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Procedural Sedation and Analgesia in Emergency Department

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1. Introduction

Emergency department (ED) is one place in the hospital where variety of patients encounter happen on a routine basis, of varied nature and severity, many of which are associated with varying degree of pain and anxiety. Hence, sedation and analgesia is an important component of acute care provided in the ED. Use of appropriate analgesia and sedation is about striking balance between patient comfort and needs and avoidance of hindering clinical findings to deliver a safe, appropriate and effective care but in comfortable and humane in nature.

2. Definitions

Conscious sedation, being used loosely in the ED for all form of sedations, was first described in 1985 as "light level of sedation where patient retains the ability to independently maintain an airway and respond appropriately to verbal commands" (1). In reality, the level of sedation used in ED is deeper than what was described as conscious sedation. In 2001, Joint Commission on Accreditation of Healthcare Organizations replaced term conscious sedation with moderate sedation/analgesia; a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation and maintain adequate spontaneous ventilation and cardiovascular function. Reflex withdrawal from a painful stimulus is not considered a purposeful response. (2) Definitions of recently launched terminology "procedural sedation" vary widely.

Procedural sedation and analgesia (PSA) is a more accurate and appropriate description. The term procedural sedation has emerged from the American College of Emergency Physician (ACEP) (3).

The concept behind PSA is to produce a state of sedation and analgesia with a minimal depression of consciousness where patient can tolerate unpleasant procedures but can maintain spontaneous respiration and airway-protective reflexes. Airway assistance ideally should not be required and the patient should be capable of responding to physical and verbal stimulus. PSA is also helpful for managing uncooperative patients in almost all the allied disciplines of healthcare including dentistry.

3. Who can perform PSA

The person performing the procedure should have sound understanding of medications used and able to monitor response and intervene to manage all potential complications. Expertise in airway management is mandatory, and the provider must be able to identify signs of airway complications both early and late in the course of procedure. Provider should be capable of maintaining airway during spontaneous ventilation and intermittent positive pressure ventilation with a mask and self-inflating resuscitation bag.

PSA is a core competency in emergency medicine residency training and existing evidence supports the PSA administration by ED physician is as safe as by anesthesiologist. Hence, graduates of emergency medicine residency are qualified to for PSA in all age group. For other ED practitioner such as physician assistants, nurse practitioners and physician's from other specialties such as family medicine working in ED; the chief of ED grants privileges for use of PSA.(3, 4)

4. Patient selection

Various patients requiring PSA in ED would be better served if the objectives of PSA are clear. Main objectives include patient safety, minimizing pain, anxiety and physical discomfort, negative psychological impact to treatment by providing analgesia and anxiolysis along with maximal potential for amnesia, patient movements during the procedure and maximizing the chances of success of procedure and returning the patient to pre-sedated state where safe discharge is possible.

Physical Status Classification

I: A normal healthy patient
II: A patient with mild systemic disease
III: A patient with severe systemic disease
IV: A patient with severe systemic disease that is a constant threat to life
V: A moribund patient who is not expected to survive without the operation
VI: A declared brain-dead patient whose organs are being removed for donor purposes

Patients undergoing PSA should be assessed for physical status. It could be done using Physical Status Classification issued by American Society of Anesthesiologists. Procedural sedation is appropriate for patients in Classes I, II and III. Procedures for class IV and higher are done in operating room.

There are no absolute contraindications, but things to consider are patients' co-morbid illness or injuries, problems with prior PSA, the ability of provider and facilities to manage the patient's airway. Patients with significant co-morbidity, minimal cardiopulmonary reserve and anticipated difficult airway should be cautiously approached. Another relative contraindication is ingestion of large food or fluid volumes shortly before procedure, less than 2 hours, for risk of aspiration. Role of fasting in emergency PSA is not very clear and risk of aspiration should be weighted over risk from delay in procedure.(5)

