Do Children Who Experience Laryngospasm Have an Increased Risk of Upper Respiratory Tract Infection?

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Background: Laryngospasm is the most frequently reported respiratory complication associated with upper respiratory infection and general anesthesia in retrospective studies, but prospective studies have failed to demonstrate any increase in risk.

Methods: A case-control study was performed to examine whether children with laryngospasm were more likely to have an upper respiratory infection on the day of surgery. The parents of all patients (N = 15,183) who were admitted through the day surgery unit were asked if their child had an active or recent (within 2 weeks of surgery) upper respiratory infection and were questioned about specific signs and symptoms to determine if the child met Tait and Knight’s definition of an upper respiratory infection. Control subjects were randomly selected from patients whose surgery had occurred within 1 day of the laryngospasm event.

Results: Patients who developed laryngospasm (N = 123) were 2.05 times (95% confidence interval 1.21–3.45) more likely to have an active upper respiratory infection as defined by their parents than the 492 patients in the control group (P = 0.01). The development of laryngospasm was not related to Tait and Knight’s definition for an upper respiratory infection or to recent upper respiratory infection. Children with laryngospasm were more likely to be younger (odds ratio = 0.92, 95% confidence interval 0.87–0.99), to be scheduled for airway surgery (odds ratio = 2.08, 95% confidence interval 1.21–3.59), and to have their anesthesia supervised by a less experienced anesthesiologist (odds ratio = 1.69, 95% confidence interval 1.04–2.7) than children in the control group.

Conclusion: Laryngospasm was more likely to occur in children with an active upper respiratory infection, children who were younger, children who were undergoing airway surgery, and children whose anesthesia was supervised by less experienced anesthesiologists. Understanding the risk factors and the magnitude of the likely risk should help clinicians make the decision as to whether to anesthetize children with upper respiratory infection. (Key Words: Complications: laryngeal spasm; upper respiratory infection. Anesthesia: pediatric.)

THE risks associated with anesthetizing children during or immediately after an upper respiratory infection (URI) remain controversial. Retrospective studies have reported an association between URI and respiratory complications most notably laryngospasm, airway obstruction, and bronchospasm.1–5 The increase in risk of developing laryngospasm for children with a URI, based on retrospective studies, may be as great as tenfold.2 However, prospective studies have failed to conclusively demonstrate an association between laryngospasm and URI.1–6 Randomized controlled trials must have large numbers of patients to detect a doubling of risk for an infrequent event. The lack of demonstrated increased risk may represent the true state of affairs, or alternatively, because of the low frequency of respiratory complications the possibility of a type II error must be considered.

The case-control study is an alternative approach to the randomized controlled trial.7,8 This study design provides a more practical way to determine whether an exposure, such as a URI, represents a risk factor for the development of an adverse event. We carried out a case-control study designed to determine if children who develop laryngospasm during elective surgical
procedures have an increased risk of URI. We have focused our attention on laryngospasm because it is the most frequently reported respiratory complication in many reports, and based on our quality assurance data, occurs with approximately ten times the frequency of bronchospasm in our operating rooms.\textsuperscript{2,3,9}

Methods

With approval of our institutional review board, we interviewed the parents of all children admitted through our day surgical unit between January 1, 1993 and June 20, 1994. During the admissions process, the children’s parents were asked if they thought their child had a URI that day (parent:active URI) or if they thought their child had a URI in the 2-week period prior to the day of surgery (parent:recent URI). If the answer to either question was affirmative, the signs and symptoms used by Tait and Knight\textsuperscript{7} were reviewed with the parent(s) to determine whether the URI met this definition of an active or recent URI (T&K:active URI and T&K:recent URI). The data gathered during this interview were not available to the anesthesia care team responsible for the patient or to the investigators.

