Dexamethasone Administration and Postoperative Bleeding Risk in Children Undergoing Tonsillectomy

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Objective: To assess whether administration of dexamethasone during tonsillectomy is associated with a dose-dependent increased rate of postoperative tonsillectomy hemorrhage.

Design: Retrospective review of 2788 children and adolescents who underwent tonsillectomy with or without adenoidectomy for sleep-disordered breathing or infectious tonsillitis and received perioperative dexamethasone between January 1, 2002, and March 3, 2009. Patients underwent 1 of 3 methods of tonsillectomy, including extracapsular electrosurgical tonsillectomy, extracapsular radiofrequency ablation tonsillectomy, or intracapsular microdebrider tonsillotomy.

Setting: Massachusetts Eye and Ear Infirmary.

Patients: Two thousand seven hundred eighty-eight children and adolescents aged 2 to 18 years (hereinafter referred to as children) who underwent tonsillectomy with or without adenoidectomy.

Interventions: Each child received 1 of 2 distinct intravenous doses of perioperative dexamethasone (0.5 mg/kg or 1.0 mg/kg) based on the protocol of the surgeon who performed the tonsillectomy; other aspects of care, including anesthetic technique, perioperative analgesia, and postoperative care, were equivalent between children.

Main Outcome Measures: Occurrence of postoperative hemorrhage based on 3 severity stratification levels.

Results: Ninety-four of the 2788 children experienced 104 episodes of postoperative hemorrhage. After adjusting for age, sex, primary diagnosis, and surgical technique, the odds ratio of experiencing a postoperative hemorrhage of any severity in children who received the 1.0-mg/kg dose compared with the 0.5-mg/kg dose was 0.66 (95% confidence interval [CI], 0.42-1.05). Children requiring readmission with or without the need for operative intervention demonstrated an adjusted odds ratio of 0.83 (95% CI, 0.51-1.36). An adjusted odds ratio of 0.71 (95% CI, 0.39-1.28) was seen in children requiring operative intervention.

Conclusion: In this observational review of children undergoing tonsillectomy or adenotonsillectomy, perioperative dexamethasone administration is not associated with a dose-dependent elevation of postoperative hemorrhage rates after adjusting for age, sex, primary diagnosis, and surgical technique.


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Dexamethasone has been advocated by the Society for Ambulatory Anesthesia for prevention of PONV in children. Furthermore, survey data suggest that perioperative steroids are widely used, particularly among members of the American Society of Pediatric Otolaryngology, with most surgeons reporting perioperative steroid use for every tonsillectomy. In the United Kingdom, a survey of anesthesiologists reported that 61% routinely use dexamethasone during tonsillectomy procedures. As such, perioperative dexamethasone administration during tonsillectomy has evolved into the standard of care at many institutions, including our own. At a minimum, perioperative dexamethasone administration during tonsillectomy is a commonly accepted practice.

In this context, a recently published randomized trial by Czarnetzki et al regarding the use of perioperative dexamethasone in children undergoing tonsillectomy is of great interest. The premature termination of this trial because of an increased risk of postoperative hemorrhage is contradictory to the widespread opinion that perioperative dexamethasone administration is essentially harmless. The trial raises profound questions with respect to our own standards of care and national and international norms.

The trial by Czarnetzki et al was designed to investigate the effects of perioperative dexamethasone administration on PONV. An interim analysis concluded that the primary outcome of a dose-escalating decrease in PONV had been identified. However, the data also suggested an increased risk of postoperative hemorrhage in children receiving perioperative dexamethasone, resulting in termination of the study. The rates of postoperative bleeding were subsequently reported to range from 2% to 24% in children who received perioperative dexamethasone, compared with 2% to 6% in children who received a placebo. The authors concluded that perioperative dexamethasone administration may be associated with a higher rate of bleeding and called for larger trials to further evaluate this association; in addition, they commented on the potential difficulties in performing such a trial.

Despite a large body of data regarding perioperative steroid therapy for tonsillectomy, minimal attention has been paid to associated hemorrhage rates. A review of posttonsillectomy hemorrhage rates among children in the United States suggests that 2.2% to 7.8% of patients undergoing tonsillectomy experience hemorrhage requiring emergency department evaluation, with 1.3% to 3.3% requiring operative intervention. Data from the United Kingdom, Germany, and New Zealand suggest that, outside the United States, 1.0% to 3.7% of children undergoing tonsillectomy similarly require operative intervention for postoperative hemorrhage control. These findings are clearly disparate from the findings of Czarnetzki et al, despite the widespread use of steroids within these audits.