5. Preparation

Preparation for PSA includes pre-sedation patient assessment, arranging equipments and choosing right pharmacological agent. Equipments necessary consists equipments to perform the procedure, monitoring and to manage potential complications. Performing time-out prior to the procedure is vital in performing right procedure in right patient. The most common reported complication of moderate sedation is respiratory depression. In PSA, multiple studies have concluded that respiratory depression can be detected early measuring end-tidal CO_2 when compared to oxygen saturation. A change of 10% in end-tidal CO_2 and loss of wave pattern in capnography are indicators of respiratory depression. Use of supplemental oxygen has not been promoted much. American society of Anesthesiologists recommends using supplemental oxygen in deep sedation but does not have similar recommendation for moderate sedation. In many EDs, PSA is performed with 3 litres of supplemental but other ED physician raise concern on use of supplemental oxygen concealing respiratory depression. Current evidence on routine use of supplemental oxygen to avoid hypoxia from respiratory depression is controversial. Low dose oxygen supplemental oxygen doesn't decrease the risk of hypoxia but high dose does. Fortunately, hypoxemia induced by respiratory depression is either self-limiting or reversible with oxygen supplementation. Hence, routine use is not recommended.

Equipments for PSA

1. Intravenous access, peripheral is adequate
2. Monitoring equipments; cardiac monitor, pulse oximetry, blood pressure cuff, capnography
3. Pharmacological agent
4. Reversal agents
5. Equipments for procedure
6. Airway equipments; oxygen supply, face mask/nasal cannula, bag-valve-mask, suction
7. Rescue airway equipments; endotracheal tube, direct laryngoscope, laryngeal mask airway
8. Normal saline

6. Pharmacological agents

A perfect agent for PSA should have rapid onset of action, short duration, rapid, smooth and complete recovery, devoid of adverse effects and able to produce adequate sedation, analgesia and amnesia. Till date, there is no perfect agent available which has all the above-mentioned properties.

7. Deep sedative agents

7.1 Propofol

Propofol is an ultrashort-acting sedative-hypnotic agent that produces dose-dependent, progressive suppression of awareness. Clinical sedation usually begins within 30 seconds from the time of injection and resolves within 6 minutes. Serum concentration drops from rapid distribution and metabolic clearance. It was first used in 1996 for PSA in ED and gained popularity after year 2000 because of its short duration of action, early and complete recovery and cost-effectiveness. Currently, it is most popular deep sedative being used in ED with over 90% satisfaction in both patients and physicians. (6) Based on current evidences, propofol is safe and efficacious in ED procedures requiring deeper level of sedation such as fracture and dislocation reduction, cardioversion, incision and drainage of abscess. It is not an optimal agent to induce minimal to moderate level of sedation. Another disadvantage is not having analgesic properties. Synergistic use of opiate analgesics is associated with higher respiratory depression and achieving near-complete analgesia using opiates prior to propofol infusion is advisable.

Cautions: There are no absolute contraindications apart from allergy to propofol, egg or soy products. Propofol is known for dose dependent hypotension that is reversible with level of sedation. Hypotension is more pronounced in volume-depleted patients and should be replete prior to procedure. Advance age is found to have higher incidence of hypotension and respiratory depression. (7) This effect is most likely related with high serum peak concentration but exact pathophysiology is not yet clear.

Monitoring: Overall, propofol is safe property but due to highly potent sedative agent and little alteration in serum concentration can make swings in level of consciousness and also produce cumulative sedation. Hence, sound understanding of pharmacological properties of propofol, abilities to monitor, intervene and resuscitate if needed for complications from deeper sedation are must for ED physician performing PSA. A dedicated nurse should be available during the procedure. At this point it is not very clear if another ED physician is needed to perform PSA in addition to physician performing procedure.

Recovery: Patients should be monitored until they return to their baseline mental status. Once they reach to baseline mental status, it is unlikely to have suppression of consciousness from redistribution but caution is advised in cases with use of protocol for longer duration with multiple doses. Emesis during recovery is infrequent, in less than 3% and no adverse events is reported post-discharge.