The anesthesia care team collected the following data for every day surgical patient during the 18-month study period: age, weight, sex, diagnosis, surgical procedure, type of preanesthetic medication, type of induction (halothane inhalation or either thiopental or propofol administered intravenously), experience of the immediate supervisor, experience level of the resident (month of residency and weeks of pediatric anesthesia training), type of airway maintenance (face mask, laryngeal mask airway, or tracheal tube), and whether laryngospasm occurred. An inexperienced immediate supervisor was considered anyone in their first year after completion of an anesthesia residency whereas an experienced supervisor was considered anyone with longer than 1 yr of postresidency experience. Airway surgery was defined as tonsillectomy, adenoidectomy, bronchoscopy, or cleft palate repair.

If the members of the anesthesia care team believed that the patient had experienced laryngospasm, one of the investigators was notified and the events were reviewed. For the purposes of this investigation, we used the following operational definition for laryngospasm: complete airway obstruction unrelieved by maneuvers to relieve soft tissue obstruction and associated with an $\text{SpO}_2 \leq 85\%$, and (1) relieved by a jaw-thrust maneuver, the application of positive airway pressure and by deepening the anesthetic; or (2) if all other methods for relieving obstruction were futile, thus necessitating the administration of succinylcholine.\textsuperscript{10,11} If laryngospasm occurred, the investigator also noted whether succinylcholine was required, whether tracheal intubation was performed, when in the course of the anesthetic the event occurred (induction, maintenance, emergence, after extubation, or in the postanesthesia care unit).

Each patient with laryngospasm was considered a case patient. Four control subjects were randomly selected using a table of random numbers matched to the last digit of the patients medical record number from the pool of patients undergoing surgery on the same day, the day before, or the day after each case patient’s laryngospasm event. If data were missing from the preoperative assessment or the intraoperative data collection, the next random number in the list was used to select a substitute control patient. Nearly 100\% of the preoperative assessments were completed, and approximately 75\% of the intraoperative records were completed. Because residents of the same level of training rotate at the same time, matching control subjects from the same day limited our ability to determine whether or not resident inexperience was a risk factor for laryngospasm. However, this was necessary to reduce potential bias caused by seasonal differences between types of viral infections.

Statistical Analysis

Sample Size. We estimated that between 10\% and 20\% of our control patients would have an active URI on the day of surgery. We calculated that between 103 and 165 episodes of laryngospasm were needed to detect a twofold increase in risk with 80\% power. After the first 103 episodes of laryngospasm, 15\% of the control patients had an active URI on the day of surgery by the most liberal definition (parent:active URI). No interim data analysis was performed at this time. Based on a URI prevalence of 15\%, a final sample size of 125 episodes of laryngospasm was determined sufficient to provide an 80\% power to detect a doubling of risk with a type I error rate of 5\%.

Analysis. For all analyses, $P < 0.05$ was considered significant. The association between individual variables and the outcome laryngospasm, was evaluated initially with univariate analysis. For categorical variables, a chi-square analysis was performed to compare differences between groups and odds ratios to quanti-
Table 1. Demographic Characteristics of Cases of Laryngospasm and Their Controls

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>123</td>
<td>492</td>
</tr>
<tr>
<td>Age (±SD) (yr)</td>
<td>3.9 ± 3.6</td>
<td>5.3 ± 7.7</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>58</td>
<td>65</td>
</tr>
<tr>
<td>Induction type (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Halothane/thiopental/propofol</td>
<td>93/2/5</td>
<td>89/4/7</td>
</tr>
<tr>
<td>Airway surgery (%)</td>
<td>22</td>
<td>13</td>
</tr>
<tr>
<td>Inexperienced supervisor (%)</td>
<td>29</td>
<td>19</td>
</tr>
<tr>
<td>Tracheal tube/mask/LMA (%)</td>
<td>47/40/13</td>
<td>48/38/13</td>
</tr>
<tr>
<td>Parent: active URI (%)</td>
<td>24</td>
<td>14</td>
</tr>
<tr>
<td>T &amp; K: active URI (%)</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Parent: recent URI (%)</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>T &amp; K: recent URI (%)</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Active or recent URI (%)</td>
<td>37</td>
<td>27</td>
</tr>
</tbody>
</table>

LMA = laryngeal mask; URI = upper respiratory infection; T & K = Tait and Knight’s definition of a URI.

