Neonatal and Childhood Perioperative Considerations

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The perioperative care of infants and children requires a team approach. Surgeons must recognize potential risk factors for adverse perioperative events and work with the anesthesiologist and other consultants to reduce or eliminate these factors to optimize the child’s perioperative care. In the past decade, there has been considerable progress in perioperative management that now makes surgery safer and less distressing for children and their families. In this review, the authors cover recent advances in preoperative evaluation and intraoperative and postoperative management, focusing mainly on the immediate perioperative period for elective surgical procedures. Consistent with the authors’ view that the optimal outcome is achieved by close collaboration of members of the surgical team, this review was written jointly by surgeons and an anesthesiologist.

Preoperative evaluation

Overview

Because many pediatric surgical procedures are elective and performed as same-day surgery, the preoperative evaluation and interventions aimed at reducing perioperative risks are commonly performed in an outpatient setting. Children who do not have acute illness or major chronic medical illnesses can be evaluated by the surgeon in the office and assessed by the anesthesiologist on the day of elective surgery. Although some institutions mandate a separate
outpatient evaluation by an anesthesiologist, most have streamlined preoperative care by eliminating this additional visit. Some institutions even use telephone surveys to identify high-risk patients who may benefit from preoperative screening before the day of surgery. Although this practice increases the convenience for families, elimination of a preoperative anesthesia evaluation increases the importance of the surgeon’s initial evaluation and can lead to delays or cancellations on the day of surgery when the evaluation is incomplete. The anesthesiologist working in the same-day surgery suite depends on accurate and timely information from the surgeon’s outpatient evaluation to make an appropriate plan for perioperative management.

“One-stop” surgery

The interest in further streamlining the preoperative evaluation among children undergoing elective surgery can be seen in the development of “one-stop” surgery programs [1,2]. The focus of these programs is to increase convenience to families by eliminating the preoperative and postoperative visits. Children who are to undergo simple procedures such as umbilical or inguinal hernia repair, circumcision, or central line removal are prescreened by their primary care provider for major risk factors for adverse perioperative events. The children at low risk are evaluated by the surgeon and the anesthesiologist on the day of the scheduled procedure. Although one-stop surgery is associated with high parental satisfaction, it has several limitations. Despite adequate preparation, about 20% of one-stop procedures are cancelled or delayed because of failure to show up, parental decisions to forego surgery after surgical consultation, the surgeon’s judgment about the need for surgery, or failure to follow preoperative feeding instructions [1,2]. This high cancellation rate requires modification of the processes used in the same-day surgery suite to avoid the costs associated with inefficient use of operating room resources.

Although major adverse events are less likely due to prescreening and the types of procedures selected for this approach, an expedited approach may not best serve the psychologic needs of many children and parents. A separate preoperative visit provides an opportunity for parents to meet with the surgeon in a less pressured environment, allows them more time to consider information about the appropriateness and potential outcomes of surgery, and may reduce parental anxiety [1,2]. In light of evidence that parental anxiety has a negative impact on the psychologic reaction of children to surgery [3], omission of the preoperative visit may not be the best choice for some families. Additional study of the impact of one-stop surgery is warranted before this option is more widely adopted.

Preoperative testing

Preoperative surgical evaluation should focus on identification of potential factors associated with frequently occurring perioperative complications
and on those associated with high potential morbidity or mortality. In most cases, children at risk can be identified by a detailed history and physical examination without the need for additional laboratory studies or other investigations. In a cohort of 8772 healthy children undergoing minor surgical procedures, anesthesiologists requested laboratory studies in 2%, most often to evaluate for suspected anemia [4]. Although almost half of these studies were abnormal, surgery was not delayed or the anesthetic management modified based on these results. Furthermore, the incidence of minor and major perioperative complications was similar to a previous period during which routine laboratory studies were obtained on all children, suggesting that a policy of selective laboratory screening is safe. In a survey of members of the Society for Pediatric Anesthesia, it was found that the most common preoperative laboratory study requested was a hemoglobin or hematocrit, being performed in up to half of children depending on their age [5]. The utility of routine screening for anemia is low because only 0.5% of pediatric same-day surgery patients are anemic and the anesthetic plan is rarely modified because of anemia [5]. A more targeted approach is to obtain hemoglobin values on children at increased risk for anemia, including infants younger than 1 year (especially the former preterm infant in whom anemia is a risk factor for postoperative apnea), adolescent menstruating girls, or those who have chronic medical illnesses. A baseline study may also be useful among children who are undergoing procedures that have an anticipated high blood loss. A hemoglobin value can be obtained at the time of placement of the intravenous cannula in the operative room, avoiding the need for venipuncture in an awake patient. The usefulness of these recommendations has not been established.

