SEDATION IN PEDIATRIC PRACTICE

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Sedation is **a** frequently overlooked but an important aspect of care of pediatric patients. It serves an important role in reducing distress or anxiety in sick children and is also **a** prerequisite to facilitate diagnostic and therapeutic procedures. The degree of anxiety and co-operation for these depend on the child's apprehension of pain, from his understanding of, and previous experiences with the procedure and the child's cognitive maturational status. The goal of sedation and analgesia is to minimize suffering and achieve a calm and co-operative subject with patient safety limiting overuse of drugs for comfort.

Despite the use of psychologic measures like hypnosis, desensitization and positive reinforcement, most children also require pharmacologic therapy for effective sedation. Children who need to be separated from parents during a procedure, those between 18 months to 5 years of age who have inadequate communicative and comprehensive skills, mentally retarded children and those with previous unpleasant experience related to diagnostic or therapeutic procedures are more likely to need sedation(l).

It is difficult to imagine a group of pediatric patients more in the need of sedative agents than those in Intensive Care Unit (ICU). In this high stress environment, sedation is required to facilitate tolerance of endotracheal tube, tracheal suction and alleviate the discomfort of noisy environs of ICU's. Furthermore, sleep deprivation may delay the process of weaning from ventilatory support. Agitation and undesirable motor activity and the associated psychological stress can result in accidental extubation or displacement of vital catheters and monitors. An optimally sedated child breathes comfortably and this remarkably decreases the work of breathing and oxygen consumption. Sedation techniques may perform additional therapeutic function by suppressing epileptiform activity and reducing cerebral demand for oxygen(2). To summarize, the goals of sedation in pediatric patients are: (i) to guard patients' welfare and safety, (ii) to minimize physical discomfort or pain, (iii) to control behavior and (iv) to return the patient to a state in which safe discharge is possible.

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Choice of Agent and Technique

Despite the diversity of patients requiring sedation, ranging from elective surgical patients to those with multisystem failure, the choice of sedative drugs is limited. An ideal sedative should be easy to administer, have a rapid short lasting action and achieve effective sedation and analgesia with minimal side effects. Although no single agent fulfills these criteria, judicious use of single drug or drug combinations can achieve these goals with varying degrees of success.

Various sedatives commonly used in pediatric practice along with their pharmacokinetic profile are given in *Table I.*

1. *Chloral hydrate and Derivatives (Trichlofos):* These are the most commonly used agents for routine pediatric sedation(3,4). Sedative doses produce somnolence but no analgesia. However, overdosage may lead to coma, cardiorespiratory depression, pin-point pupils and arrhythmias. Trichlofos has a relatively pleasant taste as compared to chloral hydrate and produces minimal gastric irritation. They produce sedation and a motionless patient within 30-60 minutes after oral administration. Rectal route may be used in patients who do not tolerate the drug orally.

2. *Antihistamines:* Promethazine (Phenergan) and trimeprazine (Vellargan), both phenothiazine derivatives are the antihistamines most often used for pediatric sedation. Promethazine is a commonly misused antihistamine and antiemetic with sedation as a potent side effect, often also used by parents to calm a fussy infant. Though a relatively safe drug, agitation, hallucination, seizures, dystonic reactions, apnea and possibly sudden infant death syndrome (SIDS) have been reported with its use especially in children less than 2 years of age(5). CNS stimulation has been seen even with therapeutic doses in some children. Considering its incrimination in SIDS, its use should be restricted to children greater than 2 years of age on the prescription of a medical practitioner(5). Trimeprazine has pharmacological actions intermediate between promethazine and chlorpromazine with a greater sedative effect than promethazine. It has chiefly been used as a premedication in the preoperative period but can produce postoperative restlessness in the presence of pain. It may cause a moderate reduction in blood pressure, and flushed appearance with circumoral pallor(6).