Results

During the 18-month study period, the parents of all (N = 15,183) children admitted through the day surgical unit were questioned whether their child had a URI. Of the 143 children (0.94%) in whom laryngospasm developed, incomplete data were available for 20. The remaining 123 children were included in the analysis. No difference existed in the percentages of case and control patients regarding the type of anesthetic induction or the type of airway used for maintenance (tables 1 and 2). Patient sex, preoperative sedative and, preoperative atropine also were not associated with laryngospasm.

Laryngospasm occurred most frequently (N = 88,72%) during induction of anesthesia. Emergence was the second most frequent time for laryngospasm, representing 23% (N = 28) of all episodes, including 15 episodes (12%) after tracheal extubation. One patient (0.8%) developed laryngospasm both on induction and during emergence. For the remaining six patients (4%) laryngospasm developed during anesthetic maintenance. During 80 (65%) episodes of laryngospasm, the SpO2 decreased to <85%, but on only three occasions did the heart rate decrease to <80% of the baseline value. A muscle relaxant was administered to treat laryngospasm during 70 of the 123 episodes (57%). Succinylcholine was administered for 68 of the 70 episodes and vecuronium was administered on two occasions.

Patients with laryngospasm were nearly twice as likely as control patients to have an active URI as defined by their parents (tables 1 and 2). Laryngospasm was not associated with active or recent URI as defined by Tait and Knight, nor a recent URI as defined by parents (table 2). Patients with laryngospasm were approximately twice as likely as control patients to have undergone a procedure involving the airway and were more likely to have been cared for by an inexperienced immediate supervisor (tables 2 and 3). Younger patients also appeared to have a predisposition for laryngospasm. In the univariate analysis, patients with laryngospasm were more than twice as likely as control patients to be younger than 1 yr (table 2). Statistical significance was not maintained when age was analyzed as a dichotomous variable in the logistic regression model (age ≤1 yr vs. >1 yr). However, increasing
Table 3. Final Logistic Regression Model* of Risk Factors for Laryngospasm

<table>
<thead>
<tr>
<th>Risk Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent: active URI</td>
<td>2.05</td>
<td>1.21–3.45</td>
<td>0.01</td>
</tr>
<tr>
<td>Age (continuous variable)</td>
<td>0.92</td>
<td>0.87–0.99</td>
<td>0.02</td>
</tr>
<tr>
<td>Sex (male vs. female)</td>
<td>0.72</td>
<td>0.47–1.12</td>
<td>0.15</td>
</tr>
<tr>
<td>Airway vs. nonairway procedure</td>
<td>2.08</td>
<td>1.21–3.59</td>
<td>0.01</td>
</tr>
<tr>
<td>Sedative (midazolam vs. none)</td>
<td>0.57</td>
<td>0.32–1.05</td>
<td>0.07</td>
</tr>
<tr>
<td>Inexperienced vs. experienced supervisor</td>
<td>1.69</td>
<td>1.04–2.7</td>
<td>0.03</td>
</tr>
</tbody>
</table>

OR = odds ratio; CI = confidence interval; URI = upper respiratory infection.
* Table includes all variables present in the initial saturated logistic regression model.

age was protective when age was analyzed as a continuous variable in the regression model (p = 0.02, table 3).