In addition to screening for anemia, it has been shown that preoperative pregnancy testing and coagulation testing before tonsillectomy are also commonly performed at many institutions [5]. The value of these preoperative tests is controversial. In a study performed at a large children’s hospital, Wheeler and Cote [6] found that routine pregnancy screening of 235 menarcheal adolescents detected pregnancy in 1%. Similar findings have been observed by others [7]. Routine pregnancy testing was favored by these investigators because of unreliable patient history, possible fetal or maternal complications related to the administration of anesthesia or the surgical procedure, and other potential liability that may occur as a result of unrecognized pregnancy. Nevertheless, there are other issues to consider, including the lack of demonstrated cost-effectiveness of routine testing, the uncertain effects of single anesthetic exposure on the fetus or mother, and the ethical and legal issues of pregnancy testing in minors [6]. Because of the controversy surrounding routine pregnancy screening in adolescents, each institution should develop recommendations that reflect the surgical team’s views and that conform to state regulations [6]. If routine pregnancy testing is instituted, a specific policy should be in place that deals with the difficult task of informing the patient and her
family about a positive test and providing counseling before the patient is discharged home.

Similar to pregnancy screening, routine coagulation screening before tonsillectomy is controversial. Tonsillectomy, commonly performed on otherwise healthy children, has a relatively high rate of postoperative bleeding (2%–4%) [8]. For many pediatric patients, this procedure is their first hemostatic “challenge.” Because results from routine coagulation testing before tonsillectomy have been obtained in several large series, previous data allow a critical evaluation of the correlation between bleeding history and the results of coagulation testing. Most current evidence suggests that routine coagulation testing is not needed before tonsillectomy unless indicated by a bleeding history [8,9]. Extensive coagulation testing in this population has also revealed that most children who have a positive bleeding history do not have an identifiable bleeding disorder and that some children who have a coagulation disorder do not have a positive bleeding history [10,11]. Even patients who have normal routine coagulation studies and an insignificant history of bleeding may have identifiable coagulation disorders if tested more extensively [10]. The high false-positive rate of routine coagulation testing and the rarity of unrecognized coagulation disorders does not support routine coagulation testing for tonsillectomy.

Studies regarding coagulation testing before tonsillectomy provide a useful paradigm for the value of screening for bleeding disorders before other routine surgical procedures. Because of the absence of studies evaluating coagulation testing for other pediatric surgical procedures, it appears appropriate to follow the recommendation of obtaining coagulation testing only when indicated by history or physical examination for most procedures with similar or lower risk of hemorrhage compared with tonsillectomy. Data obtained from a large adult series showed that the most reliable factors for detecting bleeding disorders were a history of bleeding from minor wounds, frequent bruising, and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) or platelet function antagonists [12]. In addition to children who have a positive bleeding history, coagulation studies should be considered in those undergoing procedures at high risk for bleeding; in those who have underlying medical conditions that increase the risk of coaguloapathy, such as liver disease or malabsorption; or in those receiving anticoagulants or other medications that increase the risk of a bleeding disorder.

Informed consent—surgical and anesthetic considerations

A critical aspect of preoperative preparation before pediatric surgical procedures is the informed consent process. Despite its importance, relatively little has been written about informed consent before pediatric surgical procedures. At the time of the preoperative surgical visit, families are presented with the nature of the condition, a description of the procedure, the risks associated with the procedure, and possible outcomes that may
occur after surgery. Although it is the intention of every surgeon to provide patients and family with the information needed to make informed choices, the counseling provided by the surgeon may not be adequate or in a form that is preferred by some families. One survey in a pediatric surgical clinic revealed that most parents still had questions after the office visit was complete and many believed that they had a poor or average understanding of the potential outcomes of the planned operation [13]. Most parents use sources other than their surgeon to obtain medical information pertaining to their child. These sources include the primary care physician, books, magazines, newspapers, and the Internet [13]. In a study of parents of outpatients in a pediatric surgery clinic from 2003, 63% of parents obtained information pertaining to their child’s condition using the Internet [14]. Because of the continued increase in Internet usage, this percentage is likely to be even higher today. Parents used the Internet to research several different topics including information about their surgeon (60%), treatment options (58%), the planned surgical procedure (37%), and the risks of treatment (34%) [14]. The importance of the Internet as an adjunct source of health care information for parents emphasizes the importance of accurate and updated Web site content, preferably developed with the contribution of pediatric surgeons. Although several studies have addressed the interactions between surgeons and their adult patients in an outpatient setting [15–17], this area has not been studied for pediatric surgery outpatient encounters in which parents most often serve as decision makers for their children.