7.2 Etomidate

Etomidate is an ultra-short acting non-barbiturate imidazole derivative, which is well known inducing agent for rapid sequence intubation in the ED. It produces deep sedation

similar to propofol. Onset of action is usually within one minute when administered intravenously and patient recovers from sedation with-in 6 to 16 minutes. It has minimal, if any, analgesic property but gained popularity for minimal effect on hemodynamic stability. The liver metabolizes etomidate rapidly, and the duration of effect may be longer in patients with liver failure. Indication profile for etomidate is similar to propofol but gets priority when hemodynamic stability is matter of concern. Additionally, etomidate provides excellent amnesia of the procedure; over 70% of patients have no recall of procedure.

Etomidate Administration

0.1mg/kg body weight IV as initial dose followed by half dose every 3-5 minutes titrating for clinical sedation.

Cautions: The only contraindication to etomidate is hypersensitivity to the medication, but caution should be taken during pregnancy (etomidate is a pregnancy category C drug), and the general precautions regarding procedural sedation and patient selection also should be considered. Side effects are usually rare, and there is no histamine release and hence minimal hemodynamic usability. Myoclonus is commonly reported side effect, up to 20% of cases, but not evident in rapid sequence intubation secondary to concomitant use of paralytic agent. In most cases, it is transient and does not cause respiratory distress and does not need intervention. The ED physician using etomidate should be competent in managing severe myoclonus which happens very rarely and in that scenario, opening airway is difficult. Use of benzodiazepines can decrease the probability of myoclonus. Another commonly reported side effect is emesis, up to 4% of cases, which is self-limiting. Adrenocortical suppression has been reported after the use of a single bolus of etomidate, but one time use of etomidate in otherwise healthy patient is believed to be inconsequential.

Monitoring: Monitoring in use of etomidate is similar to any deep sedative, using pulse oximetry, capnography and hemodynamic monitoring. Respiratory depression and hypoxia are possible as part of deep sedation for which supplemental oxygen is enough but rarely might require bag-and-mask ventilation.

Recovery and discharge: Recovery with use of etomidate is rapid and complete and once patient is back to baseline level of awareness, could be discharged and no adverse effect reported post discharge.

Overall, both deep sedative agents provide similar level of sedation, respiratory suppression but propofol is devoid of myoclonus and emesis and have better success rate of procedure.

8. Dissociative anesthetic agent

8.1 Ketamine

Ketamine is a dissociative agent that dissociates central nervous system from outside stimuli and produces a state of analgesia, amnesia and sedation but maintains spontaneous

respiration, protective airway reflexes and hemodynamic stability. Dissociation is produced at a dosing threshold below which patient has analgesia and disorientation and higher dose does not deepen the level of sedation. It is commonly used in short painful and emotionally disturbing procedures such as laceration repair, incision and drainage, reduction of orthopedic fractures and dislocation in children and in mentally disabled patients who are often uncooperative. It is not very popular for procedures where motionless sedation is required as occasional random movements are common in dissociative sedation.

Ketamine Administration

IV route: 1.5mg/kg in children and 1mg/kg in adults as initial dose and repeat half doses for prolonged sedation
IM route: used if no IV access, 4 to 5mg/kg as initial dose to induce sedation and repeated as half dose

Cautions: Ketamine is absolutely contraindicated in infants younger than 3-month for laryngospasm and apnea and in schizophrenia as it exacerbates the condition. To prevent the risk of laryngospasm – avoid vigorous stimulation of posterior pharyngeal wall, use in anatomical defect of airway such as stenosis or recent surgery etc, upper respiratory tract infection and in asthma. Ketamine decreases re-uptake of catecholamines, which leads to increased sympathomimetic activity. For this reason ketamine should be avoided in children and adult with known or possible coronary artery disease, congestive heart failure and hypertension. Sympathomimetic action is exacerbated in patients with porphyria and thyroid disease, hence should be used with caution. Ketamine increases intracranial and intraocular pressure and should be avoided in hydrocephalus, intracranial masses/abnormalities, acute globe injury and glaucoma but no more contraindicated in head injury as cerebral vasodilatation caused by ketamine is potentially beneficial.

