Chapter 11: Pre-procedure Medications

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INTRODUCTION

FOCUS POINTS

1. Preoperative oral midazolam reduces perioperative anxiety and provides anterograde amnesia within 10 minutes of administration.
2. Ketamine provides good sedation and analgesia while preserving upper airway muscular tone and respiratory drive. The intramuscular (IM) route of administration is very useful for children who are uncooperative, refuse oral medications, and become combative.
3. Fentanyl can be administered intranasally to provide both pain relief and sedation prior to a procedure.
4. Dexmedetomidine is a highly selective alpha-2 agonist that can be given intranasally with ease of separation from parents for most patients at 30 minutes after administration.
5. Topical preparations of local anesthetics can alleviate pain due to venipuncture or intravenous (IV) catheter insertion.

In the preoperative period, children have significant anxiety and behavioral and pharmacological interventions are used to mitigate these symptoms prior to surgery. Although this is true for adults as well, in the young pediatric patient it is related to a limited understanding of the nature of the illness, the need for surgery, and the unfamiliarity of the environment. Anxiolysis is the primary aim of premedication use, although other clinical goals include amnesia, optimization of preoperative conditions, and prevention of physiological stress.

Nearly 50% of children demonstrate signs of significant preoperative fear and anxiety.[1] Heart rate and blood pressure measurements correlate with behavioral ratings of anxiety.[2] Anesthesiologists may use either parental presence or sedative premedication to alleviate physiological and psychological effects of preoperative anxiety, since separation from parents and induction of anesthesia are considered the most stress-inducing phases of the perioperative experience. Anesthesiologists who favor parental presence during induction of anesthesia tend to use sedative premedications least frequently, and vice versa.[3,4] Both approaches are considered appropriate depending on the clinical scenario.

The most popular premedicant available in the past were long acting (eg, morphine and pentobarbital) but their administration delayed postoperative recovery and increased the incidence of postoperative nausea and vomiting. In addition, these medications were not available via oral route. This resulted in underuse of sedative premedication in many children with anxiety compromising their psychological welfare for the goal of efficiency and rapid discharge. The introduction of oral midazolam as premedication is the main reason pharmacological sedation has regained popularity in modern pediatric anesthesia practice, especially in the ambulatory setting. Oral midazolam remains the most commonly used premedication for pediatric practice, with several other medications (eg, alpha agonists) available depending on the specific clinical needs.

Premedication versus Parental Presence for Induction

Early studies suggested reduced anxiety and improved patient cooperation if parents were present during induction.[5,6] The majority of parents prefer to be present during induction of anesthesia regardless of the child's age or previous surgical experience,[7] and regardless of their experience with prior parental presence or premedication of their child in the case of repeated surgery.[8] Concerns regarding parental presence for induction (PPI) do include a negative behavioral response to stress when a parent is present, and an upsetting experience for the parents, especially when watching their

child become unconscious or needing to leave their child after induction.[9,10] This experience correlates with an increase in heart rate and skin conductance levels in mothers.[11] Oral midazolam has been shown to be more effective in reducing a child's anxiety than PPI, and parental presence combined with oral midazolam was not superior in reducing a child's anxiety than sedation alone.[12] PPI is most helpful in children older than 4 years of age who share a calm baseline personality with the accompanying parent.[13,14] However, limitations to controlled studies such as these may be that randomization in subject recruitment may not reflect the everyday practice of anesthesiologists who largely individualize their approach to each child and parents.