Aspects of the anesthetic are similarly presented by the anesthesiologist on the day of the procedure or at a separate preoperative visit. Using interviews with a small cohort of parents of same-day surgery patients, Sobo [18] identified major themes of parental worries and fears. These worries included concerns about the child’s fear or their possible noncooperativeness, their powerlessness as parents to control the child’s safety, the risks of anesthesia, the risks related to performing procedures in younger patients, potential surgical or postoperative complications, and the potential need to alter the treatment plan intraoperatively or postoperatively. With regard to information about anesthesia, Wisselo and colleagues [19] identified specific areas of information needed by parents, the most frequent being information about induction, side-effects, emergence from anesthesia, and pain relief. Most parents like to know (or believe that they have a right to know) about all possible anesthetic complications, even those that are potentially life threatening. When parents were given highly detailed information about the conduct and potential complications of the planned anesthetic, no significant increase in parental anxiety was observed compared with those given less detailed information [20]. Most parents preferred a pamphlet or a preoperative visit with the anesthesiologist as a method for receiving information about anesthesia. Almost half of parents preferred receiving this information during the week before the procedure as opposed to the day before or the day of the operation [19].
Unique considerations arise when anesthesia is planned for the child who has a do-not-resuscitate (DNR) status. Although a DNR order may be in place, a child may require surgery to improve quality of life or to correct a self-limited medical condition. Examples of these procedures include placement of a gastrostomy for supplemental feeding, an appendectomy for appendicitis or the establishment of vascular access. In a recent report from the American Academy of Pediatrics, a panel that included pediatric surgeons and pediatric anesthesiologists developed recommendations for handling this problem [21]. An approach of “required reconsideration” of the DNR order is recommended when surgery is planned for any child who has DNR status. This approach includes a discussion with the child’s parents or caregivers about the likelihood of requiring intraoperative resuscitation, the type of resuscitation methods that might be used, and the anticipated outcome should resuscitation be required. The potential benefits of perioperative suspension of DNR status should also be reviewed. Members of the perioperative team should be fully aware whether DNR status will be upheld or continued and should participate only if willing to uphold the wishes of the family. The child’s perioperative DNR status and decisions to use other aspects of medical care such as ICU monitoring should be considered independently. When DNR status is held in the perioperative period, a plan should be in place should an arrest occur perioperatively and when continued support is likely to result only in prolonging the process of dying [21].

**Perioperative adverse events**

**Overview**

The goal of preoperative evaluation and perioperative management is to minimize morbidity and mortality. The focus should be to reduce uncommon but potentially life-threatening complications such as major respiratory events and to reduce common complications such as vomiting (Table 1). It is important to understand the frequency of these adverse events and the location at which they occur in the immediate perioperative period. In a review of 24,165 anesthetics administered over a 30-month period, Murat and colleagues [22] identified 1829 adverse events occurring in the operating room or recovery room. In the operating room, 724 adverse events were noted (31:1000 anesthetics). Most (53%) of these events were respiratory events. Adverse intraoperative events occurred more frequently in infants younger than 1 year than in older children. Respiratory and cardiac events were more frequent among infants and among those who had an American Society of Anesthesiologists (ASA) physical class higher than 2. In the recovery room, 1105 adverse events occurred (48:1000 anesthetics). Vomiting was the most common (77%) adverse event, and the incidence of vomiting increased with age. Respiratory events in the recovery room were more frequent in
infants than in older children. Compared with children undergoing other types of procedures, intraoperative respiratory events and vomiting in the recovery room were more common among children undergoing ears, nose, and throat (ENT) procedures [22].

**Respiratory complications**

Two recent studies have identified potential independent risk factors for respiratory complications in children undergoing elective surgical

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*Abbreviations:* ASA, American Society of Anesthesiologists; ENT, ears, nose, and throat; LMA, laryngeal mask airway; URI, upper respiratory tract illness.
procedures [23,24]. Mamie and colleagues [23] found that respiratory complications (laryngospasm, airway obstruction, bronchospasm, or oxygen desaturation) were less frequent in older children when anesthesia was administered by a pediatric anesthesiologist, when endotracheal intubation using a relaxant rather than a mask was used, or when a non-ENT procedure was being performed. The risk of respiratory complications decreased by 8% with each year of age. In a similar study, Bordet and colleagues [24] identified age less than 6 years, the presence of a respiratory tract infection, and the use of a laryngeal mask airway as independent factors associated with airway complications. Although each study described multivariate models constructed with different inputs, both showed the importance of age and the method of airway management as important factors contributing to respiratory complications.