Although overall the prevalence of URI varied with the season, the patients with laryngospasm always had a higher incidence of URI than the control patients (fig. 1). Of the 125 children in whom laryngospasm developed, 121 had no change in their planned postanesthesia care unit disposition. A 2.5-yr-old child, and a 1.5-yr-old child required oxygen after the postanesthesia care unit, and the younger child required observation in the intensive care unit overnight. Both children had an active URI as defined by their parents, and both underwent adenoidectomy and tonsillectomy because of preoperative airway obstruction. Whether the laryngospasm event, preexisting airway obstruction, the URI, or a combination of these factors resulted in persistent hypoxemia (SpO₂ < 94% in room air) is uncertain. ¹²

Discussion

Children in whom laryngospasm developed during induction, maintenance, or emergence from anesthesia were nearly twice as likely to have an active URI, as defined by their parents on the day of surgery. Conversely, we found no evidence that a recent URI predisposes children to an increased risk of laryngospasm. Meeting the criteria for an active or recent URI developed by Tait and Knight¹ was not predictive of an increased risk of laryngospasm. Children with only one or two signs or symptoms are believed by their parents to have a URI but may not meet more stringent criteria.

Although retrospective studies have shown children with an active URI to have increases in risk for laryngospasm as high as tenfold, prospective studies using Tait and Knight’s criteria have failed to show any such increase in risk.¹²⁻⁴ These retrospective studies lack uniform definitions for URI and for the complications investigated. Problems with previous prospective studies include small sample size and possible inappropriate patient assignment. For example, only 40% of our patients in the parent-active URI group, met Tait and Knight’s criteria for a URI.¹ This suggests that in studies that have used Tait and Knight’s criteria, patients with a URI might have been more likely to be assigned to the healthy patient group than to the URI group. While it is possible that some of the children believed by their parents to have a URI are experiencing allergies or other noninfectious processes instead of a URI, our data suggest that when a parent believes his/her child has a URI, that process, whatever it may be, is related to an increased risk of laryngospasm.

We found that younger age was an independent risk factor for laryngospasm. However, we were unable to demonstrate a particular age cutoff at which one could expect an increased risk. That the univariate data were similar when age was dichotomized with cutoffs of either 1 yr or 3 yr and that statistical significance was not achieved in the logistic regression model when age was dichotomized (cutoff at 1 yr), implies the lack of a distinct age cutoff.

The experience of the resident was not important in determining the patients whose anesthesia was in their first year. Increased risk of URI was not noted among patients with children who were in their first year of practice.

Laryngospasm in patients without a URI was used to define the URI group. Many children without a URI had a URI as determined during the consent process, and the risk factor double-counted 29 episodes of laryngospasm in patients who could have had URI but for whom the first URI was recorded as being without an URI. All operations for which URI had been recorded were included in the analysis, regardless of the time of postanesthesia care unit admission.

Laryngospasm was not recorded in our study if the patient did not have URI. The patient’s airway was evaluated once every 10 min postoperatively, and the patient was awakened from general anesthesia if URI had been recorded. Of the 22 children with URI who were recorded as awake from general anesthesia, 15 had URI and 7 did not. Only the URI was entered as a risk factor for laryngospasm. The hospital dietitian estimated food and fluid intake postoperatively and recorded it in the patient chart. If the patient had received anything in the past 2 hr before the laryngospasm episode, it was recorded as a risk factor. Only the URI was entered as a risk factor for laryngospasm. If the patient had received anything in the past 2 hr before the laryngospasm episode, it was recorded as a risk factor. Only the URI was entered as a risk factor for laryngospasm.

The decision as to whether a child with a URI was entered as a risk factor or not was made by the attending anesthesiologist. The decision was based on the patient’s respiratory tract at the time of the URI. The patient’s respiratory tract was evaluated postoperatively by the attending anesthesiologist. The decision was based on the patient’s weight, age, and postoperative course.

Fig. 1. The histogram represents the percentage of patients with upper respiratory infection in the control group (N = 92, open boxes) and laryngospasm group (N = 123, shaded boxes) for each season during the study period. During the study, the total number of surgical patients admitted through the day surgery unit was fairly stable from one season to the next, ranging between a minimum of 2,404 and a maximum of 2,691.
determining the risk of laryngospasm. However, patients whose anesthesia was supervised by anesthesiologists in their first postresidency year had a twofold increased risk of laryngospasm. Whether experience caring for adults after residency or specific experience with children would be necessary to diminish risk is uncertain.