If PPI is deemed to be in the child's best interest, a clear explanation that describes what the parent can expect to witness during the peri-induction period can significantly decrease parental anxiety and increase their level of satisfaction, which may be reflected in the child's behavior.[15–17] Predictive characteristics for children who would probably benefit from sedative premedication include children between the ages of 2 and 6 years, who have a history of prior stressful medical encounters, who are shy and inhibited, and who were accompanied by an anxious parent.[7,18] In the extremely anxious child, premedication is indicated to avoid a traumatic anesthetic induction and consequently a possible postoperative psychological disturbance.[19]

PREMEDICATIONS

The major objectives of preanesthetic medications are to decrease the stress response with preservation of hemodynamic parameters, facilitate anesthesia induction, and produce amnesia. The child's age, body weight, medication history, allergic status, and underlying medical or surgical conditions are factors that need to be taken into consideration prior to administration of any premedication. In most cases, oral or nasal medications are preferred over rectal, intramuscular, or IV routes if no IV access is already in place. Oral premedication administration does not increase the risk of aspiration pneumonia.[20] A variety of different medications and classes may be used as premedication.

BENZODIAZEPINES

Midazolam is the most commonly used sedative premedicant in the preoperative holding area.[3] After appropriate administration of midazolam, the following is expected: sedation, induction of sleep, reduction in anxiety, anterograde amnesia, muscle relaxation, and anticonvulsant effects.[21]

Midazolam can be administered orally, intranasally, intravenously, rectally, and intramuscularly.

When administered orally its favorable characteristics are the short onset and offset of action. Bioavailability is highly sensitive to changes in pH. As a standard syrup preparation, midazolam exists in both an open and a closed ring structure. The closed ring formulation is lipophilic and physiologically active, and its proportion in the preparation is dependent on pH values.[22] The drawback is its bitter taste. The most common oral dose used is 0.5 mg/kg, but ranges from 0.25 to 1 mg/kg have been described. Higher doses of midazolam appear not to offer any additional benefits and may cause more side effects. Commercially prepared oral midazolam formulation is rapidly absorbed with most patients demonstrating a satisfactory degree of sedation and anxiolysis within 10 minutes of consumption, with an even higher percentage appropriately sedated at 20 minutes after administration. The dose of oral midazolam should be adjusted in children taking depressants or inducers of the cytochrome oxidase system, such as anticonvulsants or barbiturates. All doses should be administered under direct supervision with the patient placed in a closely monitored bed space in the preoperative holding area.

The bioavailability of different routes of administration and suggested doses are as given in Table 11-1.

Table 11-1

Bioavailability and Suggested Doses of Midazolam

	Oral	Nasal	Intramuscular	Rectal
Bioavailability (%)	30	57	90	40–50
Suggested dose (mg/kg)	0.25–0.75	0.2	0.1-0.2	1

A sublingual route of administration (0.2mg/kg) has also been described.[23–29]

After IV administration, the time to peak central nervous system (CNS) electroencephalographic effect is 4.8 minutes. It is preferable to wait this interval of time prior to administering any additional dose of midazolam to avoid oversedation. To avoid the added trauma of venipuncture, IV midazolam is best reserved for children who already have a functioning IV line.

When administered intranasally, peak plasma concentrations of midazolam occurs in only 10 minutes; however, discomfort due to irritation has been associated with this route. Intranasal midazolam with preservative has been shown to induce neurotoxic effects in an animal model.[30] A preservative-free midazolam preparation is recommended when using this route of administration.

There is synergism between propofol and midazolam on gamma-aminobutyric acid (GABA) receptors.[31] Oral midazolam decreases the infusion requirements of propofol by one-third during a propofol-based anesthetic.[32] After premedication with oral midazolam (0.5 mg/kg), in children 1 to 3 years of age post-adenoidectomy after induction of anesthesia with propofol, and maintenance with sevoflurane, emergence and early recovery were shown to be delayed with no change in discharge times.[33] Spontaneous eye opening and discharge time were delayed as compared with placebo after 25 minutes of sevoflurane anesthesia.[34] Extubation, awakening, and discharge times were not affected after sevoflurane anesthesia in children 1 to 10 years of age receiving a similar dose of oral midazolam.[35]