The management of the child who has an acute upper respiratory tract illness (URI) and is scheduled for an elective procedure is a frequent problem because healthy children may have up to several URIs per year [25]. Children who have a recent (within 1 month) or active URI are more likely to have respiratory complications including breath holding, oxygen desaturation, and severe coughing [26,27]. Among those undergoing anesthesia during an active URI, significant independent risk factors for adverse respiratory events included copious secretions, the use of endotracheal intubation in children younger than 5 years, history of prematurity, nasal congestion, parental smoking, history of reactive airway disease, and surgery involving the airway [27].

Because URIs contribute to respiratory complications, the surgical team needs to decide when the morbidity of these events justifies postponement of surgery. When respiratory events related to a URI occur, most are easily managed and few lead to unplanned hospitalization (<0.5%) or other long-term sequelae [27,28]. There is considerable variation in the approach to this problem that reflects the diversity of patients, procedures, and practitioners involved. A survey of anesthesiologists showed that many factors are considered, including the presence of asthma, whether intubation is required, and the anesthesiologist’s fear of potential litigation or past experience anesthetizing children who had a URI [29]. When surgery is postponed, the recommended time until rescheduled surgery ranges from 1 to more than 6 weeks, with most recommending a delay of 4 weeks or less. When a decision is made to proceed with surgery, modifications in the anesthetic technique include added hydration, use of an antismialogogue, avoidance of endotracheal intubation, humidification of the anesthetic circuit, and the use of regional techniques [29]. Tait and Malviya [26] proposed an algorithm for managing the child who has a URI (Fig. 1). Factors considered include the urgency of the procedure, the likelihood that symptoms are due to an infectious etiology, the severity of symptoms, the planned mode of anesthesia administration, potential risk factors for respiratory complications, and related nonmedical factors.
Cardiac complications

Although perioperative cardiac events are less common than adverse respiratory events, they are associated with significantly higher morbidity and mortality. The Pediatric Perioperative Cardiac Arrest (POCA) Registry was established in 1994 to identify risk factors for perioperative cardiac events and to develop strategies to reduce them [30]. In 2000, 289 cardiac arrests were reported to the POCA Registry [31]. Nearly half of these events (48%) were unrelated to anesthesia, occurring most commonly among children who failed to wean off bypass or who had early post-bypass heart failure or uncontrollable surgical bleeding. The incidence of anesthesia-related cardiac arrests was 1.4 events per 10,000 instances. Events related to medications or to cardiovascular events were most common [32]. Medication-related events were most often associated with the use of halothane and were more common among children who had an ASA physical class 1 to 2 than those with higher ASA classes. Although most (55%) anesthesia-related cardiac arrests occurred in infants younger than 1 year, sufficient data were not
available to control for factors such as prematurity and congenital defects that may have had a confounding effect. Death occurred in 26% of children who had an anesthesia-related cardiac arrest. Independent factors associated with mortality included undergoing an emergency procedure and having an ASA physical class greater than 2, but did not include age [31].

Based on observations made from POCA Registry data, several strategies may help prevent cardiac arrest in children (see Table 1). Because medications are the leading cause of perioperative cardiac arrest, the medications used should carefully considered, particularly in infants [32]. Halothane was commonly used in anesthetic practice in the past because of its nonpungent effects that limited the potential for airway irritation. For this reason, it was the agent of choice for the inhalation induction of anesthesia in infants and children for many years. It has potent negative inotropic and chronotropic effects, which can lead to profound hypotension and bradycardia. These effects can be more problematic in dehydrated infants who had been nil per os for prolonged periods. Recently, sevoflurane has been introduced as an acceptable alternative that has fewer cardiovascular effects than halothane and is especially useful in the neonatal and infant populations who are at the greatest risk for halothane-induced cardiovascular depression.

Because of the importance of cardiovascular mechanisms as a cause of arrest, children who have cardiac disease must be identified preoperatively to appropriately modify the anesthetic plan. Although cardiac anomalies may already be known, occult defects may be found only at the time of the preoperative evaluation. One way that these defects are found is by the detection of a cardiac murmur. When a murmur is found, the main consideration is to identify occult cardiac lesions that (1) may have hemodynamic consequences during surgery (eg, pulmonary artery hypertension or left-to-right shunts) or (2) have no hemodynamic consequences but require administration of antibiotic prophylaxis (eg, a small ventricular septal defect). All infants younger than 1 year who have a murmur should undergo formal evaluation by a cardiologist before surgery because a significant cardiac lesion may have not yet become clinically apparent [33]. Most older children who have an “innocent” murmur without symptoms or signs of cardiovascular disease can safely undergo surgery. A preoperative cardiology evaluation is recommended for those discovered to have other types of murmurs or who have symptoms or signs of cardiovascular disease. Antibiotic prophylaxis should be considered before an emergency procedure not classified as clean when the etiology of the murmur is unclear [33].