Monitoring: Pulse oximetry, cardiac monitoring and capnography are recommended. Capnography is increasingly recommended for early detection of respiratory compromise. Co-administration of anti-cholinergic agents to decrease oral secretions, benzodiazepines to decrease recovery reaction, antiemetic agents for emesis that is common with intramuscular administration of ketamine is being practiced. Based on current evidences, prophylactic use of these agents is no superior than as needed basis use. Respiratory depression is uncommon with ketamine but can happen with IV dosing, 1-2 minutes after dose.

Recovery and discharge: Ketamine is known for hallucinations, agitation and emesis during recovery. Recovery reactions are more common in late adolescents and can be rapidly taken care of with use of short acting benzodiazepines. Emesis could occur hours after the procedure. Ataxia has been reported post-discharge and close observation by family member is recommended. At this point, there are no standard guidelines for discharge. Once patient returns to pre-treatment level of awareness, vocalization and activity is achieved, could be discharged.

8.2 Benzodiazepines and opioids

Benzodiazepines act by binding to benzodiazepine-specific receptors on the gamma-aminobutyric acid (GABA)-benzodiazepine receptor complex and potentiate GABA inhibitory action in the CNS and produce sedation, amnesia, anxiolysis, anticonvulsant effects and respiratory depression.

Midazolam is the most commonly used benzodiazepines for PSA, as it has early onset of action producing more complete amnesia, less pain on injection and improved awakening when compared with diazepam. Midazolam possesses a relatively high volume of distribution (Vd) compared with other benzodiazepines because of its lipophilicity. The Vd is greatly amplified in obese patients, resulting in an increased half-life from 2.7 hours to 8.4 hours. On usual dose, sedation is induced within 1-2 minutes and lasts up-to 30 minutes. Midazolam is frequently combined with a short acting opioid; this combination is titrated easily and widely available.

Midazolam Administration
0.02 mg/kg body weight IV in adults and 0.1 mg/kg IV in children less than 5 years of age as initial dose followed by 1mg IV every 3 minutes during prolonged sedation

Fentanyl is a favored opioid as it has prompt onset and short duration of action, and it also has minimal cardiovascular depressive effects and hypotension unlike morphine. Fentanyl binds with stereospecific receptors at many sites within the CNS and increases pain threshold, alters pain reception, and inhibits ascending pain pathways. In addition to analgesia, opioid agonists suppress the cough reflex and cause respiratory depression, drowsiness, and sedation. Onset of analgesia begins within 1-2 minutes and lasts up-to 30 to 60 minutes.

Fentanyl Administration
1 to 1.5mcg/kg body weight IV in adults as initial dose followed by 1mcg/kg every three minutes for prolonged analgesia

8.3 Barbiturates

This group of drug is one of the oldest classes of drug and their role is mostly restricted to operating room and occasionally ICU, occasionally they may be used for providing sedation outside operating rooms setting. They have been traditionally classified on the basis of their duration of action. Methohexital, thiopental and thiamylal are short acting; pentobarbital is intermediate and phenobarbital fall under long acting group. Their have been few studies on their role in providing sedation to pediatric population in radiological suite during early and late 90s, however due to availability of better and safe alternative they are not the

preferred drugs to provide sedation among anesthesiologists and emergency care physician anymore.

8.4 Remifentanyl

Remifentanyl is a recent addition in the list of pharmacological agents that has gained popularity amongst anesthetist and emergency physician, it's a short acting μ-receptor opioid agonist and achieves peak analgesic effect in less than a minute and has an elimination half life of about ten minutes. Due to this short action of the drug, sustained analgesia may require an additional dose or an intravenous infusion. Different dose regimens are in use but the most often used ones were an intravenous bolus dose of 1 μg/kg over 1 minute. Alternatively it can also be titrated to individual needs with an infusion rates ranging from 0.025 - 0.1 μg/kg/min for conscious sedation (8). Recent studies have proved safety and efficacy of remifentanyl for PSA when used along with propofol (9 - 11).