Midazolam has the advantage of producing anterograde amnesia. Memory usually becomes impaired within 10 minutes after oral administration.[36] This effect is beneficial in children who require repetitive interventions. Midazolam, like other benzodiazepines, increases the seizure threshold for CNS toxicity but does not affect the threshold for cardiovascular toxicity. Therefore, cardiovascular collapse after regional anesthesia toxicity may occur unrelatedly to CNS symptoms of toxicity after a patient has received premedication with midazolam or another benzodiazepine. Other secondary effects of midazolam may include a paradoxical effect with behavioral changes: anxiety, agitation, involuntary movements, aggressive or violent behavior, uncontrollable crying or verbalization, and hiccups. These adverse effects may occur independently of the mode of administration, ie, rectal, nasal, or oral. They seem to be related to the altered state of consciousness or disinhibition produced by the drug. To directly reverse such midazolam, flumazenil, a competitive benzodiazepine antagonist[37], can be administered. TP mitigate side effects, ketamine at 0.5 mg/kg IV38 or antipsychotic medications such as haloperidol can be administered.

Lorazepam can be administered orally, intravenously, or intramuscularly. It has a slow onset and offset of action and may be better used for inpatients. It is metabolized by the liver to inactive metabolites. The usual dose is 0.05 mg/kg administered orally or intravenously to older children; however, a dose of 0.025 mg/kg has been shown to be adequate for decreasing preoperative anxiety.[39] Lorazepam has good amnestic properties and produces less tissue irritation than diazepam.

Diazepam has a greater fat solubility than midazolam and a faster CNS effect after IV administration (1.6 minutes). Diazepam undergoes oxidative metabolism to pharmacologically active metabolites by demethylation, hydroxylation, and glucuronidation in the liver. The main active metabolite is desmethyldiazepam (nordiazepam) with pharmacologic activity equal to the parent compound.[40] Other active metabolites include temazepam and oxazepam. Diazepam has a biphasic half-life of about 1 to 3 days, and 2 to 7 days for the active metabolite desmethyldiazepam.[41] Diazepam is a less popular choice as a preoperative premedicant in young children because of their immature liver function that may lead to a prolonged half-life. The average oral dose for premedicating healthy children with diazepam ranges from 0.1 to 0.3 mg/kg. When administered rectally, diazepam appears to be less effective than rectal midazolam.[42] The intramuscular route is not recommended because it is painful and absorption is erratic.[43] Use of

diazepam should be avoided in individuals with ataxia, severe hypoventilation, acute narrow-angle glaucoma, severe hepatic and renal deficiencies, severe sleep apnea, severe depression, particularly when accompanied by suicidal tendencies, psychosis, myasthenia gravis, and hypersensitivity or allergy to any drug in the benzodiazepine class. Paradoxical side effects have been reported, including nervousness, irritability, excitement, insomnia, worsening of seizures, and muscle cramps. These adverse reactions are more likely to occur in children, the elderly, and individuals with a history of drug or alcohol abuse and/or aggression.[44] In some patients, diazepam may increase the tendency toward self-harming behaviors.[45]

BARBITURATES

Barbiturates have become less commonly used for premedication in children since the advent of shorter-acting benzodiazepines. IV **methohexital**, still in use, has a relatively short elimination half-life (3.9 ± 2.1 hours) than thiopental (9 ± 1.6 hours) because of a faster hepatic metabolism.[46] A major disadvantage of barbiturates is hyperalgesia, which can induce agitation in children who experience postoperative pain. Methohexital, in a rectal dose of 20 to 30 mg/kg, may result in sleep/sedation in 15 to 20 minutes but has unpredictable systemic absorption and side effects including hiccups, apnea, airway obstruction, laryngospasm, seizures, and possible allergic reaction.[47,48] An increase in absorption through rectal mucosa abnormality may lead to cardiorespiratory arrest. Contraindications to methohexital include porphyria, hypersensitivity, and temporal lobe epilepsy.[49]