**Perioperative anxiety**

Although uncommonly associated with major morbidity, perioperative anxiety and emergence delirium are disturbing for patients and their families. Significant anxiety is observed in as many as 65% of children before
surgery and during induction [34]. In addition to leading to potential delays in induction, high levels of preoperative anxiety appear related to the development of emergence delirium and the postoperative development of new maladaptive behaviors and negative behavior changes, including general anxiety, separation anxiety, sleep anxiety, eating disturbances, aggression, and apathy/withdrawal [35]. Risk factors associated with perioperative anxiety include younger age, parental anxiety, lower social adaptive capabilities, and a temperament with low sociability [3].

Preoperative interventions to reduce anxiety are appropriate, particularly for children at risk (see Table 1). Preoperative preparation programs are now available in most hospitals but vary in content and approach [36]. These programs include child life preparation (coping skills instruction), modeling using a videotaped program, play therapy, tours of the operating room, and written materials [37]. Among these interventions, coping skills instruction is the most effective for reducing preoperative anxiety but also the most expensive to employ. Although child life preparation effectively reduces anxiety in the preoperative holding area and on separation from parents, this intervention has little impact on anxiety during induction, in the recovery room, or after hospital discharge [38]. Some methods of preoperative preparation such as modeling and operating room tours may increase perioperative anxiety, particularly among younger children and previously hospitalized children. For this reason, preoperative preparation must be modified to meet the needs of each child [37].

A common method that is used to decrease perioperative anxiety is allowing a parent to be present with the child during induction of anesthesia. This practice has significantly increased in the United States during the past decade [39]. The potential benefits include avoiding the need for premedication, avoiding the child’s resistance to separation from parents, and decreasing perioperative anxiety and postoperative behavioral problems related to perioperative anxiety [37]. Although initial studies suggested that parental presence effectively reduced anxiety, more recent evidence suggests that this practice should be selectively applied and requires proper parental preparation to be effective. Children who most benefited from parental presence were those older than 4 years who had either a calm baseline personality or a mother who had a calm baseline personality [40]. To be effective, parents need to learn effective support techniques such as the use of distraction [41]. Although it has limitations, presence during induction is viewed favorably by parents; most believe that they have contributed to reducing their child’s stress [42]. Compared with premedication with oral midazolam, however, parental presence during induction was found to be less effective at reducing anxiety [43]. The addition of parental presence did not significantly reduce anxiety more than using premedication alone [44]. Despite the appeal of parental participation for many parents, it is likely that parental presence will be applied more selectively and effectively in the future [37].
Postoperative management

Overview

Although outpatient surgery is appropriate for many pediatric surgical procedures, the surgical team needs to be alert to postoperative complications that require further management. Perioperative events may be identified in the hospital, leading to a prolonged recovery room stay or direct hospital admission. Other problems are identified only after discharge from the same-day surgery unit and require return to the hospital for admission. In a study of 3331 children undergoing day surgery, 130 (4%) had a prolonged recovery room stay and 61 (2%) were admitted to the hospital [45]. The main reasons for prolonged recovery room stays were nausea and vomiting or respiratory complications. Most children who had these complications recovered and were sent home, but 14% required admission to the hospital for further management. The most common reasons for unplanned hospital admission for the same-day surgery unit were respiratory complications or surgical reasons (including the surgeon’s desire for a longer period of observation or a more extensive surgical procedure than planned). Although the ASA physical status of children did not differ between those who had a prolonged recovery room stay and those who did not, children admitted to the hospital after day surgery had a higher ASA physical status than those who were discharged. Although most children have an uneventful recovery after day surgery, the possibility of admission after day surgery should be communicated to families, particularly for children who have higher ASA physical status [45].

