Preoperative evaluation, premedication, and induction of anesthesia in infants and children

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Purpose of review
Preparation for and induction of anesthesia in children has evolved significantly over the last decade, with particular reference to the reduction of perioperative anxiety reduction by nonpharmacologic and pharmacologic means. Several new large population studies and meta-analyses further scrutinize the current techniques.

Recent findings
Many nonpharmacologic methods to reduce anxiety are effective λU similar to sedative premedications, with the exception of parent present induction of anesthesia. Healthcare providers can be taught to increase anxiety-reducing behaviors through an educational intervention. Clonidine and dexmedetomidine have many similar or superior qualities to midazolam.

Summary
Larger studies still need to be conducted before wide-scale application of many nonpharmalogical interventions such as parental acupuncture. Similarly, more investigation should be done on outcomes such as onset, emergence, and discharge times, as well as the postoperative response with reference to emergence delirium and postoperative nausea and vomiting prevention to outline the differences among sedative premedications such as midazolam, clonidine, and dexmedetomidine.

Keywords
clonidine, dexmedetomidine, perioperative anxiety

INTRODUCTION

Recently, many publications have advanced the science of anesthesia with regard to the preparation for and induction of anesthesia by adding to years of vast research on the topic. Several of the newer studies have included large populations and meta-analysis of smaller studies, increasing the power of the data and the generalizability of individual findings. Particular advancements have been in correlation between preoperative status and intraoperative complications, nonpharmacologic reductions of preoperative anxiety, and critical evaluation of newer sedative premedicants, as well as evaluating the incidence of complications for induction techniques.

PREOPERATIVE EVALUATION

An important addition to common preoperative evaluation included a large study examining 9297 preoperative questionnaires and intraoperative records to look for associations between preoperative status and respiratory events [1▪]. This study used an extensive modification of the International Study Group for Asthma and Allergies in Childhood questionnaire to look at ordinary predictors such as upper respiratory infection, but also evaluated the history of eczema, as well as family history of asthma, or smoking as risk factors for intraoperative events. The authors found an association between preoperative coughing, asthmatic episodes, and eczema with preoperative airway complications such as bronchospasm, laryngospasm, and desaturation, which, however, very rarely were severe. Limitations of the study included potential reporting bias of the parents during the preoperative questionnaire, anesthesiologists not blinded to

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KEY POINTS

- Although many nonpharmacologic methods to reduce anxiety are effective, parent present induction of anesthesia has not been shown to reduce anxiety or improve cooperation.
- Healthcare providers can be trained to increase anxiety reducing behaviors and decrease anxiety increasing behaviors for their pediatric patients.
- Clonidine and dexmedetomidine have many promising sedative properties similar or superior to midazolam but have long onset times.

questionnaire findings, widely varying forms of anesthetic management, and different levels of anesthesia providers.

PREMEDICATION

When discussing premedication, one of the areas that must be considered first is that of nonpharmacologic interventions. There has been no shortage of interest and research on this essential subject. A large Cochrane review of the topic by Yip *et al.* [2▪▪] included 17 trials, involving 1796 children, parents, or both for any nonpharmacological intervention implemented on the day of surgery compared with any other intervention, or no intervention. The review included trials of parental presence (including presence of an anxious parent), clown doctors, interactive cartoon computer packages, midazolam, handheld video games, hypnotherapy, decreasing sensory stimulation at induction, music therapy, and relaxational parental acupuncture. According to their analysis, parental presence during induction of anesthesia in children has not been shown to reduce anxiety or improve cooperation of children. Other interventions such as parental acupuncture, clown doctors, hypnosis, low sensory stimulation, and handheld video games appear to be helpful in reducing children's anxiety and improving their cooperation during induction of general anesthesia, but large randomized controlled trails are needed.

These findings are consistent with smaller studies. Although it has been reported that parents and children prefer to stay together during procedures such as lumbar puncture, immunizations, and induction of anesthesia [3], obvious drawbacks include concerns about disruption of the operating room routine, crowded operating rooms, and parents' possible adverse reactions [4]. In addition, increased parental anxiety can result in increased child's anxiety, prolonged anesthetic induction, and additional stress on the anesthesiologist, especially if a complication develops.

Both parent and nursing specific behaviors can reduce anxiety, while certainly others increase distress [5–7]. For instance, using nonprocedural and distracting talk, humor, giving actual choices to child with clear limitations, and medical reinterpretation of visible equipment reduces anxiety. Many of these behaviors are intuitive and displayed often. However, so are many of the undesirable behaviors, such as using reassuring, apologetic, and empathetic statements, which likely lead to the results described by Yip. Unfortunately, these behaviors that increase distress in patients are similar to giving implied, unlimited choices offered to child, medical reinterpretation of nonvisible equipment, and excessive talk. Luckily, specific methods can teach anesthesiologists to increase desired behaviors and decrease undesired behaviors associated with anxiety in a new study by Martin *et al.* [8▪▪]. An intervention, Provider-Tailored Intervention for Perioperative Stress, was developed to train healthcare providers to increase behaviors that promote children's coping and decrease behaviors that may exacerbate children's distress. Rates of healthcare provider behaviors were coded and compared between preintervention and postintervention. Also, rates of parents' behaviors were compared between those that interacted with healthcare providers before training to those interacting with healthcare providers after the intervention. The intervention successfully modified both healthcare and parent behaviours, and a larger study is now underway to launch the training method at several centers.