NONBARBITURATE SEDATIVES

Chloral hydrate is an orally administered nonbarbiturate (20 to 75 mg/kg with a total maximum dose of 2 g). It is devoid of analgesic properties and has a bitter taste. Its principal advantage is that it can be administered orally or rectally with relatively good sedation within 30 to 45 minutes. Its use is less frequent than midazolam as a premedicant because of its slow onset and long elimination half-life.[50] It is not recommended in neonates and patients with liver disease because of impaired metabolism, and the potential accumulation of toxic metabolites leading to metabolic acidosis, renal failure, and hypotonia.[51] The active metabolite of chloral hydrate, trichloroethanol, has a long half-life in toddlers and in preterm infants (39.8 ± 14.3 hours) with a risk for residual drug effect and prolonged sedation or resedation.[52] Airway obstruction may occur in children with tonsillar hypertrophy.[53] Deaths after administration of chloral hydrate for sedation have been reported.[54] Concerns for potential carcinogenicity with chronic administration exist. Other adverse effects include irritation of the skin, mucous membranes, and gastrointestinal tract, possibly in relation to the metabolism of chloral hydrate to trichloroacetic acid.

Phenothiazines

Promethazine (0.25 mg to 0.5 mg/kg intravenously, intramuscularly, or orally) possesses several beneficial properties. It is sedating, and it is an antihistamine (H1 blocker), an antiemetic/anti-motion sickness medication, and an anticholinergic. However, it is not a popular premedicant in pediatric ambulatory anesthesia because of ineffective sedative effects as sole premedication and because of long elimination half-life (8 to 12 hours). It may also cause dystonic reactions.

Ketamine

Ketamine is a phencyclidine derivative that antagonizes the *N*-methyl-d-aspartate (NMDA) receptor (NMDAR). The principal effect of ketamine is due to the central dissociation of the cortex from the limbic system. Ketamine provides good sedation and analgesia while preserving upper airway muscular tone and respiratory drive. Ketamine also relaxes the smooth musculature of the airway stimulated by the release of histamine, an effect with the potential risk for bronchoconstriction. The most common adverse reaction to ketamine is postoperative vomiting, which occurs in 33% of children.[55] The dextro-isomer of ketamine has more potent analgesia and a reduced incidence of side effects.[56] Other side effects associated with the administration of ketamine include sialorrhea and hallucinations. It is recommended to administer an antisialagogue (atropine or glycopyrrolate) with ketamine in order to decrease the amount of oral secretions that may occur and therefore to decrease the risk of laryngospasm. Hallucinations during recovery from ketamine may occur mostly in older children, although oral ketamine has been reported to reduce emergence delirium. Coadministration of benzodiazepines or subsequent administration of general anesthetic agents reduces the incidence of hallucinations to approximately 4%.[57] It is preferable to recover patients who have received ketamine in a quiet environment with the least stimulation in order to help decrease the incidence of undesirable effects such as hallucinations, nightmares, and delirium.

NMDAR antagonism is responsible for the anesthetic, amnestic, dissociation, and hallucinogenic effects of ketamine. Activation of *k*-opioid receptors and possibly sigma and mAch receptors may also contribute to its hallucinogenic properties.[58] The mechanism of action for the possible antidepressant effects of ketamine at lower doses is being investigated.[59] Ketamine blocks voltage-dependent calcium and sodium channels, attenuating hyperalgesia; it alters cholinergic neurotransmission and inhibits the reuptake of serotonin and norepinephrine.[60]

Ketamine can be administered via the oral, intramuscular, and nasal routes. Bioavailability and peak concentrations for each route are as mentioned in Table 11-2. After oral administration, ketamine undergoes first-pass metabolism, where it is biotransformed in the liver by CYP3A4, CYP2B6, and CYP2C9 isoenzymes into norketamine, hydroxynorketamine, and finally dhydronorketamine.[61] Norketamine is the major metabolite of ketamine and is one-third to one-fifth as potent, and plasma levels of this metabolite are three times higher than ketamine following oral administration.[62]

