.^{4,5} However, the association between NPO status and vomiting during or following sedation is not well established in the pediatric literature. Several observational studies found no clear association between adverse events and NPO status.⁹⁻¹²

Monitoring

Before initiating the PSA, baseline vital parameters (temperature, heart rate, respiratory rate, blood pressure, and pulse oximetry) should be documented. The minimal monitoring recommendation includes close patient observation by a trained provider, pulse oximetry, heart rate and intermittent assessment of the level of sedation. Monitoring in moderate and deep sedation includes continuous monitoring of oxygen saturation, heart rate, and intermittent recording of respiratory rate and blood pressure. In addition, the Ramsay sedation scale can be used to assess sedation level.¹³ Other non-invasive monitoring options include the use of capnography to detect hypoventilation and Bispectral index (BIS) to measure the depth of sedation (Table 1).

Capnography

There are 2 types of hypoventilation. The first one is bradycardic hypoventilation commonly observed with opioid use and characterized by increased end tidal carbon dioxide (ETCO₂) and increased partial pressure of carbon dioxide (PaCO₂). The second is hypopneic hypoventilation occurs most commonly with sedative hypnotic drugs and is characterized by a normal or decreased ETCO₂ and an increased PaCO₂.

Capnography is believed to detect hypoventilation during sedation before it becomes apparent by clinical examination or pulse oximetry.^{4,5,14} Several investigators reported early detection of hypoventilation in sedated pediatric patients when capnography is compared to conventional monitoring with pulse oximetry and patient observation.¹⁵⁻¹⁹ However, routine capnography use

Table 1. The studies for monitoring procedural sedation with end tidal carbon dioxide and Bispectral index in pediatric emergency departments

Authors, date of publication, type of study	Age of patients (year)	Monitoring type, number of patients (n)	Procedure. (%)	Administered drugs (%)	Outcomes
Hart et al. ¹⁵ , 1997, prospective observational for ETCO ₂ , randomized controlled for drugs	2-11	ETCO ₂ , 42	Laceration repair (52.4) Fracture reduction (28.6) Dental procedures (14.3) Incision, and drainage of an abscess (4.7)	Fentanyl (47.5) Fentanyl-midazolam (31) Meperidine-promazine-chlorpromazine (21.5)	Number of transient respiratory events (SpO ₂ <90%): 8 Number of hypercarbia (ETCO ₂ >50%) without hypoxia: 6 8 respiratory depression events while only two of them were able to detected by pulse oximetry
Tobias ¹⁶ , 1999, prospective observational case series	1-6	ETCO ₂ , 50	Painful, invasive procedures (it is not clear in the study)	Glycopolate-midazolam-ketamine (100)	Number of adverse event (decrease in oxygen saturation greater than 3%, ETCO ₂ >50% or airway obstruction): 3 The practitioner recognized one patient who experienced upper airway obstruction during procedure by the loss of ETCO ₂ waveform
McQuillen and Steele ¹⁷ , 2000, prospective observational case series	1.2-16.6	ETCO ₂ , 106	Fracture reduction (55) Laceration repair (37) Incision, and drainage of an abscess (4) Lumbar puncture (4)	Midazolam (12.4) Midazolam and ketamine (41.5) Midazolam and opiate (43.4) Ketamine (0.9) Midazolam, ketamine and opiate (1.8)	34% of patients receiving a combination of midazolam and morphine or fentanyl had an increase of 10 mmHg or more in end tidal CO ₂ Maximal hypoventilation was found after the procedure completed
Langhan et al. ¹⁸ , 2011, prospective observational case series	1-19	ETCO ₂ , 58	Fracture reduction (54.5) Laceration repair (18.8) Incision and drainage of abscess (16.8) Arthrocentesis (6) Other (2.9)	Ketamine with or without midazolam (100)	50% of children experienced hypopneic hypoventilation during sedation with ketamine with or without midazolam 5 (72%) of seven children with prolonged hypoxia episodes were preceded by decrease in ETCO ₂
Langhan et al. ¹⁹ , 2015, randomized controlled trial	1-20	ETCO ₂ , 154 (intervention group: 77, control group: 77)	Fracture reduction (55.2) Laceration repair (18.8) Incision and drainage of abscess (18.2) Arthrocentesis (3.25) Dislocation (3.25) Other (1.3)	Ketamine with or without midazolam (98) Midazolam (2)	No difference in procedures and medications between intervention and control group. The treating team was blinded to the screen on the capnograph in control group; the capnograph was viewable by all staff in Intervention group. Intervention group with access to capnography provided fewer but more timely interventions for hypoventilation that led to fewer episodes of hypoventilation and of oxygen desaturation. All episodes of hypoventilation were caused by hypopnea that goes with decreased ETCO ₂