Although we recognize the value of randomized controlled trials, we believe that important information regarding posttonsillectomy hemorrhage rates may be obtained from observational data. A trial designed to evaluate the hypothesis of a dose-dependent increase in posttonsillectomy hemorrhage associated with perioperative dexamethasone administration would require a large sample size and may be additionally complicated by ethical concerns given the proposed benefits of decreasing PONV vs the potentially life-threatening risk of hemorrhage. As such, a large, well-defined database of surgical data may alternatively prove useful not only to provide further insight into the question at hand but also to help define the utility of conducting such a trial.

Given the discordance between the literature and the results of the trial, we sought to better understand the role of perioperative dexamethasone administration in children undergoing tonsillectomy. At our institution, the 2 senior authors (M.J.C. and C.J.H.) have a long-standing practice of perioperative dexamethasone administration, each surgeon using a different dexamethasone dosing regimen (0.5 and 1.0 mg/kg). Many aspects of our perioperative care are highly protocolized, based on information gained from the combination of a high-volume pediatric otolaryngology operative service and previous joint participation in tonsillectomy studies. As such, few differences exist concerning patient selection, anesthetic technique, and postoperative management. One of the few differences between tonsillectomies performed is the dexamethasone dose. Given this unique position, we undertook a review of our experience with perioperative dexamethasone administration and tonsillectomy in hopes of better evaluating our own outcomes and reassessing the safety of current practices in light of the findings of Czarnetzki et al.

**METHODS**

**DESIGN AND DATA EXTRACTION**

To conduct a retrospective review of our experience with perioperative dexamethasone administration for tonsillectomy, a database was created to identify all children and adolescents (hereinafter referred to as children) who underwent tonsillectomy at the Massachusetts Eye and Ear Infirmary between January 1, 2002, and March 3, 2009. The creation of the database was reviewed and approved by our institutional review board.

The database was constructed in a stepwise fashion. Initially, patients undergoing tonsillectomy were identified from billing data using Current Procedural Terminology codes corresponding to tonsillectomy (42820, 42821, 42825, and 42826), with limits placed on service date and attending surgeon. The service date was limited to those after January 1, 2002, when both staff surgeons (M.J.C. and C.J.H.) were established as members of the full-time faculty. From this query, a primary database identifying all children who underwent tonsillectomy during the period of interest was created that included patient demographics, service dates, attending surgeon, and procedure performed, as well as primary and secondary diagnoses.

Subsequently, the medical record numbers of all children who underwent tonsillectomy were cross-referenced with the medical record numbers of children with diagnostic codes (International Classification of Diagnosis, Ninth Edition) consistent with postoperative hemorrhage or hemorrhage from the throat (998.11 and 784.8) or Current Procedural Terminology codes consistent with control of hemorrhage (42960, 42961, and 42962) to initially identify all children with postoperative hemorrhage. In addition, each record for children undergoing tonsillectomy was searched for an evaluation in our emergency department or an inpatient admission at any time after tonsillectomy. In this group of children, if none of these hem-
orrrhage codes were identified, a manual search of the child's record was performed to identify the occurrence of a postoperative hemorrhage. The final element of the database included identifying the tonsillectomy technique, which was obtained by a query of facility fees associated with disposable items used in tonsillectomy procedures.

STUDY POPULATION

Our study population consisted of all patients aged 2 through 18 years who underwent tonsillectomy with or without adenoidectomy at the Massachusetts Eye and Ear Infirmary between January 1, 2002, and March 3, 2009, by 2 attending physicians (C.J.H. and M.J.C.).

PROCEDURES

All children underwent tonsillectomy within our institution while under general anesthesia. Standard practices for anesthesia in children at our institution include preoperative medication as needed with an oral benzodiazepine, induction with a volatile anesthetic or propofol, and maintenance with volatile anesthetics. Children undergo endotracheal intubation with or without the use of muscle relaxants. Intraoperative and immediate postoperative analgesia is obtained with intravenous narcotics.

Each child receives a perioperative dose of intravenous dexamethasone administered by the anesthesia provider. The magnitude of the dose is determined by the attending surgeon. Each attending surgeon in this report strictly adheres to a protocol based on a combination of existing evidence and personal experience. One surgeon uses a single dose of 0.5 mg/kg of body mass with a maximum dose of 10 mg administered after induction of anesthesia. The other surgeon administers 1.0 mg/kg of body mass with a maximum dose of 40 mg divided over 2 doses, 0.5 mg/kg of body mass with a maximum of 20 mg per dose after induction of anesthesia, and 0.5 mg/kg of body mass with a maximum of 20 mg per dose 6 to 12 hours postoperatively, depending on the child's discharge plan.