Table 11-2

Bioavailability and Peak Concentrations of Ketamine

	Oral	Intramuscular	Intranasal
Bioavailability (%)	17	93	25–50
Peak plasma concentration (minutes)	30	5–15	10–15

Peak plasma concentrations of ketamine are reached within a minute intravenously, but in 5to 15 minutes when administered intramuscularly.[60]

IV ketamine has a fast onset of effect (<1 minute). Duration of action of a single IV dose is 5 to 8 minutes (α-elimination half-life of 11 minutes and a β-elimination half-life of 2.5 to 3 hours).[63] Ketamine is administered in very low doses intravenously (0.25 to 0.5 mg/kg) or intramuscularly (1 to 2 mg/kg) preferably in combination with low-dose midazolam (0.05 mg/kg) along with atropine (0.02 mg/kg) for sedation. The dose of ketamine needed to prevent gross movement in infants younger than 6 months of age is four times greater than in children 6 years of age.[64]

The intramuscular route of administration is very useful for children who are uncooperative, refuse oral medications, and become combative. These children become adequately calm in around 3 minutes and will then accept a mask inhalation induction of anesthesia. There is no documentation of prolongation of the hospital discharge times after IM ketamine administration (2 mg/kg) even after brief surgical procedures and there is only a minimal likelihood of delirium or bad dreams during recovery.[65] However, the combination of intramuscular ketamine (2 mg/kg) and midazolam (0.1 to 0.2 mg/kg) may prolong recovery and discharge times after brief ambulatory procedures.[66] A larger dose (4 to 5 mg/kg) sedates children with 2 to 4 minutes, and a dose of 10mg/kg usually produces deep sedation. Larger and repeated doses are associated with hallucinations, nightmares, vomiting, and a prolonged recovery from anesthesia.

Oral ketamine alone and in combination with midazolam have been used for premedication in healthy children and those with congenital heart defects. Sedation is usually achieved after a dose of 5 to 6 mg/kg of oral ketamine in most children within 12 minutes; the depth of sedation is sufficient to obtain IV access in more than half of children. Larger doses may prolong recovery from anesthesia. The combination of oral midazolam (0.5 mg/kg) and ketamine (3 mg/kg) is synergistic in its efficiency for preoperative sedation and does not seem to prolong recovery time for procedures longer than 30 minutes.[67]

Only preservative-free ketamine should be given intranasally to avoid neurotoxicity, and the 100 mg/mL concentration is preferable to minimize volume administered.[68] Nasal transmucosal ketamine at a dose of 6 mg/kg is also effective in sedating children within 20 to 40 minutes before induction of anesthesia.

Rectal ketamine administration has a bioavailability of only 25% and can result in an unpredictable effect.[69]

Ketamine should be used with caution in any child with a history of psychiatric or seizure disorder because of its psychotropic and epileptogenic effects. Although ketamine was considered to increase intracranial pressure (ICP) as a result of cerebral vasodilation, with adequate ventilation this

effect may be minimal. Ketamine was also thought to produce an increase in intraocular pressure (IOP), although this effect is clinically not significant.

Opioids

Opioids are a useful preanesthetic medication for children with preoperative pain, as preemptive analgesia. However, common opioid-related side effects such as respiratory depression, dysphoria, pruritus, and nausea/vomiting should be considered when these medications are administered. If opioids are used in combination with other sedatives such as benzodiazepines, the dose of each drug should be appropriately adjusted to avoid the risk of respiratory depression. Neonates are very sensitive to the respiratory depressant effects of opioids, and they are rarely used to premedicate in this age group.