Laryngospasm is an uncommon event with an incidence of 0.94% in our study. Approximately three quarters of all laryngospasm events occurred in patients without a URI. Assuming that the prevalence of an active URI as defined by parents averaged 14%, then approximately 2,000 children with a URI were anesthetized during the course of the study. Assuming that this risk factor doubles the risk of laryngospasm, half of the 29 episodes of laryngospasm associated with an active URI could have been prevented. Therefore, canceling all operations for children with an active URI would have resulted in nearly 2,000 cancellations to prevent approximately 15 episodes of laryngospasm.

Pulmonary function is altered by the presence of a URI but the impact of these alterations on anesthesia and surgery remains uncertain. Long-term complications from anesthetizing children with URI such as pneumonia and postoperative complications such as croup have not been demonstrated. Intraoperative and immediate postoperative hemoglobin oxygen desaturation appears to occur more frequently in children with URI. However, the oxygen hemoglobin desaturation associated with a URI appears to be treatable with supplemental oxygen and is likely to resolve by the time of postanesthesia care unit discharge.

The decision as to whether to cancel surgery for a child with a URI may be difficult. It is important to emphasize that our results pertain only to healthy children whose URI symptoms are limited to the upper respiratory tract. Children with fever (≥38.5°C), wheezing, or malaise were not anesthetized during this study. The patient’s age, the urgency and nature of the procedure, the patient’s history and physical examination, the anesthesiologist’s experience, and parental attitudes must all be taken into account before proceeding with anesthesia and surgery. Recognizing that perioperative hemoglobin oxygen desaturation may occur more frequently and that there is a small increased risk of laryngospasm should help practitioners and families arrive at the best decision for each individual patient. During the study period, only 0.5% of patients who arrived at our hospital for a scheduled day surgical procedure had their operation canceled (all possible causes). Given the average incidence of URI in our patient population, this indicates that at our institution, the majority of patients with a URI were deemed well enough to proceed with surgery.

The case-control study design is the optimal means of detecting risk factors when an outcome event is rare. Several issues may cloud the validity of the results when the case-control design is used. Appropriate selection of control subjects and controlling for confounding variables are of paramount importance. We randomly selected our control patients from the same surgical population and from the same operative day, and we prospectively collected the necessary data on all patients to eliminate recall bias. We sought to have the control group exposed to the same house staff, the same types of surgery, and to the same seasonal infectious pathogens as the laryngospasm group. We did not match control patients for potential risk factors in the study design because we wanted to maintain the ability to evaluate all potential risk factors in the analysis. We believe that we adequately eliminated the effects of confounding variables by controlling for these variables in the regression analysis.

Investigator bias is always of potential concern and can occur in situations where those diagnosing the outcome variable are aware of the presence or absence of the risk factor being studied. We had separate groups performing the preoperative questionnaire, inducing anesthesia, and making the determination if an event met the definition of laryngospasm. It is difficult to fully mask the anesthetic team to the presence or absence of a URI. However, by selecting a rigorous definition of laryngospasm, we hope to have diminished the likelihood of investigator bias occurring through selective reporting of laryngospasm events. Although our rigorous definition of laryngospasm may have missed the more mild episodes, we believe that it served to minimize the possibility of including patients with soft tissue obstruction in the laryngospasm group. We believe that it also served to provide information on risk factors for a more meaningful clinical outcome.

In summary, healthy children undergoing elective surgical procedures in whom laryngospasm developed were approximately twice as likely to have an active URI as defined by their parents than control patients. Recent URI and Tait and Knight’s definition of a URI were not related to laryngospasm. Children with laryngospasm were also more likely to be younger, to be scheduled for airway surgery, and to have their anes-
anesthesia supervised by a less experienced anesthesiologist than children in the control group.

The investigators thank the nursing staff of the day surgical unit, and Shirley Hui, R.A.

References


Anesthesiology, V 85, No 3, Sep 1996