During the study period, 3 methods of tonsillectomy were performed by the 2 attending surgeons. Extracapsular tonsillectomy was performed with a standard spatula tip monopolar electrocautery device at a power of 20 W (Vallleylab, Boulder, Colorado) or with a radiofrequency ablation plasma wand designed for tonsillectomy procedures (Arthrocare Corporation, Austin, Texas). Hemostasis was obtained with monopolar electrocautery or the bipolar electrocautery feature of the plasma wand. Intracapsular tonsillectomy was performed with a microdebrider technique using blades specifically designed for this purpose from 1 of 2 microdebrider systems (Gyrus ACM ENT Division, Bartlett, Tennessee, or Medtronic-Xomed, Jacksonville, Florida); hemostasis in these cases was obtained with suction monopolar electrocautery. All children had a gastric tube passed at the completion of the surgery.

On anesthetic emergence and extubation, children were transferred to the postanesthesia care unit for first-stage recovery, until they met admission criteria for transfer to the pediatric floor. Based on a variety of factors, including age and preoperative diagnosis, children were discharged home on the day of surgery or after overnight observation, once they had adequate pain control and tolerated liquids. All children discharged on the day of surgery were observed for a minimum of 6 hours postoperatively. Oral narcotics and oral or rectal acetaminophen were used for analgesia on the floor and at home. No children received nonsteroidal anti-inflammatory drugs (NSAIDs) at any point during their care. At discharge, each family received an instruction sheet that was verbally communicated by the surgeon and the nursing staff outlining postoperative care. Salient points include the complete avoidance of NSAIDs and strict instructions to call our institution or report to our emergency ward for any evidence of bleeding.

PRIMARY OUTCOME

The primary outcome of interest was the number of children experiencing a posttonsillectomy hemorrhage. This outcome was stratified into 3 levels of severity. Level 1 included all children who were reported to have any history of a postoperative hemorrhage, whether or not there was clinical evidence of bleeding. This level included all children with any history of postoperative hemorrhage who underwent evaluation and/or treatment by a physician in the emergency department, inpatient unit, or operating room. Level 2 included all children who required inpatient admission for postoperative hemorrhage regardless of the need for operative intervention. This level of severity excluded children undergoing evaluation in the emergency department for reported postoperative hemorrhage who had no clinical evidence of hemorrhage or clot formation and were deemed safe for discharge. Level 3 included all children who required return to the operating room for control of a posttonsillectomy hemorrhage.

These outcomes were chosen because this method represents a graded severity. Contrary to many reporting systems of postoperative hemorrhage rates, such a graded reporting system provides additional clinical relevance by providing insight into the degree of bleeding that actually occurs and what clinical resources are subsequently consumed. Furthermore, this stratification system provides an observational framework to serve as proxies to the categories reported by Czarnecki et al10 in their trial.

STATISTICAL ANALYSIS

Baseline characteristics compared the group receiving the 0.5-mg/kg dose of dexamethasone with the 1-mg/kg group using Pearson χ2 tests. A 2-sided P < .05 was considered statistically significant.

Given that our primary objective was to compare our observational experience with the findings of a recent randomized trial, we sought to identify and control for all possible confounders for which data were available. Subsequently, a logistic regression model was constructed for each level of the postoperative hemorrhage outcome. Therefore, 3 models were constructed corresponding to the 3 levels of severity described.

Model construction initially determined crude associations based on a simple univariate analysis of dexamethasone dose and the outcomes. In subsequent steps, individual variables were introduced into a bivariate logistic regression model. Continuous and categorical variables were assessed for departures from linear trend by using likelihood ratio tests of logistic regression models considering such variables compared with models using indicator variables. A linear relationship was assumed if P > .10. Confounding was identified by comparing crude and adjusted estimates. Variables were considered confounders if the estimates differed by 10% or more. A multivariate main effects model was then constructed that included the confounding variables. For models in which technique and diagnosis were both found to be confounders, an interaction term was generated. The interaction term was retained in the model if the model fit was improved. Model fit was assessed by the likelihood ratio test of the model including the interaction term to the nested model (P < .10) and Pearson goodness-of-fit test.