Fentanyl may be administered by parenteral, transdermal, nasal, and oral routes. The optimal oral dose as a preanesthetic medication with minimal desaturation and preoperative nausea appears to be 10 to 15 mcg/kg. Children begin to show signs of sedation within 10 minutes after receiving this dose. Recovery is similar to that after 2 mcg/kg given intravenously. Doses greater than 15 mcg/kg are not recommended because of opioid side effects, particularly respiratory depression. Fentanyl may also be administered nasally (1 to 2 mcg/kg) as a premedication, but it is most frequently utilized after induction of anesthesia as a means of providing analgesia in children without IV access.

Sufentanil is 10 times more potent than fentanyl. Several instances of reduced chest wall compliance have been reported in children after nasal sufentanil, as well as a higher incidence of nausea and vomiting and a prolonged discharge time when compared to nasally administered midazolam.[70] These potential side effects and prolonged hospital stay after nasal sufentanil makes it an unpopular choice for premedication.

Morphine sulfate may be administered intramuscularly (0.1 to 0.2 mg/kg) or intravenously (0.05 to 0.1 mg/kg) or orally.

Codeine has been a commonly prescribed oral opioid, which must undergo *O*-demethylation in the liver to produce morphine to provide effective analgesia. Five percent to 10% of children lack the cytochrome isoenzyme (CYP2D6) required for this conversion and therefore do not derive analgesic benefit. The combination of codeine with acetaminophen is effective in relieving mild to moderate pain but its use in the United States has fallen out of favor because of several deaths in pediatric patients; the Food and Drug Administration (FDA) in 2017 recommended against the use of this medication in pediatric patients.[71]

Alpha-2 Agonists

Clonidine causes dose-related sedation by its effect in the locus coeruleus through inhibition of adenylate cyclase and reduction in norepinephrine release. Clonidine acts both centrally and peripherally to reduce blood pressure and therefore it attenuates the hemodynamic response to intubation. The plasma concentration peaks at 60 to 90 minutes after oral administration.[72,73] The need to administer clonidine 60 minutes before induction of anesthesia makes its use impractical in most clinical settings. An oral dose of 3 mcg/kg given 45 to 120 minutes before surgery produces comparable sedation to that of diazepam or midazolam.[74] Clonidine if given at 4 mcg/kg is effective in the reduction of postoperative pain. In most studies reviewed, the side effects were minimal, but some investigators added atropine to prevent bradycardia and hypotension.

Dexmedetomidine is a newer, more highly selective alpha-2 agonist than clonidine, with more favorable pharmacokinetics. Commonly used in the intraoperative period to smooth emergence and reduce opioid use, dexmedetomidine also demonstrates utility when used as an anesthetic premedication. Meta-analyses recommend its use as superior to midazolam in that it produces better preoperative sedation and parental separation, and reduction of postoperative pain.[75,76] It can be given intravenously or intranasally with onset of action of 5 to 30 minutes, respectively. It is most commonly administered via nasal route at 1 to 2 mcg/kg with ease of separation from parents for the majority of patients at 30 minutes after administration.[77] Statistically but not clinically significant reductions in heart rate and blood pressure may be seen, but discharge time from the recovery room is not prolonged in comparison with midazolam.[75,76]

Antihistamines

Antihistamines are not commonly used because their sedative effects are somewhat variable. **Diphenhydramine** is an H1 blocker with mild sedative and antimuscarinic effects. The dosage for children is 0.5 mg/kg intravenously or intramuscularly.[78] Although the duration of action is 4 to 6 hours, it does not appear to interfere with recovery from anesthesia. **Hydroxyzine** has antiemetic, antihistaminic, and antispasmodic effects with minimal respiratory and circulatory changes. It is usually administered intramuscularly at a dose of 0.5 to 1 mg/kg.

ANTICHOLINERGIC DRUGS

Anticholinergic agents were commonly used in the past to prevent the undesirable bradycardia associated with some anesthetic agents (halothane and succinylcholine), and to minimize autonomic vagal reflexes and reduce secretions. Current inhalational anesthetics are not associated with bradycardia and do not stimulate salivary or tracheobronchial secretions; therefore, the routine use of an anticholinergic drug is not generally needed prior to induction. In the majority of cases, anticholinergics are given after IV access is established.