Postoperative nausea and vomiting

Although postoperative nausea and vomiting (PONV) is rarely associated with significant morbidity, it is the most frequent complication in the recovery room and is distressing to the child and parents [22]. Independent predictors of PONV include older age, duration of surgery more than 30 minutes, history of motion sickness, history of postoperative vomiting in the child or the child’s immediate family, and strabismus surgery [46]. Management strategies used to reduce PONV include an alteration in the anesthetic technique to eliminate emetogenic factors and pre-emptive treatment strategies (see Table 1). Effective control of PONV begins with the elimination of factors or medications that may increase its incidence. Although not extensively studied in the pediatric population, experience in the adult population has demonstrated that specific anesthetic induction agents (etomidate, ketamine) and maintenance agents (nitrous oxide) increase the incidence of PONV. With the advent of shorter-acting, less soluble anesthetic agents such as sevoflurane or desflurane, the addition of nitrous oxide to the maintenance anesthetic adds little to ensure a rapid awakening. In addition, propofol (for anesthetic induction, maintenance, or just before
emergence) can be added to the anesthetic technique to reduce PONV. Other risk factors for PONV include the reversal of neuromuscular blocking agents and the use of perioperative opioids. For many of the outpatient pediatric surgical procedures, postoperative pain can be effectively managed with a regional anesthetic technique (caudal or peripheral block) and acetaminophen or NSAIDs, thereby decreasing the need for opioids. In many centers, routine pre-emptive antiemetics (5-HT3 antagonists such as ondansetron) are used. In adults, small doses of dexamethasone have been shown to lessen the incidence of PONV when used alone and have a synergistic effect when administered with agents such as ondansetron. Alternatively, agents such as ondansetron or phenothiazines can be used to treat PONV when it occurs. Although phenothiazines are effective, adverse effects such as dystonic reactions, hypotension, sedation, and respiratory depression have limited their perioperative use in some centers.

Postoperative pain management

The past 20 years have seen many changes in the understanding and treatment of acute pain in infants and children. The first step was to disprove the previously held misconceptions that neonates, infants, and children did not feel or react to pain like adults. This belief was based on the misconception that the immaturity of the central nervous system of infants made them less likely to perceive pain. This theory, compounded by fears of addiction and adverse effects from opioids, resulted in the inadequate treatment of pain. Recent studies have shown that infants and children experience a severity of postoperative pain similar to adults and that even premature infants demonstrate alterations in heart rate, blood pressure, and oxygen saturation in response to painful stimuli [47].

Considerations in the treatment of acute pain include the severity of the pain and the setting in which it is treated (inpatient versus outpatient). One approach is to use a three-step ladder (Box 1), initially described by the World Health Organization for the treatment of cancer-related pain [48]. Mild pain such as that following a soft tissue surgical procedure is initially treated with a nonopioid analgesic agent such as a prostaglandin synthesis inhibitor (acetaminophen, acetylsalicylic acid, or ibuprofen). Moderate pain such as that following a bony orthopedic procedure can usually be controlled with a combination of a prostaglandin synthesis inhibitor and a weak opioid (eg, a preparation of acetaminophen with codeine) for the outpatient or intravenous opioids or a regional anesthetic technique for the inpatient. More severe pain (thoracotomy or an exploratory laparotomy) generally requires a regional anesthetic technique or parenteral opioids. NSAIDs, acetaminophen, and salicylates act through the inhibition of the enzyme cyclooxygenase, thereby blocking the synthesis of prostaglandins that stimulate the free nerve endings of the peripheral nervous system. In distinction to opioids, these agents demonstrate a ceiling effect so that after a specific
plasma concentration is achieved, no further analgesia is provided by increasing the dose. A more comprehensive review of the prostaglandin synthesis inhibitors can be found in other sources [49]. Those that are used most commonly in children and their various preparations are listed in Table 2.

Prostaglandin synthesis inhibitors can be used as the sole agent for minor pain, may be combined with weak opioids for oral administration to control moderate pain, and may be added to parenteral opioids and regional anesthetic techniques for severe pain. Its addition to opioids provides adjunctive analgesia and lowers the total amount of opioid required [50,51]. Because most opioid-related adverse effects are dose related, modalities that decrease total opioid consumption play a significant role in decreasing or preventing opioid-associated adverse effects. A technique used frequently by Tobias and colleagues [52] in the perioperative setting is the combination of the oral premedication (midazolam) with acetaminophen (15 mg/kg) or ibuprofen elixir (10 mg/kg). If preoperative administration is not chosen, then an acetaminophen suppository (40 mg/kg) can be placed following anesthetic induction. Because absorption is decreased with rectal administration, a larger dose of acetaminophen is required to achieve effective plasma levels [53]. A third option is the postoperative administration of ibuprofen or acetaminophen when the child complains of pain in the recovery room. This latter option is less desirable because the onset of activity of any of these agents following oral or rectal administration is 20 to 30 minutes. The

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**Box 1. The World Health Organization ladder for pain treatment**

*Mild pain*
1. NSAIDs
2. Acetaminophen

*Moderate pain*
1. NSAIDs or acetaminophen with a weak opioid (oxycodone, hydrocodone, codeine)
2. Intravenous opioids (with addition of fixed-interval NSAID or acetaminophen)
   A. Intravenous opioid by patient-controlled analgesia (PCA)
   B. Continuous infusion of opioid with as needed rescue doses of opioid
   C. Fixed-interval dosing of opioid
3. Regional anesthetic techniques