3. *Barbiturates:* These are sedative hypnotics with no analgesic effect. In sedative doses they do not affect respiratory drive, hemodynamic status and airway reflexes though myocardial depression and hypotension may occur if the patient is hypovolemic or has compromised cardiac status prior to administration. In the presence of pain they may increase the sensitivity to painful stimuli leading to agitation and hyperkinetic behavior(7). Overdosage may lead to coma, miosis, respiratory depression, laryngospasm, hypotension, hypothermia and dysrrhythmias. Extravasation into the subcutaneous tissue is painful and may lead to tissue necrosis due to the alkalotic pH of the solution. As they lower cerebral blood flow, they may be preferred for intubation of patients with raised intracranial pressure. Barbiturates are contraindicated in patients with porphyrias.

4. *Benzodiazepines:* These produce sedation with amnesia and skeletal muscle relaxation. Diazepam, lorazepam and midazolam are the commonly used drugs in this group. Dosages of diazepam required for sedation and immobility may have profound cardiorespiratory effects (hypotension,

TABLE I—*Sedatives Commonly Used in Pediatric Practice*

Agent (Trade name)	Usual dose (Formulation)	Duration (Effect)	Cautions and comments
Opiates			
- Morphine	0.1-0.2 mg/kg IV (15 mg/ml)	7 h (pain) 1-3 h (sedation)	* Raised intracranial pressure secondary to CO_2 retention in event of respiratory depression is a serious drawback * Painful recall of intercurrent events * Use of opiates may delay the onset of enteral feeds
- Meperidine (Demerol)	1-2 mg/kg IV (50 mg/ml)	2-4 h (pain) 1-3 h (sedation)	
- Fentanyl (Sublimaze)	2-3 mg/kg IV 0.05 mg/ml)	0.5-1 h (pain) < 1 h (sedation)	
Benzodiazepines			
- Diazepam (Valium)	0.25-0.5 mg/kg IV (5 mg/ml)	60 min (sedation)	* Modest risk of physical dependence and toxicity
Midazolam (Versed)	0.05-0.2 mg/kg IV (1 mg & 5 mg vials)	6 h (sedation)	* Diazepam and lorazepam produces cardiac depression
- Lorazepam (Ativan)	0.05 mg/kg (2 mg/ml)	8-10 h (sedation)	* Variable response of midazolam in small children (At dosage >0.25 mg/kg, anxiety and distress may be increased)
Chloral hydrate			
- Tricloryl	50-75 mg/kg PO (500 mg/5 ml)	1-2 h (sedation)	* Tolerance to sleep induction occurs rapidly May reduce airway secreton
Antihistamines			
- Promethazine (Phenergan)	0.5-1 mg/kg PO (5 mg/5 ml)	Variable	* Contraindicated in hemodynamically unstable patients because of α-receptor blocking action
- Trimeprazine (Vellergan)	2-4 mg/kg PO (30 mg/5 ml)	Variable	* Dystonias, hallucinations and convulsions encountered in children after large doses * May produce drowsiness

TABLE I (*Contd.*)

Agent (Trade name)	Usual dose (formulation)	Duration (Effect)	Cautions and comments
Barbiturates			
- Pentobarbital (Nembutal)	2-6 mg/kg IV	2-4 h (sedation)	* Respiratory depression is a serious problem * May produce increased anxiety and distress in patients in pain
- Thiopental (Pentothal)	2-3 mg/kg IV (250 mg/vial)	<30 min (sedation)	* Hypotension with barbiturates is related to very high dose or rapid administration
Ketamine			
(Ketalar)	0.5-2 mg/kg IV (10 mg, 50 mg/ml)	1-10 min (dissociative anesthesia)	* Benzodiazepines should be given concurrently to avoid bizzare and disturbing memories

apnea and respiratory depression) in young infants(3). Midazolam a water soluble agent is a useful, rapidly acting sedative when administered intramuscularly or intranasally in patients undergoing invasive radiologic procedures(8,9).