Table 1 continued. The studies for monitoring procedural sedation with end tidal carbon dioxide and Bispectral index in pediatric emergency departments

Authors, date of publication, type of study	Age of patients (year)	Monitoring type, number of patients (n)	Procedure, (%)	Administered drugs (%)	Outcomes
Agrawal et al. ²³ , 2004, prospective observational study	0.4-16.7	BIS, 20	Orthopedic reduction (35) Diagnostic imaging (30) Arthrocentesis (20) Laceration repair (5) Chest tube placement (5) Gastrostomy tube replacement (5)	Fentanyl-midazolam (70) Pentobarbital (30)	Good correlation between BIS values and modified Ramsay sedation scale Bispectral index scores between 60 and 90 predicted with moderate accuracy and reliability clinical levels of sedation typically encountered during ED procedural sedation and analgesia in children
Overly et al. ²⁴ , 2005, prospective observational study	2-17	BIS, 47	Fracture/dislocation (34) Laceration repair (12.8) Dental extraction (34) Head CT (14.9) Lumbar puncture (4.3)	Midazolam and ketamine (55) Methohexital, propofol or midazolam and a narcotic (45)	The Observer's Assessment and Alertness/Sedation Scale sedation scale predicts the BIS value for pediatric patients undergoing procedural sedation when sedated with certain medications, excluding ketamine
Gamble et al. ²⁵ , 2012, prospective observational study	3-15	BIS, 42	Orthopedic reduction (93) Diagnostic procedure (2.3) Laceration repair (2.3) Nailbed repair (2.3)	Fentanyl and propofol (100)	Most of the pediatric procedural sedation patients spend at least a period in a general anesthetic state During most procedural sedations, the physicians involved are likely underestimating the maximal depth of sedation for their patients (93% of the sedating physicians' and 88% of the procedural physicians' assessments of maximal sedation underestimated the maximum level of sedation)

ETCO₂: End tidal carbon dioxide, SpO₂: Oxygen Saturation, CO₂: Carbon dioxide, BIS: Bispectral index, ED: Emergency departments

for all patients is not recommended in the current guidelines.^{4,5}

The Bispectral Index

The BIS is based on the principle that electroencephalography (EEG) waveforms change with the level of alertness. The index generates a numerical scale of 0-100 by placing two electrodes on the frontal-parietal areas. The BIS index is used for monitoring patients during general anesthesia to decrease the anesthetic drug dose which lead to a shorter recovery time.²⁰ However, BIS has limited value in children receiving nitrous oxide (N₂O) and infants younger than 6 months of age when sedated with ketamine.^{21,22}

Recent studies found a strong correlation between BIS score and modified Ramsay sedation scale.^{23,24} Investigators also noted poor association between the BIS and depth of sedation in patients sedated with ketamine.^{24,25}

Common Procedural Sedation Agents Used for Fracture Reduction in Randomized Control Trials in Pediatric Emergency Departments

Ketamine: Ketamine is a phencyclidine derivative that acts as a dissociative sedative through binding of the N-methyl-D-aspartate receptor. It provides sedation, analgesia and amnesia while preserving spontaneous breathing and protective airway reflexes. Ketamine has rapid onset of action and short half-life. Therefore, it is the preferred agent for brief painful procedures, such as fracture reduction due to its rapid onset, relatively short duration of action and excellent sedative and analgesic properties.²⁶⁻²⁸

The disadvantages of ketamine include vomiting, increased salivation and airway secretion, and hallucinations during recovery. A rare life-threatening complication associated with intramuscularly (IM) ketamine is

laryngospasm.²⁶⁻³⁰

Ketamine can be administered either IM or intravenously (IV). However, IM ketamine is associated with longer recovery time, respiratory adverse effects (especially laryngospasm) and vomiting.²⁹⁻³¹