Caution: Combination of propofol and remifentanyl has good safety profile as compared to the combination of remifentanyl and midazolam and is being increasingly used due to its safety profile as compared to other agents.

Monitoring: Standard monitoring of PSA is recommended, using pulse oximetry, capnography, and cardiac monitoring

8.5 Dexmedetomidine

Dexmedetomidine is a selective α-2 adrenoceptor agonist was approved by FDA in the year 1999 for sedation in intensive care (13). It causes hyperpolarization of noradrenergic neurons, thereby suppressing the neuronal firing in locus ceruleus along with inhibition of norepinephrine release and activity in descending medullospinal nor-adrenergic pathways. This drug has recently being in focus due to its sedative, analgesic, perioperative sympatholytic properties. Along with all these properties, it is also hemodynamically stable with minimal effect on respiratory drive making it an ideal sedative agent and useful in various clinical scenarios. This drug has now become a safe alternative to benzodiazepine/opioid combination for monitored anesthesia care (14). The recommended dose range for dexmedetomidine is 0.2 – 0.7 μg / kg/hr. Although it preserves respiratory drive at higher doses it may lead to hypotension and bradycardia.

8.6 Reversal of sedation

Reversal of sedation is rarely required if pharmacological agents are carefully chosen based on nature of procedure. The commonly used agents are:

Naloxone: It is administered to antagonize opioid induced respiratory depression and sedation. Naloxone is non-selective opiod antagonist and can precipitate sudden severe pain. It has a very fast onset of action with peak effect in 1-2 minutes and effect of total dose of 0.4 to 0.8 mg lasting for 1 to 4 hours. Incremental dose of 20 to 40 μg may be given every few minutes till the ventilation of the patient improves. Infusion rate between 3-10 μg/hr may be started if prolonged ventilatory depression is anticipated.

Flumazenil: It is a pure benzodiazepine antagonist which promptly reverses the hypnotic effect of benzodiazepine. This drug has chemical structure which is similar to benzodiazepine, except that it has carbonyl group in place of phenyl. It's onset of action is less than one minute, and undergoes rapid hepatic metabolism with a half life of 1 hour. When it's used to antagonize the action of benzodiazepine with long duration of action, there are chances of recurrence of the symptoms. The usual total dose is 0.6 to 1.0 mg given as a gradual titrated dose of 0.2 mg / minute until the desired level of reversal is achieved. It is given as IV infusion if over dosage with a long-acting benzodiazepine is suspected. This review will not be complete without adding a note of caution that use of flumazenil may precipitate seizure activity that are being chronically treated with benzodiazepine or in those group of patients who are being treated with drugs that reduces seizure threshold like tricyclic antidepressants.

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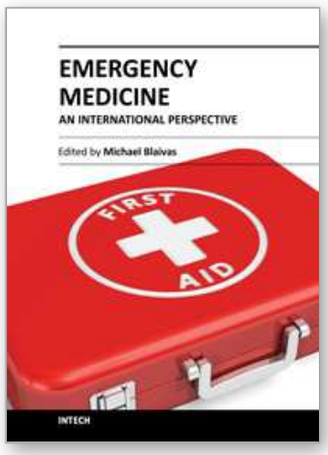
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Emergency Medicine is an expanding field that has spread beyond the shores of North America and has taken on different characteristics around the world. Although many of the struggles of emergency practitioners are similar, the field and its principles have adapted to local needs and resources. This book seeks to educate readers not only on emergency medicine theory, science and practice, but also reflects that multinational nature of emergency medicine, allowing readers to learn from experiences of others. This diverse group of authors presents a true international view of emergency medicine practice and science that will be educational for any reader.

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