*Severe pain (continue use of NSAID or acetaminophen)*
1. Intravenous opioid by PCA
2. Regional anesthetic techniques
administration of a small dose of an intravenous opioid (fentanyl, 0.5 μg/kg; morphine, 0.02 mg/kg; or nalbuphine, 0.02–0.04 mg/kg) can be used to provide immediate analgesia while waiting for the onset of the oral/rectal acetaminophen or ibuprofen. When the patient is ready for discharge home, ongoing analgesia can be provided with acetaminophen or ibuprofen. Although it is most common to administer these agents on an “as-needed” basis, fixed-interval dosing may provide more effective analgesia. This process entails administering the medication around the clock for the first 24 to 48 hours and not waiting for the child to complain of pain. For this purpose, acetaminophen (10–15 mg/kg) every 4 hours or ibuprofen (10 mg/kg) every 6 hours can be used. If the patient is receiving acetaminophen as a fixed-interval dose and complains of pain, an “as needed” or supplemental dose of ibuprofen can be administered and vice versa. These techniques can be used for all types of acute pain.

When moderate pain needs to be treated on an outpatient basis or when the first step of the ladder fails in what was thought to be mild pain, the NSAID, aspirin, or acetaminophen can be combined with a weak opioid (codeine, oxycodone, or hydrocodone), which are available in tablet and liquid formulations. Acetaminophen with codeine elixir contains 120 mg of acetaminophen and 12 mg of codeine per 5 mL. Dosing is based on the codeine component, ranging from 0.5 to 1.0 mg/kg every 4 to 6 hours. Tablet preparations contain 325 mg of acetaminophen with 15, 30, or 60 mg of codeine. Codeine is metabolized by hepatic microsomal enzymes to morphine for a significant part of its analgesic effect. In a cohort of 96 children, Williams and colleagues [54] reported that 47% had genotypes associated with a reduction of the activity of the enzymes necessary for the conversion of codeine to morphine and that no morphine or metabolites were detected in 36% of the patients given codeine. Alternatives to codeine for oral administration include oxycodone or hydrocodone preparations, which are also

<table>
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<tr>
<td>Ibuprofen</td>
<td>Oral suspension</td>
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<td></td>
<td>Infant drops</td>
<td>50 mg/1.25 mL</td>
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<td></td>
<td>Chewable tablets</td>
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<td>Children’s caplets</td>
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<td>Tablets</td>
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<tr>
<td>Choline magnesium</td>
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<td>trisalicylate</td>
<td>Tablets</td>
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<td>Naproxen</td>
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<tr>
<td>Tolmetin</td>
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</tr>
<tr>
<td></td>
<td>Capsules</td>
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<tr>
<td>Acetylsalicylic acid</td>
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</table>
available in liquid and tablet forms with acetaminophen or acetylsalicylic acid. Hydrocodone (7.5 mg) combined with 200 mg of ibuprofen is also available as a tablet. The dose should be based on the oxycodone or hydrocodone component, starting at 0.1 to 0.15 mg/kg every 4 to 6 hours. Regardless of the preparation used, increasing the dose may result in exceeding the amount of recommended acetaminophen (15 mg/kg/dose or 60–90 mg/kg/d).

In patients who cannot tolerate or will not accept oral or rectal medications, intravenous administration is possible with ketorolac, a parenteral NSAID. When first released, the initial clinical trials suggested that ketorolac was as effective as opioids in treating acute pain; however, its current clinical use is similar to that of other NSAIDs as an adjunct to opioid analgesia [55]. Because ketorolac is more expensive than nonparenteral NSAIDs, future studies are needed to determine its advantages over more inexpensive agents and routes of delivery (oral or rectal) in various acute pain situations. The authors’ current practice includes fixed-interval administration of ketorolac for the initial postoperative period or immediately following the acute pain issue, with the switch to acetaminophen or ibuprofen after the patient is able to tolerate oral or rectal medications. In the adult population, a ceiling effect has been reported so that no further analgesia was noted with doses of ketorolac higher than 7.5 to 10 mg [56]. Although there are no comparable studies in pediatric-aged patients, the authors’ current practice includes dosing at 0.5 mg/kg up to a maximum of 10 mg every 6 hours. After the patient is able to tolerate oral medications, the switch is made to an oral NSAID or acetaminophen. Ketorolac is contraindicated in patients who have bleeding dyscrasias or in settings in which acute hemorrhage is a concern (eg, in patients who have abnormal coagulation function, in the trauma patient, or following intracranial or ENT surgery).