The initial ketamine dose is 1-2 mg/kg administered over 30 to 60 seconds.^{27,30,32,33} Chinta et al.³⁴ reported in a prospective small trial for fracture reduction that smaller ketamine doses (0.7-0.8 mg/kg) with a rapid infusion (5 sec) technique achieved effective brief sedation and rapid recovery. Ketamine is the most popular agent for sedation in PED. Most studies combined it with midazolam.³⁵⁻³⁷ Investigators evaluated different combination medications including ketamine/midazolam, fentanyl/midazolam and propofol/midazolam.³⁵⁻³⁸ Ketamine/midazolam was found to be more effective in relieving pain and anxiety compared to fentanyl/midazolam.³⁵ Favorable reduction in respiratory depression was noted with ketamine/midazolam compared to propofol/midazolam.³⁶ The combination of propofol/fentanyl had shorter recovery and total sedation time with more desaturation than ketamine/midazolam.³⁶⁻³⁸ Midazolam premedication was associated with an increased frequency of oxygen desaturation.³⁹

Ketamine is contraindicated in patients younger than three months, and psychosis. History of cardiac disease and increased intracranial or intraocular pressure are relative contraindication.³²

Propofol: Propofol is a nonopioid, nonbarbiturate sedative hypnotic, first reported pediatric use for PSA in the ED was described in 1996.⁴⁰ It is highly lipophilic and extensively distributed in tissues. It acts on neuronal lipid membranes to potentiate γ -aminobutyric acid effect, producing rapid sedation.^{41,42}

The common adverse effects of propofol are respiratory depression, apnea, bradycardia and hypotension.⁴²⁻⁴⁹ It can also cause pain during administration and injection and the recommendation is to use large vein and injecting lidocaine prior administration.⁴²

Because of the high lipophilic properties, unintended greater depth of sedation can occur. Propofol has several advantages over other agents, including rapid onset of action, short recovery time and reducing intracranial pressure. Several studies have examined the safety profile of propofol in the ED.⁴⁵⁻⁴⁸ Because propofol has no analgesic effect, it is often combined with an analgesic agent, opioid, which increases the potential for respiratory depression.⁵⁰

The recommended initial IV bolus dose for propofol is 0.5-1 mg/kg for brief procedures and it can be repeated every 3-5 minutes to maintain sedation to a maximum total

dose 3 mg/kg.^{43,44} In a prospective observational study, Young et al.⁴⁹ showed that 2 mg/kg initial bolus dose for pediatric sedation was well tolerated during a wide range of procedures.⁴⁵

Two randomized controlled trials evaluated the safety and efficacy of propofol for PSA during orthopedic fracture reduction in PEDs. In their study, Godambe et al.³⁶ noted a higher event rate of respiratory depression in the propofol/fentanyl group compared to ketamine/midazolam. Havel et al.⁵¹ found no differences in Ramsay sedation scores or complication rates between propofol/morphine and midazolam/morphine. However, they did not specifically report sedation or pain scores at the time of reduction and the study may not have enough power to detect clinically important adverse events.

Propofol formulation contains egg lecithin and soybean oil. For that reason, some authors suggest being careful when using propofol in children with allergies to these components.⁵²

Ketamine + Propofol (Ketofol): The combination of ketamine and propofol, known collectively as ketofol, has been used for pediatric fracture reduction for the last ten years.⁵³ The combination is believed to decrease the adverse effects from using either medication alone. Ketamine's sympathomimetic effect could theoretically decrease propofol-associated respiratory depression and hypotension. Propofol's sedative and anti-emetic properties could hypothetically counter the ketamine-associated recovery agitation and emesis.^{41,54}

No standard dosing regimen has been established; a 1:1 ratio provides ease of administration and has been documented in several recent articles.

We found one randomized controlled trial that assessed the safety and efficacy of ketofol on PSA for orthopedic reduction at PEDs. Shah et al.⁵⁵ compared ketofol 1:1 and ketamine alone in 137 children for fracture reduction and found slightly faster recovery, fewer episodes of vomiting, and higher satisfaction scores in the ketofol group.⁴¹

Another study reported shorter recovery time and 3 incidences of airway compromise requiring intervention.⁵⁶ In adult randomized controlled clinical trials, ketofol did not provide superior sedation or reduce clinically important adverse effects when compared to propofol alone.^{57,58}

Etomidate: Etomidate is an ultrashort imidazole-derived sedative hypnotic agent with a rapid recovery time. It has rapid onset of action, short recovery time, and few side effects. Since etomidate reduces intracranial pressure and maintains hemodynamic stability, it is a better agent for patients with multisystem trauma, hypotension, and increased intracranial pressure.^{26,27}