Training for healthcare providers is particularly helpful, as 83.5% of all pediatric surgical procedures in the USA are on an outpatient basis, which does not allow the opportunity for in-hospital preoperative preparation for anesthesia [9]. In order to address this issue, an abbreviated preparation program on the day of surgery is frequently used, but this is not a practical solution because of production pressures on the day of surgery and the very limited time with families on the day of surgery (e.g. 1–4 min). Martin's study showed that parents mimicked the healthcare provider behaviors, which means that training the provider has extended impact beyond just what it can accomplish to reduce the stress directly for the patient.

Another interesting area of study is that of preoperative anxiety in teens [10▪]. This subgroup of pediatric patients has not been exclusively studied and has many complex psychosocial behaviors that might confound research if they are included with younger pediatric patients. For instance, teens may exhibit less of a relationship between observable

measures of anxiety and physiological indices such as heart rate and skin conductance. Despite an outward appearance of calmness, over 80% of adolescents reported significant anxiety at the time of induction, which had steadily increased from the preoperative holding area to the induction. Self-reported anxiety increased significantly at each time point (holding, separation from parents, and mask introduction), with significant increases in both heart rate and skin conductance were found from holding to mask introduction. They also found several risk factors to predict higher anxiety at mask introduction, including baseline anxiety and depression, somatizing problems, and fearful temperament.

Despite many advances in nonpharmacologic interventions, practitioners still rely on sedative premedicants. The rate of sedative premedication use for the treatment of preoperative anxiety in the USA varies widely among age groups and geographic locations [11]. Historically, the most commonly used premedicant for children in the preoperative holding area is midazolam, usually dosed 0.5 mg/kg orally. Other common medications in the past have included ketamine, transmucosal fentanyl, and meperidine [4], but newer favorites have been α2-antagonists clonidine and dexmedetomidine [12]. Midazolam has been shown to produce anterograde amnesia in as little as 10 min [13] and increase parental satisfaction [14]. A recent study showed that midazolam reduced the amount of required propofol and provides a more favorable environment for insertion of laryngeal mask airway (LMA) [15]. This is consistent with the prior studies which found that propofol infusion requirements decrease by one-third which may be because of synergism of propofol and midazolam on γ-aminobutyric acid receptors [4].

There have been conflicting results about midazolam's effect on emergence times, discharge times, emergence delirium, postoperative behavior disturbances [16], and the debate about its use rages on. Because the majority of pediatric surgical patients are treated on an outpatient basis, the concerns about delays in emergence or discharge times coupled with an emphasis on selecting a premedication that will allow for efficient utilization of the operating room may pressure anesthesiologists to premedicate pediatric patients inadequately [4].

Clonidine is an α2-adrenergic agonist that was found to have analgesic, anxiolytic, and sedative properties [17,18] over a decade ago. At that time, orally administrated clonidine at a dose of 4 μg/kg was reported to cause sedation, decrease anesthetic requirements, and decrease requirement for postoperative analgesics [17,18]. Preoperatively administered clonidine has been reported to be as effective as intraoperatively administered fentanyl (3 μg/kg) for postoperative analgesia in children undergoing tonsillectomy [19]. However, the data regarding these issues have been controversial and were recently addressed in a meta-analysis [20▪▪]. Ten publications fulfilling the inclusion criteria were analyzed and it was found that premedication with clonidine, in comparison with midazolam, exhibited a superior effect on sedation at induction, decreased the incidence of emergence agitation, and produced a more effective early postoperative analgesia. However, the superiority of clonidine for postoperative nausea and vomiting (PONV) prevention remains unclear, because nausea prevention was not used in some of the studies included in the analysis (even for strabismus surgery) and this might interfere with the interpretation of the results. All studies included in the meta-analysis studied minor and short-duration ambulatory surgery, so patients' recovery and discharge were not evaluated in the included studies. Consequently, no recommendation could be drawn concerning the use of clonidine during ambulatory surgery. Similarly, multiple factors introduced heterogeneity in this meta-analysis, so its broad application cannot be ensured.