Opioids may act as pure agonists (bind and activate both µ and κ receptors) or as agonists/antagonists (bind and activate κ receptors while binding to but not activating µ receptors). Agonists/antagonists including nalbuphine, butorphanol, and pentazocine should not be administered to patients who have been chronically receiving opioids because these can precipitate withdrawal symptoms or reverse analgesia. Although these agents have a decreased potential to cause respiratory depression, there is also a ceiling effect for their analgesia. With dose escalation for increasing or persistent pain, there is a limit to the amount of analgesia achieved. Their potency and efficacy for severe pain is less than that of pure agonists. They may be useful for mild to moderate pain when oral administration of other agents such as acetaminophen with codeine is not feasible or when a more rapid onset of action is desired. The authors’ practice frequently includes the intravenous administration of a single dose of these agents to treat moderate pain in the postanesthesia area, followed by the switch to oral agents when the patient is discharged home. An additional benefit of a drug such as nalbuphine is that it causes more sedation than other opioids and may be beneficial for the agitated postoperative patient. The agonists/antagonists should also be
considered when supplemental intravenous analgesia is required in patients who are receiving or have received epidural or intrathecal opioids within the last 24 hours (see Tobias [49] for a full discussion of neuraxial opioids). The respiratory depression that can occur with the combination of intravenous and neuraxial opioids may be less if an agonist/antagonist is used rather than a pure agonist such as morphine. In these situations, the authors’ practice is to administer incremental doses of nalbuphine (0.02–0.03 mg/kg) every 5 to 10 minutes as needed until the desired level of analgesia is achieved.

When opioids are chosen for postoperative analgesia, three choices must be made: (1) which opioid to use, (2) the mode of administration, and (3) the route of administration. Respiratory depression is similar if equipotent doses are administered. The authors’ practice is to use morphine or hydromorphone. Meperidine is generally avoided given its higher incidence of dysphoric reactions and the potential for seizures related to the accumulation of the metabolite normeperidine. Morphine is metabolized in the liver to morphine-6-glucuronide, which is significantly more potent than the parent compound. Morphine-6-glucuronide is water soluble, penetrates the central nervous system poorly, and is of little consequence in most circumstances. It is cleared by the kidneys and can accumulate in patients who have renal insufficiency, resulting in respiratory depression. In such patients, alternative opioids such as hydromorphone (see later discussion), which has no active metabolites, should be considered. Hydromorphone may also be advantageous when adverse effects related to histamine release, such as pruritus, occur with morphine, which may be more common in adolescents and young adults.

The second decision regarding opioid analgesia is the mode of administration. Options include on demand (as-needed dosing), fixed-interval administration, continuous infusion, or patient-controlled analgesia (PCA) pumps. For optimal analgesia, opioids should be administered in a manner that maintains a steady-state serum concentration. For moderate to severe pain, on-demand administration generally does not provide adequate analgesia because of the delay in obtaining the medication. The optimal mode for the delivery of opioids remains PCA. PCA allows the patient to administer a preset amount of opioid at specific intervals. These devices may be used in children as young as 5 to 6 years [57,58]. Before instituting PCA administration of narcotics, pain must be controlled. An opioid is titrated in small, intravenous bolus doses (morphine 0.02 mg/kg every 5 minutes) to the desired level of analgesia before the PCA device is started. Its use may be limited in certain patients due to age, underlying illness, or mental capabilities. Many centers still use PCA in these types of patients, but allow the device to be activated by the bedside nurse. In this setting, the PCA device eliminates the delay in opioid administration that occurs while the nurse signs out the medication and draws it up. Murphy and colleagues [59] showed equivalent levels of analgesia and equivalent opioid consumption for PCA compared with nurse-controlled analgesia.
Regional anesthetic technique is an alternative that continues to increase in popularity. Depending on the site of surgery and the severity of the postoperative pain, this may include a neuraxial approach (caudal, lumbar, or thoracic epidural) or a peripheral nerve block. For unilateral surgery, a peripheral nerve block may be chosen. For outpatients, a single shot approach using only local anesthetic agents is used, such as a caudal epidural block with bupivacaine following inguinal herniorrhaphy. For the inpatient, more prolonged analgesia can be provided by a single shot approach using a combination of local anesthetic with opioid (morphine) or clonidine or by the placement of a catheter for a continuous infusion. Whenever neuraxial opioids are administered, ongoing monitoring of respiratory status is suggested given the potential for respiratory depression.

Summary

The safety of surgery and anesthesia for infants and children has improved over the past several decades. Same-day surgery is now feasible for most pediatric surgical procedures and has been widely adopted. The focus of preoperative management should be to identify children at high-risk for complications that are common and complications that are less common but potentially life-threatening. Psychologic preparation of children and their families is essential to reduce preoperative anxiety and the likelihood of short- and long-term adverse psychologic responses to surgery. Although additional work is needed, we have a better understanding of factors associated with major and minor adverse events that occur intraoperatively and postoperatively.

References