Table 2. The randomized controlled studies that compare medications of procedural sedation and analgesia for orthopedic reductions in pediatric emergency departments

Authors, date of publication	Age of patients (year)	Group A (treatment, n)	Group B (treatment, n)	Complications	Outcomes
Evans et al. ⁶⁵ , 1995	4-15	50% nitrous oxide, n=15	IM Meperidine (2 mg/kg, max: 100 mg) and IM Promethazine (1 mg/kg, max: 50 mg), n=15	No severe adverse event	Similar pain scores (CHEOPS) and amnestic effects for each group, shorter recovery time and higher patient satisfaction in N2O group
Kennedy et al. ³⁵ , 1998	5-15	Fentanyl (≤0.5 µg/kg every 3 min. to a max: 2 µg/kg IV) Midazolam (≤0.1 mg/kg every 3 min. to a max: 0.3 mg/kg IV), n=130	Ketamine (≤0.5 mg/kg every 3 min. to a max: 2 mg/kg IV) Midazolam (≤0.1 mg/kg every 3 min. to a max: 0.3 mg/kg IV), n=130	Respiratory complications more frequent with F/M Vomiting more frequent for K/M	K/M more effective for relief of pain, anxiety and reducing procedural distress (OSDB-r) than F/M Recovery time longer with K/M group
Havel et al. ⁵¹ , 1999	2-18	Morphine (0.05-0.1 mg/kg, repeated if required IV) Propofol (1mg/kg and 67-100 µg/kg/min. infusion, 1mg/kg bolus repeated if required IV), n=43	Morphine (0.05-0.1 mg/kg, repeated if required IV) Midazolam (0.1 mg/kg bolus, 0.05-0.1 mg/kg, repeated if required IV), n=46	No significant differences on complications	Similar Ramsay sedation scores (pre and post reduction), Considerably less recovery time with propofol
Godambe et al. ³⁶ , 2003	3-18	Ketamine (1-2 mg/kg IV) Midazolam (0.05 mg/kg IV), n=54	Propofol (1mg/kg IV) Fentanyl (1-2 µg/kg IV), n=59	Respiratory complications more frequent with P/F group (more frequent desaturation and airway obstruction event)	P/F comparable to K/M on reducing procedural distress (OSDB-r) Quicker off-set and smoother recovery time with P/F
Di Liddo et al. ⁶² , 2006	2-18	Morphine (0.05-0.1 mg/kg; max: 5mg/dose IV) or fentanyl (1 µg/kg; max: 50 µg/dose IV) Etomidate (0.2 mg/kg; max: 10 mg IV), n=50	Morphine (0.05-0.1 mg/kg; max: 5mg/dose IV) or fentanyl (1 µg/kg; max: 50 µg/dose IV) Midazolam (0.1 mg/kg; max: 5 mg IV), n=50	Similar desaturation events between groups More often injection pain with etomidate myoclonus with etomidate	Etomidate adequately and significantly sedated of more patients with a mean Ramsay sedation score than midazolam Shorter induction and recovery times with etomidate Etomidate more efficacious than midazolam
Luhmann et al. ⁶⁶ , 2006	5-17	Ketamine (1 mg/kg IV) Midazolam (0.1 mg/kg; max: 2.5 mg IV), n=55	50% nitrous oxide Hematoma block (2.5 mg/kg of 1% buffered lidocaine), n=47	Increase incidence of desaturation events with K/M	Minimal change of pain scores (PBCL) for each group. Less pain score, both parents and patients reported less pain (VAS), shorter recovery time with N2O and hematoma block
Lee-Jayaram et al. ³⁷ , 2010	5-17	Ketamine (1 mg/kg IV) Midazolam (0.05 mg/kg; max: 2 mg IV), n=11	Fentanyl (1 µg/kg IV) Etomidate (0.2 mg/kg IV), n=12	More desaturation event with E/F	Significantly lesser observed procedural distress (OSDB-r), both parents and patients reported significantly less pain (VAS), both parents and orthopedic practitioner satisfaction (LSSS) significantly much with K/M

Table 2 continued. The randomized controlled studies that compare medications of procedural sedation and analgesia for orthopedic reductions in pediatric emergency departments