The relationship of the dexamethasone dose to outcome was considered not to be significant if P > .05 for the Wald test on
The final multivariate logistic regression model coefficient. All statistical analyses were performed using commercially available software (Stata IC, version 10; StataCorp, College Station, Texas).

RESULTS

PATIENTS

We identified 2788 patients aged 2 to 18 years who underwent a tonsillectomy by 1 of 2 surgeons between January 1, 2002, and March 3, 2009. Of these children, 1237 received a perioperative dexamethasone dose of 0.5 mg/kg, and 1551 received a total dose of 1 mg/kg. Regarding surgical technique, 1577 underwent an extracapsular monopolar electrosurgery tonsillectomy, 960 underwent an intracapsular microdebrider tonsillectomy, and 251 underwent an extracapsular radiofrequency ablation tonsillectomy. Baseline sex, median age, primary diagnosis category, and technique are presented in Table 1. Between the 0.5-mg/kg and 1.0-mg/kg groups, significant differences were noted in surgical technique, thus severely limiting any conclusions regarding causality between steroid use and increased hemorrhage rates.24,25 One retrospective review reporting a 15-year history of tonsillectomy in adults and children suggested that the rate of postoperative hemorrhage at the institution was increasing.24 During the period of the increased hemorrhage rate, several variables were evident, including alterations in tonsillectomy techniques, the introduction of intraoperative and postoperative steroid use, and the introduction of postoperative NSAID use. The database used in that study did not provide patient-level data regarding the use of steroids or surgical technique, thus severely limiting any conclusions regarding causality between steroid use and increased hemorrhage rates. A second retrospective review of 430 cases noted an increase in hemorrhage rate associated with the introduction of intraoperative and postoperative steroids.25 Once again, this study precludes any statement on the effects of steroids because their use was not individually stratified. Children receiving steroids demonstrated a significantly increased rate of hemorrhage compared with those receiving the 0.5-mg/kg dose. Adjusted odds ratios control for age, sex, primary diagnosis, and surgical technique.

After adjusting for potential confounders, the 95% confidence intervals of the odds ratios at each of the 3 outcome levels contain the value of 1 and therefore suggest that there is no association of a different hemorrhage rate based on the dexamethasone dose (Table 3). Furthermore, the point estimate of each odds ratio is less than 1; this suggests that, if significant, a dose of 1.0 mg/kg would actually confer a protective effect against postoperative hemorrhage.

COMMENT

Perioperative dexamethasone administration for children undergoing tonsillectomy is widely practiced nationally and internationally. Support of this practice has been expressed by expert panels and is widely stated in textbooks.6,21-23 Few studies exist with demonstrative data suggesting adverse consequences of perioperative dexamethasone administration. Two studies supported the notion that perioperative steroid use increases hemorrhage rates.24,25 One retrospective review reporting a 15-year history of tonsillectomy in adults and children suggested that the rate of postoperative hemorrhage at the institution was increasing.24 During the period of the increased hemorrhage rate, several variables were evident, including alterations in tonsillectomy techniques, the introduction of intraoperative and postoperative steroid use, and the introduction of postoperative NSAID use. The database used in that study did not provide patient-level data regarding the use of steroids or surgical technique, thus severely limiting any conclusions regarding causality between steroid use and increased hemorrhage rates.24,25 One second retrospective review of 430 cases noted an increase in hemorrhage rate associated with the combination of steroids and intraoperative use of topical vasoconstrictors.25,26 Once again, this study precludes any statement on the effects of steroids because their use was not individually stratified. Children receiving steroid...
roiids also received intraoperative topical vasoconstrictors that, as described by the authors, may have been a more plausible mechanism of increased hemorrhage risk.22

The trial by Czarnetzki et al10 is the first prospective study to report a detrimental effect of perioperative dexamethasone administration in children undergoing tonsillectomy. As such, the trial warrants close examination to determine its clinical significance on future practice. The trial was designed to determine the effect of a single dose of perioperative dexamethasone on PONV and analgesic efficacy. Children aged 2 to 17 years were randomized to 1 of 4 treatment arms based on dexamethasone dosing: 0.05, 0.15, or 0.50 mg/kg or placebo. The children were then observed as inpatients for 24 hours and underwent an outpatient visit at 10 days. Because the trial was designed to determine the effects of intraoperative dexamethasone administration on PONV, no a priori hypotheses regarding postoperative hemorrhage were generated. During an interim analysis, an increased rate of postoperative hemorrhage was noted and the trial was terminated early.