Benzodiazepines are devoid of any analgesic effect hence intramuscular administration of diazepam is painful with a slow and unpredictable absorption. Propylene glycol contained in the IV preparation may lead to direct myocardial depression(3).

5. *Opioids:* Morphine-the prototype of this group is a narcotic analgesic with a dose dependent depression of the respiratory drive which may persist longer than the sedative effect. Infants less than 1-2 months of age are particularly sensitive to this depression. Vasodilatation related to histamine release may lead to significant hypotension in hypovolemic patients or if used concurrently with benzodiazepines. Otherwise it produces virtually no cardiovascular effects when used alone. Nausea and vomiting commonly seen are due to stimulation of the chemoreceptor trigger zone in the brain stem. Because analgesia occurs with a lower dose than that required for sedation, it is rarely used alone for sedation, its use being mainly limited to ventilated patients(10).

Fentanyl is a short acting opioid "with a rapid onset of action and is now the preferred sedative analgesic for short procedures like bone marrow aspiration, fracture reduction, suture of lacerations, endoscopy and dental procedures. It is 100 times more potent than morphine and largely devoid of hypnotic or sedative activity. It has minimal hemodynamic effects and is thus the opioid of choice for trauma, cardiac and intensive carepatients(ll).

Meperidine, a synthetic opioid is mainly used as preanesthetic medication for sedation. At equianalgesic doses there is little quantitative difference between meperidine and morphine as regards sedation, analgesia, miosis and respiratory depression(l0). 'Lytic cocktail'-A combination sedative of meperidine, promethazine and chlorpromazine is now rarely used due to a high incidence of side effects reported with its use and prolonged sedation of more than 7 hours in some patients(12).

6. *Ketamine:* This produces a state of dissociative anesthesia characterized by analgesia and amnesia in a conscious cooperative and motionless patient A sympathetic response is evoked with increase in heart rate and blood pressure in usual doses of 0.5-2 mg/kg, though higher doses may produce a direct myocardial depression. Airway reflexes may be depressed and oral secretions increased. Occasionally ketamine may cause an increase in skeletal muscle tone which mimics a tonic seizure. Its use is not recommended in patients with raised intracranial pressure and intraocular pressure. Half the patients may have dreams, hallucinations and delirium during the recovery period which can be prevented by the concomitant use "of diazepam, though both the drugs should not be mixed in the same syringe. Atropine may be used 20 minutes before administration of ketamine for its antisialogogue effect. Ketamine may be administered intramuscularly (5-10 mg/kg) or intravenously (0.5-2 mg/kg)(13,14).

Problems with Current Sedative Agents

Critically ill patients vary widely in both pharmacodynamic and pharmacokinetic responses to sedative-hypnotic agents. These patients often have a background of multisystem failure, disturbed acid-base status, need for a number of concomitant

medications and a reduced serum albumin concentration. These numerous pharmacological variables limit the use of sedative agents in critically ill children(15). Also, use of sedatives in children with acute hepatic failure may precipitate hepatic encephalopathy.

Sedative medications may mask pain and hinder neurological assessment. They should not, therefore, be used on a regular basis in conditions requiring ongoing neurological evaluation or where pain is used as an indicator of severity of disease *(e.g.,* acute abdomen). Short acting sedatives may, however, be used when needed. Sedatives also preclude the diagnosis of brainstem death in patients who are on advanced life support systems and could be potential organ donors.

Most sedatives cause respiratory depression and should, therefore, be used very cautiously if facilities for mechanical ventilation are not available. In such situations a good airway should be assured and agents that have reversible (opiates) or least effect (chloral hydrate/Ketamine) should be used.

