Adenotonsillectomy (AT) is one of the most common surgical procedures performed in children internationally. Historically, it was used to treat children with chronic tonsillitis; however, today most children presenting for AT have sleep-disordered breathing and obstructive sleep apnea syndrome (OSAS) caused by tonsillar hypertrophy. Perioperative respiratory adverse events (PRAEs) are common complications after AT, and an increase in childhood obesity is associated with an increase in the incidence of upper airway obstruction and sleep-disordered breathing, further complicating perioperative medication management.

Preoperative pharmacologic anxiolysis is frequently administered in young children, most commonly the benzodiazepine midazolam or, more recently, the α-2 agonist dexmedetomidine. Both medications are available as intranasal formulations, which is beneficial for administration to pediatric patients without intravenous access before inhalational induction. Combined with analgesics, including opioids, and anesthetics, these anxiolytics may further contribute to increased incidence of PRAEs; however, observational and retrospective studies have been inconclusive or contradictory. Thus, Shen et al conducted a double-blinded, randomized clinical trial in 384 children undergoing AT to compare the incidence of PRAEs after preoperative intranasal administration of midazolam, dexmedetomidine, or saline (control). The intention-to-treat analysis demonstrated a higher incidence of PRAEs in the midazolam group (56.5%) compared with both the dexmedetomidine (24.2%) and saline control (40.8%) groups. No significant differences were observed between the groups at the time of induction of anesthesia.

Comparisons of midazolam and dexmedetomidine for preoperative anxiolysis have been an important topic for discussion in pediatric anesthesiology, particularly with regard to effectiveness and the incidence of emergence delirium. Although both are similarly effective for anxiolysis, the most recent studies favor dexmedetomidine for preventing emergence delirium. In fact, benzodiazepines are independently associated with increased risk of delirium in hospitalized patients. The study by Shen et al takes this comparison a step further to evaluate PRAEs and attempts to control for factors contributing to respiratory complications, excluding obese children and performing all extubations awake at the end of surgery (including extubation in the postanesthesia care unit, which is not routine practice throughout the US). However, the study design and inclusion criteria did not control for key clinical factors that increase the risk for perioperative airway obstruction and respiratory complications. Additionally, the authors hypothesize that preoperative midazolam and dexmedetomidine will reduce the occurrence of PRAEs, in contrast to their preliminary data, which demonstrated 60% incidence of PRAEs with midazolam compared with 20% in the control group.

Children with OSAS are at increased risk for major PRAEs when undergoing AT at a rate 5 times higher than that in children without OSAS. Furthermore, it is well documented that patients with severe OSAS have higher sensitivity to opioids, and it is recommended that opioid dosing be reduced by half in these patients to mitigate respiratory depression. Although Shen et al note different frequencies of OSAS between groups, the severity of disease was not accounted for, and the method for diagnosing OSAS was not standardized. No patient underwent polysomnography, the criterion standard diagnostic test to identify the presence and severity of OSAS. Instead, patients were
designated as having OSAS according to a clinical diagnosis made by the otolaryngologist. Clinical diagnosis of OSAS has poor accuracy, with rates ranging from 30% to 85%. Therefore, the randomized groups may have represented an unequal distribution of patients with severe OSAS because the patient population was not appropriately screened, diagnosed, and controlled for in the analysis.

In addition, this trial did not standardize the perioperative anesthetic medications administered during and after AT. First, it is unknown whether standard medications, like dexamethasone, which is associated with reduced postoperative pain after AT, were administered for all patients. Although the authors describe dexamethasone use for patients undergoing intravenous anesthesia induction, it is unclear whether patients undergoing inhalation induction also received dexamethasone. Second, there is no discussion about the treatments used for children experiencing emergence delirium. Pain and emergence delirium can be challenging to differentiate in children because of the overlap in symptoms, and the diagnostic approach is unclear. Treatment for emergence delirium may include additional dexmedetomidine and/or narcotics, which increase the risk of respiratory depression. Additionally, there was inconsistent administration of reversal agents for neuromuscular blockade. Despite conflicting reports about whether reversal of neuromuscular blockade increases or decreases PRAEs, it is recommended that patients who receive intraoperative neuromuscular blockers receive reversal agents at the conclusion of surgery. Furthermore, dexmedetomidine has mild analgesic properties, and its duration of action exceeds that of midazolam. Shen et al report that patients receiving dexmedetomidine required substantially less fentanyl postoperatively. Therefore, it is possible that fewer patients in the dexmedetomidine group required postoperative fentanyl for analgesia and, therefore, did not experience the opioid respiratory depressant effects. Without standardization of the anesthetic regimen, it is difficult to attribute any postoperative complications to just one preoperative medication.

In summary, the study by Shen and colleagues may highlight more questions than answers. Two of the most important questions when discussing anesthesia and the developing brain are as follows: Is less more? Which outcomes matter most? Nonpharmacologic approaches to preoperative anxiolysis and postoperative emergence agitation are well described. The anxiolytic medications we use are predictable when used alone, but polypharmacy creates complexity in the broad spectrum of children for whom we care. The benefits of dexmedetomidine in pediatric patients with AT may seem clear, but the decision to administer any preoperative anxiolytic should never be automatic. Each and every medication should be carefully considered in the context of the individual child's needs and risks.

ARTICLE INFORMATION
Published: August 9, 2022. doi:10.1001/jamanetworkopen.2022.25482
Open Access: This is an open access article distributed under the terms of the CC-BY License. © 2022 Dalesio NM et al. JAMA Network Open.

Corresponding Author: Sapna R. Kudchadkar, MD, PhD, Department of Anesthesiology and Critical Care Medicine, Division of Pediatric Anesthesiology, Johns Hopkins University School of Medicine, 1800 Orleans St, Baltimore, MD 21287 (sapna@jhmi.edu).

Author Affiliations: Department of Anesthesiology and Critical Care Medicine, Division of Pediatric Anesthesiology, Johns Hopkins University School of Medicine, Baltimore, Maryland.

Conflict of Interest Disclosures: None reported.

REFERENCES

August 9, 2022