A review of the methods of the trial by Czarnetzki et al reveals the stratification of postoperative hemorrhage into 3 levels of escalating degree of severity. The most inclusive category included all children readmitted with a history of postoperative hemorrhage, whether or not there was clinical evidence of bleeding. The second category of reporting included all children who were readmitted and demonstrated clinical evidence of a postoperative hemorrhage but did not require operative intervention. The most stringent category included only children who required operative intervention to control the bleeding. This method of stratification provides insight into the various levels of bleeding that may or may not occur. Most audits, trials, and reports that chronicle postoperative hemorrhage focus on primary vs secondary hemorrhage rates and refers to hemorrhage occurring within 24 hours (primary) or after 24 hours (secondary) of surgery. Although some studies stratify by operative or nonoperative intervention, most data are not stratified by severity of bleed. Unfortunately, this variability in reporting methods has caused some difficulty in interpreting postoperative hemorrhage rates and thus limits comparisons.

The trial by Czarnetzki et al10 was terminated owing to an increased rate of postoperative bleeding in the children randomized to receive dexamethasone. In conjunction with the hospital ethics committee, the investigators believed that they were potentially placing children at risk of serious harm (posttonsillectomy hemorrhage) with a nonvital treatment (perioperative dexamethasone). Furthermore, at the time of trial termination, the primary outcome measure of a dose-dependent decrease in PONV had been documented.

As such, the investigators reported hemorrhage episodes stratified on the 3 escalating severity levels described. A staggering rate of 24% of children experienced at least 1 episode of postoperative hemorrhage in the 0.5-mg/kg arm. Furthermore, the authors found that, for the 9 surgeons whose patients experienced postoperative hemorrhage, the median number of surgical procedures performed per hemorrhage was 7. These data appear drastically different from our own experience and that of the posttonsillectomy hemorrhage literature.11-19

Further review of the data from Czarnetzki et al10 reveals several findings. Of the variables recorded—technique, indication, NSAID exposure, vomiting in the first 24 hours, body mass index, surgeon, and age—only age was identified as a confounder, and this was determined to be in a negative direction. The adjusted analyses using a logistic regression model suggest that the relative risk of postoperative hemorrhage requiring readmission is increased across each dexamethasone dose compared with children who received placebo. The greatest risk is associated with the 0.50-mg/kg dose. The confidence intervals of the relative risk for the 0.05-mg/kg and 0.15-mg/kg doses are quite wide and include the value of 1. Because there were no episodes of postoperative hemorrhage requiring operative intervention in the placebo group, the logistic model was invalid and comparisons were made by Fisher exact test to account for small sample size. The resultant P values for the 0.05-, 0.15-, and 0.50-dose groups were .24, .49, and .05, respectively. As pointed out by Gunter et al20 and reflected in the wide confidence intervals, the authors logistic regression model was limited by the small number of outcome events.

The necessity to end the trial owing to ethical concerns with the resultant small sample size represents one
of the primary weaknesses of the trial regarding the conclusions made about postoperative hemorrhage. The small sample size presents the opportunity to magnify treatment effects. Once again, this constraint is demonstrated in the wide confidence intervals of the trial’s effect measures.

In an effort to explain the study’s findings, the authors highlight that that the randomized nature of the trial should control for known and unknown potential confounders. They forward several biological plausibility models, including interactions of glucocorticoids with NSAIDs and wound repair inhibition. However, as the authors stated, their data suggest that there is no association between postoperative hemorrhage and NSAID use postoperatively.

Given these concerns and the lack of any sound data to further support the findings of the trial, we sought to determine how the question of postoperative hemorrhage associated with dexamethasone administration could be best answered. A randomized trial designed to test the outcome of bleeding would be ideal. However, in light of the findings of this trial, the question arises concerning the ethical responsibility associated with subjecting children to a therapy that may risk greater harm than proposed benefit in the setting of a research study. Furthermore, enrollment and management of such a trial would require a significant volume of resources. A trial with 2 arms designed to detect a doubling in hemorrhage rate from 4% (the hemorrhage rate in the placebo arm of the trial) to 8% with 80% power would require approximately 600 children per arm.