Persistent sedation due to drug accumulation can prolonged the hospital stay. In addition, prolonged exposure to a drug raises the possibility of both tachyphylaxis and physical dependence. Physical dependence is managed by gradual reduction of drug dosage once it is no longer required. Addiction *per se* is not an indication for stopping the use of an agent in a distressed patient. As the patients are being weaned off sedatives, they are monitored for the signs of withdrawal that may impair recovery. In general, symptoms of withdrawal are unlikely if dose is tapered over 5-10 days. Agents given by continuous intravenous infusion are generally tapered by 10%-20% once daily. One important caution is that shorter acting agents are not to be withdrawn more rapidly than longer acting agents(16).

Monitoring of Depth of Sedation

Sedation of pediatric patient has serious associated risks such as hypoventilation, apnea, airway obstruction, cardiopulmonary impairment, these risks should be avoided or rapidly diagnosed and appropriately treated. In recognition of expanding need for both elective and emergency use of these agents, American Academy of Pediatrics has presented guidelines for the use of depressant agents in children(17).

These guidelines are preffered with the awareness that regardless of intended level of sedation or route of administration, the sedation of a patient represents a continuum and may result in loss of the patient's protective reflexes; a patient may move easily from a high level of sedation to obtundation. The distinction between conscious sedation and deep sedation is made for the purpose of describing the appropriate levels of physiologic monitoring.

Conscious sedation is a medically con trolled state of depressed consciousness *(i)* that allows protective reflexes to be maintained, *(ii)* retains the patient's ability to maintain a patent airway, and *(iii)* permits appropriate response by the patient to physical and/or verbal command. The drug and technique used should carry a margin of safety wide enough to render unintended loss of consciousness highly unlikely. Trichlofos, antihistaminic agents, opioids and paraldehyde can be safely used for the purpose of conscious sedation. These agents should be administered at the health care fa cility where appropriate monitoring can be instituted.

TABLE II—*Suggested Drugs for Various Depths of Sedation*

	Depth sedation	Indication	Drugs used	Guidelines for monitoring
1.	Conscious sedation	- Combative child - Respiratory distress - ICU inpatients to allay environmental anxiety - Preoperative sedation - Minor invasive procedures	Trichlofos, Antihistamine Benzodiazepines	- Document name, route, site, dosage and time of administration - Time based record of heart rate, respiratory rate, blood pressure and oxygen saturation - Check head position to ensure patency of airway - Patient is fit to be discharged if he is arousable, can talk and is able to sit up unaided.
2.	Deep sedation	- Endoscopy bone marrow aspiration, liver & kidney biopsy - During CT scan MRI & other invasive radiological producers - Chest tube placement, venous cutdown and other minor surgical procedures - Children for endotracheal intubation - Patient on ventilator and other advanced life support system	Ketamine + Benzodiazepines, Ketamine Opioids (Fentanyl) ketamine Opioids (Morphine) Opioids, Barbiturates	Same as above - One medical personnel skilled in airway management and cardiopulmonary resuscitation must be present - ECG monitor and defibrillator should be readily available - Ensure adequate hydration

Deep Sedation

Deep sedation is a medically controlled state of depressed consciousness from which the patient is not easily aroused. Deep sedation may be accompanied by a partial or complete loss of protective reflexes, including the inability to maintain patent airway independently and to respond purposefully to physical stimulation or to verbal command. Benzodiazepines, barbiturates and ketamine are the drugs frequently used to achieve a state of deep sedation. The state of deep sedation regardless of how it is achieved warrants constant vigil over patients vital signs, airway patency and adequacy of ventilation. At least one individual must be present who is trained and capable of providing pediatric basic life support. A functioning suction apparatus must be present.

The varying depth of sedation, indications, drugs and appropriate guidelines for their use are illustrated in *Table II.*

Conclusion

When judiciously used and with proper precautions, sedatives can improve the quality of care for children. Because the medical literature is incomplete in describing the pharmacology of sedatives in children, the response of a child to a particular sedative agent cannot be predicted, hence each use is an individual experiment in which the response of the child is assessed. Guidelines given in *Table II* should be strictly adhered to prevent adverse outcomes with the use of sedative agents.

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