Authors, date of publication	Age of patients (year)	Group A (treatment, n)	Group B (treatment, n)	Complications	Outcomes
Shah et al. ⁵⁵ , 2011	2-17	Ketofol (Ketamine 0.5mg/kg and propofol 0.5 mg/kg IV) followed by propofol (0.5 mg/kg IV every 2 min.), n=67	Ketamine (1 mg/kg IV) followed by Ketamine (0.25 mg/kg IV every 2 min.), n=69	Similar respiratory complications (desaturation, airway obstruction) Less vomiting in K/P group	Ketofol produced slightly faster recoveries, higher satisfaction scores than Ketamine alone. Similar efficacy in each group
Dişel et al. ⁶¹ , 2015	7-18	Fentanyl (1 µg/kg IV) Etomidate (0.2 mg/kg IV) same dose repeated if required, n=24	Ketamine (1 mg/kg IV) same dose repeated if required, n=20	No significant differences on complications	The similar Ramsay sedation scores between two groups. Relatively shorter induction and longer action times with ketamine

IMI: Intramuscularly, IV: Intravenously, min: Minimum, max: Maximum, CHEOPS: Children's hospital of eastern ontario pain score, OSDB-r: Observational score of behavioral distress revised, PBCL: Procedure behavior checklist, VAS: Visual analog score, LSSS: Likert satisfaction scale score

The common adverse events with etomidate are respiratory depression, vomiting and nonepileptiform myoclonus. The recommended IV bolus dose is 0.1 to 0.3 mg/kg. Additional dose of 0.05 mg/kg may be given every 5 minutes up to a maximum 0.6 mg/kg total dose.^{26,27,59}

Recent literature suggested that etomidate is a safe and effective agent for PSA.^{37,60,61} Liddo et al. reported that etomidate was more effective for fracture reductions with shorter induction and recovery times compared to midazolam and, similar incidence of adverse events in both groups.⁶²

Etomidate inhibits 11-beta hydroxylase enzyme that has an important role at adrenal steroid production pathway. It is contraindicated in adrenal insufficiency and severe sepsis.^{26,27}

Nitrous Oxide: N₂O is a colorless anesthetic gas that provides sedation, amnesia and anxiolysis. The typically concentrations of N₂O used for PSA are 50% to 70%. The most common adverse effects of N₂O are nausea, vomiting and dysphoria.^{63,64}

Two randomize controlled trials evaluated the effectiveness of N₂O in comparison to other PSA drugs in orthopedic reductions. Evans et al.⁶⁵ compared 50% N₂O to intramuscular meperidine and promethazine in 30 children for orthopedic fracture reduction (FR) in PED. There was no significant difference between pain scores in the two groups. However, patients in the N₂O had a significantly shorter recovery time. Luhmann et al.⁶⁶ compared ketamine/midazolam with 50% N₂O and a hematoma block (2.3 mg/kg of 1% buffered lidocaine) for PSA during fracture reduction of 102 children. In this study, patients who received N₂O had a shorter recovery time and significantly less episodes desaturation events compared to the ketamine/midazolam group. Both parents and patients reported less pain during procedure with N₂O.^{66,67} A clinical survey on 111 pediatric emergency physicians revealed that N₂O and ketamine were most commonly used in PS for FR.⁶⁸

The effect of N₂O on ventilation is dose-dependent. Mechanical failure of the delivery system resulting in the delivery of 100% N₂O is rarely associated with death.⁶³ Equipment must be periodically tested to ensure adequate safety. N₂O is contraindicated in pneumothorax, pneumoensefalon, and bowel perforation due to its diffusion effect. Use of N₂O pregnancy that increases the risk of spontaneous abortion.^{26,27,63,64}

In Table 2, we presented a summary of the available literature on randomize controlled trial for FR in PEDs.

Summary: Sedation and analgesia in the PED is safe and effective for common painful procedures such as closed fracture reduction. Published guidelines provide

an excellent framework for providing safe and effective minimal to moderate sedation. When the PED physician is planning for sedation, patient safety is a top priority to avoid undesirable complications. Patient assessment, monitoring, choice of appropriate medication, and physician competence in managing potential airway compromise are essential. In choosing sedation medication, the physician should consider patient's risk factors, type of procedure, required duration to complete procedure, and medication side effects.

Ethics

Peer-review: External and Internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Alkan Bal, Hallim Hennes, Concept: Alkan Bal, Hallim Hennes, Design: Alkan Bal, Hallim Hennes, Data Collection or Processing: Alkan Bal, Hallim Hennes, Analysis or Interpretation: Alkan Bal, Literature Search: Alkan Bal, Hallim Hennes, Writing: Alkan Bal, Hallim Hennes.

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