Atropine (0.02 mg/kg) and **scopolamine** (0.01 mg/kg) both have CNS effects, although the sedating effects of scopolamine is 5 to 15 times greater than atropine. The central sedative effects of both atropine and scopolamine may be antagonized with physostigmine. Atropine is more commonly used and is a better vagolytic agent than scopolamine, whereas scopolamine is a better sedative, antisialagogue, and amnestic. **Glycopyrrolate** is a quaternary amine and as such it does not cross the blood-brain barrier and does not produce CNS side effects including sedation. When compared to atropine, it is less effective in attenuating bradycardia during induction.

Anticholinergic agents are very useful as an adjuvant to ketamine anesthesia because of their antisialagogue and central sedative effects. The recommended doses of anticholinergics are scopolamine 0.005 to 0.01 mg/kg, atropine 0.01 to 0.02 mg/kg, and glycopyrrolate 0.01 mg/kg intravenously or intramuscularly.

TOPICAL ANESTHETICS

Topical anesthetic applications are commonly used as an attractive alternative to intradermal local anesthetic infiltration for obtaining IV access when this is indicated prior to induction of anesthesia.

EMLA cream (eutectic mixture of local anesthetic, Astra Zeneca, Wilmington DE) is a mixture of two local anesthetics (2.5% lidocaine and 2.5% prilocaine). One-hour application of EMLA cream to intact skin with an occlusive dressing provides adequate topical anesthesia for an IV catheter insertion. However, EMLA causes venoconstriction and skin blanching, making IV cannulation more difficult. Methemoglobinemia may occur secondary to prilocaine.[79] A 1-hour application of EMLA cream and a maximum dose of 1 g did not induce methemoglobinemia when applied to intact skin of full-term neonates younger than 3 months of age.[80]

Ametop, a 4% tetracaine topical preparation, has the advantage of no venoconstriction or skin blanching and no risk of methemoglobinemia. Its onset time is 30 to 40 minutes.

ELA-Max (4% lidocaine) decreases pain associated with IV catheter insertion after only a 30-minute application with lesser skin blanching and better vein dilation compared to EMLA cream. There is no risk of methemoglobinemia with this formulation.

Synera is a eutectic mixture of lidocaine and tetracaine (70 mg of each per patch) that uses a controlled heating system to accelerate delivery and analgesic effect of the local anesthetic. An application time of 20 minutes lessens pain associated with venipuncture in children and is associated with only mild and transient local erythema and edema and no skin blanching.[81] Methemoglobinemia has not been reported with this formulation.

The **J-tip Needle-Free Injection System** (National Medical Products, Irvine CA) uses a carbon dioxide–driven dispersion method to distribute lidocaine 1% into the intradermal space. It demonstrates equivalent to superior analgesia as compared with EMLA when used for peripheral venous access, with analgesia achieved in 1 to 2 minutes.[82,83]

The primary goal of premedication in children is to reduce anxiety by facilitating a smooth separation from parents and ease the induction of anesthesia. Other pharmacological effects (amnesia, prevention of physiologic stress, reduction of total anesthetic requirements, decrease in risk of aspiration of acidic stomach content, and analgesia) may also be achieved. Special considerations for patients with deteriorating mental status, with airway obstruction, or patients with hemodynamic instability/intolerance to hypercapnia (such as those with significant increases in pulmonary artery pressure/pulmonary arteriolar resistance) or with systemic organ failure should be taken into account prior to administration of premedication. In these cases, parental presence may be the preferable choice. Pediatric premedication should be administered with caution, and under supervision and close monitoring. Skilled staff should be immediately available to rescue the airway and initiate resuscitation should it be needed.

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