These limitations raise the possibility of using observational data to answer questions raised by a clinical trial. The success of observational studies in the past has been to answer questions in a clinically relevant way outside the strict confines of a trial or, alternatively, in a setting where the ability to conduct a trial is limited by ethical or resource considerations. The large volume of tonsillectomies worldwide may allow significant power to be achieved through observational methods. However, to obtain meaningful data for the question at hand requires strict control of potential confounding factors. An ideal situation would involve a single surgeon using multiple dexamethasone doses (including a dose of zero) in an environment characterized by high use of protocols to ensure standardized treatment. Our data represent the experience of 2 surgeons at a single institution using 2 doses of dexamethasone. The operative environment is well governed by protocol owing to previous joint participation in tonsillectomy studies. In this setting, variability between individual surgeons in dexamethasone dosing appears to be one of the primary differences between children undergoing tonsillectomy.

The stratification of our data by dexamethasone dose while maintaining a large sample size within each strata provides valuable insight into our experience. Although we lack a control arm of children who did not receive perioperative dexamethasone, we did not experience the rates of posttonsillectomy hemorrhage seen by Czarnetzki et al. Our data conform closely to previously published studies that used varying doses of perioperative steroids.

The lowest dose of dexamethasone in our experience is equivalent to the highest dose of dexamethasone in the trial by Czarnetzki et al, which was the only dose of dexamethasone to suggest significance at all 3 levels of hemorrhage. Furthermore, analysis of our data demonstrates no difference in the incidence of posttonsillectomy hemorrhage between the 0.5-mg/kg and 1.0-mg/kg doses. The findings of Czarnetzki et al suggest that we should expect a high rate of hemorrhage at the 0.5-mg/kg dose and possibly an even higher rate at the 1.0-mg/kg dose. If dexamethasone administration is causally related to an increased rate of hemorrhage, a positive dose-response relationship would be expected.

The weaknesses of our study center primarily on the retrospective, observational nature of the data. Perhaps the greatest concern is our ability to adequately identify and capture all children who experienced posttonsillectomy hemorrhage, a concern that has been appropriately raised with similar audits in the past. We can only state that we believe we have captured most of the children who experienced postoperative bleeding for several reasons. First, all patients were clearly instructed in writing and verbally to telephone or report directly to our institution if they suspected any degree of hemorrhage. Second, all children were scheduled for an outpatient postoperative follow-up visit. Finally, the data were derived from a 2-surgeon data set in which each surgeon had a nurse dedicated to making and receiving postoperative telephone calls relative to such hemorrhage issues.

In addition, the nature of our study did not allow a separation of individual surgeon variation from dexamethasone dosing, regardless of the technique used. This limitation was unavoidable in our design. However, both surgeons were trained in a similar fashion and mutually agreed on specifics regarding how tonsillectomy and tonsillotomy should be performed. If dexamethasone administration introduced a dose-dependent increase in postoperative hemorrhage, observation of the relationships seen in our data would require the surgeon variation associated with postoperative hemorrhage to be of similar magnitude in an opposite direction. This magnitude would have to be large based on the findings of the trial. Although this situation is possible and cannot be disproved, from a statistical standpoint it seems unlikely to have occurred given the tight confidence intervals of our effect measures and unlikely to have occurred from a clinical standpoint given the similar training, attitudes, and practice patterns of the individual surgeons. Furthermore, the point estimates of the odds ratios suggest a protective effect of an increased dose of perioperative dexamethasone.

Whereas the data from the trial of Czarnetzki et al suggest that children at their institution who received perioperative dexamethasone were at increased risk for posttonsillectomy hemorrhage, their findings do not appear to translate to children undergoing tonsillectomy at our institution since 2002. The apparent contradiction is particularly important given the widespread practice of perioperative dexamethasone use. To definitively answer the question at hand and determine a dose-response relationship, a large-scale, prospective, placebo-controlled trial designed with postoperative hemorrhage as an end
point at multiple dexamethasone doses is necessary. However, our large sample size, coupled with the generalizability of including all children undergoing tonsillectomy by 2 different surgeons during a 7-year period, provides no compelling evidence that perioperative dexamethasone administration confers any increased risk of postoperative hemorrhage.

Submitted for Publication: August 17, 2009; final revision received November 22, 2009; accepted February 20, 2010.

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Author Contributions: Drs Brigger and Hartnick had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Brigger and Hartnick. Acquisition of data: Brigger and Hartnick. Analysis and interpretation of data: Brigger. Drafting of the manuscript: Brigger and Cunningham. Critical revision of the manuscript for important intellectual content: Cunningham and Hartnick. Statistical analysis: Brigger. Administrative, technical, and material support: Brigger. Study supervision: Cunningham and Hartnick.

Financial Disclosure: None reported.

Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, the Department of Defense, or the US government.

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