Previously, Fazi *et al.* [21] compared the effects of oral clonidine (4 μg/kg) and midazolam (0.5 mg/kg) on the preoperative sedation and the postoperative clinical recovery process of children undergoing tonsillectomy. Their findings were quite the opposite of the meta-analysis, showing children in the clonidine group exhibiting higher levels of anxiety preoperatively, with lower mean arterial pressures intraoperatively and postoperatively, greater opioid requirements, and higher maximum excitement and pain scores. Also, there were no differences between the groups with regard to discharge readiness or postoperative emesis. Therefore, the investigators concluded that oral midazolam is a better sedative for the children undergoing tonsillectomy.

Also, one major drawback to the use of clonidine as a sedative premedicant is its slow onset of action [21]. Clonidine must be administered orally 60–90 min before surgery. In fact, an earlier study [17] recommended that children be separated from their parents 105 min after oral clonidine administration. This is a major disadvantage in a busy operating room setting, especially in ambulatory surgery centers.

Dexmedetomidine is another α2-adrenergic agonist, with increased specificity over clonidine [22]. With administration, it produces sleep or drowsiness, but maintains ease of arousability and cooperation once aroused [12]. The sedation is dose-dependent and there is minimal respiratory depression, even at

large doses. Dexmedetomidine has a shorter duration of action than clonidine but may be more suitable as premedication, especially in ambulatory surgery. Dexmedetomidine has a low bioavailability when given orally (15%) but may be more effective when given intranasally. Yuen [23] also found 1 mg/kg of intranasal dexmedetomidine was more effective as a sedative than 0.5 mg/kg oral midazolam [22] when both medicines were given in acetaminophen syrup. Dexmedetomidine has a slow onset time of 30–45 min [24], which is still shorter than that of clonidine. The duration of sedation was 85 min. Dexmedetomidine and clonidine may have similar efficacy to midazolam in producing sedation, but the α2-adrenergic agonists may have some advantages in avoiding respiratory depression, providing analgesia, fewer paradoxical reactions, and less agitation on arousal [12]; however, the long onset time could remain a problem for their use clinically.

INDUCTION

Moving past preinduction anxiety management, one discovers a thorough study of induction. Using electronic medical record database query, a new study evaluated 1070 children who underwent a rapid sequence induction (RSI) at a single institution over a 5-year period to determine the incidence of complications of this anesthetic technique [25▪]. Of over 1000 patients aged 3–12 years, 20 (1.9%) developed moderate hypoxemia (SpO_2 80–89%), 18 (1.7%) demonstrated severe hypoxemia (SpO_2 <80%), five (0.5%) developed bradycardia (heart rate <60), and eight (0.8%) developed hypotension (systolic blood pressure <70 mmHg). Only one patient had emesis of gastric contents, but no evidence of pulmonary aspiration or hypoxemia was seen. Eighteen (1.7%) children were noted to be difficult to intubate and required more than one intubation attempt, but all were eventually intubated without significant complications. A subgroup analysis showed that children between 10 and 19 kg had a higher incidence of severe hypoxemia when compared to older children. There were no long-term or permanent complications. The study was limited to children over 3 years, because the authors felt that a large proportion of emergency cases were above the age of 3 and that inclusion of younger children would necessarily involve anatomic and physiological airway changes that would be inconsistent with an older pediatric population.

Other publications about the induction of anesthesia included a timely discussion of childhood obesity [26] and its pathophysiology and implications for anesthesia, particularly during induction. The prevalence of obesity in children is increasing, with approximately 20% of European and 32% of American children and adolescents currently overweight. This epidemic carries increased risks for perioperative complications of airway management and ventilation. The authors make the following suggestions for mitigating risks during induction: positioning 25° head up in older children, preoxygenating for 3 min, mask ventilation with positive end-expiratory pressure (PEEP) 10 cm H_2O, desufflating stomach, having equipment for difficult intubation at hand, tracheal intubation or LMA as indicated by type of surgical procedure, and prevention of atelectasis with PEEP.

CONCLUSION

Exciting frontiers remain, with particular reference to perioperative anxiety reduction by both nonpharmacologic and pharmacologic means. For areas such as parental acupuncture, hypnosis, low sensory stimulation, and handheld video games, large randomized controlled trials are needed. Similarly, we await the result of the large-scale application of the healthcare provider behavior modification intervention. These modifications of proximal factors [9,27,28] of distress could provide a more favorable risk/benefit ratio than sedative premedicants, but issues related to time and cost cannot be ignored.

The administration of sedative premedication to appropriately selected children who are about to undergo anesthesia and surgery can result in beneficial effects during the preoperative and postoperative periods by decreasing anxiety, increasing cooperation during anesthesia induction, and reducing negative postoperative behavioral responses in children [4]. The choice of the individual sedative premedication will vary widely based on the patient's age, ideal body weight, comorbidities, emotional level, personality, anesthetic history, the surgical procedure, and duration. To further elucidate the differences and superiority of different premedications, more investigation should be done on outcomes such as onset, emergence, and discharge times, as well as the postoperative response with reference to emergence delirium and PONV prevention.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 393).

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