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Dexmedetomidine as a Primary Sedative Agent after Single-Stage Airway Reconstruction

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Abstract

Objective. To examine the outcomes of children receiving dexmedetomidine after single-stage airway reconstruction.

Study Design. Historical cohort study.


Subjects and Methods. Of 61 eligible patients, 50 children undergoing single-stage airway reconstruction were included in the study. Thirty children received dexmedetomidine (Dex) as a primary sedative agent, and 20 received a more traditional sedation protocol (no Dex). Primary outcomes included complications, intubation lengths, and lengths of pediatric intensive care unit (PICU)/hospital admission. Secondary analysis incorporating polypharmacy and age was performed using multivariate linear regression models.

Results. Median age was 18.0 months. Age, sex, and weight were similar between the groups. Intubation length was equal in the 2 groups, and there were no statistical differences between lengths of PICU or hospital stay after extubation. Similarly, overall and individual complications were all similar, and there was no difference between the 2 groups in the amount of polypharmacy administered. On multivariate analysis, polypharmacy and younger age were independently correlated with an increase in overall complications, and polypharmacy alone was correlated with an increased length of stay after extubation.

Conclusion. The use of dexmedetomidine as a primary sedation agent after single-stage airway surgery does not appear to improve outcomes or decrease the need for additional pharmacologic agents. Polypharmacy was associated with an increase in overall complications and an increased length of stay after extubation. Although success can be expected in greater than 90% of these surgical patients, the optimal postoperative sedation management remains challenging.

Keywords
dexmedetomidine, single-stage laryngotraceo-plasty, pediatric airway, postoperative sedation, subglottic stenosis

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The management of subglottic stenosis in children has continued to evolve over the past decade with the development and refinement of endoscopic techniques.1,2 Open airway surgery, including both laryngotraceo-plasty and cricotracheal reconstruction, remains the most effective option for more severe and longer segment stenoses. Single-stage laryngotraceo-plasty and cricotracheal resection are typically followed by a period of intubation and stenting of the reconstructed airway in a pediatric intensive care unit (PICU).3-6 Adequate sedation during this immediate postoperative period is critical for proper healing and surgical success.7 Conventional pharmacologic sedatives and analgesics used during this postoperative period include opioids, benzodiazepines, neuromuscular blocking agents, and propofol, but these carry risks of dependence and withdrawal and other increased complications.3,8,9

Dexmedetomidine (Precedex; Hospira, Inc, Lake Forest, Illinois) is a centrally acting α2-agonist that is currently approved by the Food and Drug Administration (FDA) for use in both nonintubated adults as a procedural sedative and in mechanically ventilated adults for less than 24 hours.10,11
Cardiovascular anomaly 13.3 15.0 .868
Syndrome 20.0 35.0 .236
Developmental delay 23.3 10.0 .229
Bronchopulmonary dysplasia 26.7 10.0 .149
Gastroesophageal reflux 56.7 55.0 .907
Prematurity 56.7 60.0 .815
Subglottic stenosis grade 2.43

During the postoperative intubation period. Special attention was paid to medication administration for demographic data, operative details, and postoperative between November 2005 and June 2012. Charts were reviewed identified for children who had undergone single-stage airway surgery (www.irbear.org) prior to collection of data. Charts were identified for children who had undergone single-stage airway surgery between November 2005 and June 2012. Charts were reviewed for demographic data, operative details, and postoperative course. Special attention was paid to medication administration during the postoperative intubation period. Postoperative intubation length was determined on an individual basis by a number of factors, including surgeon preference, comorbid conditions, and age. Exclusion criteria included inadequate records, intubation period less than 48 hours, and confounding major medical conditions. Patients were divided into 2 groups based on whether or not dexmedetomidine was considered a primary sedative agent. This was defined as administration of dexmedetomidine for ≥50% of the intubation period. The allocation of children into these 2 groups was based primarily on a longitudinal practice change in 2008 (prior to January 2008, most patients undergoing single-stage laryngotracheoplasty did not receive dexmedetomidine, whereas after January 2008, most patients did) and also on the preferences of the pediatric intensivists at our institution.

Primary analysis compared the groups with respect to complications (unplanned extubations, reintubations, withdrawal, pneumonia or tracheitis, and cardiac events) and lengths of intubation and PICU/hospital stay after extubation. Univariate statistical analysis was performed using the Student t test and χ² test. Multivariate linear regression models were created to determine the independent effects of dexmedetomidine, polypharmacy, and age.

Results
Sixty-one children met criteria and their charts were reviewed; 11 children were excluded and 50 children were included in the final analysis. Thirty children received dexmedetomidine for ≥50% of their intubation and were designated the “Dex” group (median of 91.3% of intubation). The other 20 children were assigned to the “no Dex” group (median of 23.6% of intubation). There were no differences in age, sex, or weight between the 2 groups (Table 1). Similarly, there were no differences in the grade of subglottic stenosis or comorbid conditions. Surgical success in each group, as defined by the avoidance of a tracheostomy, was 100% in each group.

Table 2 details the complications and lengths of intubation and stay for each group. On univariate analysis, there was no difference between the 2 groups when comparing overall (P = .322) and individual complications. There were no differences in intubation length (P = .429), length of PICU stay after extubation (P = .847), and length of hospital stay after extubation (P = .142) (Figure 1). Polypharmacy was identical in each group both in terms of absolute number of days of polypharmacy (P = .069) and in the percentage of intubation requiring polypharmacy (P = .152).

Multivariate linear regression models were created using dexmedetomidine, polypharmacy, and age as independent variables. There was no significance found for the models.
for any individual complication, intubation length, or PICU stay after extubation (data not shown). The model for overall complications (Table 3) reached overall significance (overall analysis of variance [ANOVA], \(P = .044\); adjusted \(R^2 = .105\)), and polypharmacy was independently correlated with the occurrence of complications (Figure 2; \(P = .035\); 95% confidence interval [CI], 0.003-0.078).

Length of hospital stay after extubation also reached overall significance on multivariate linear analysis (Table 4; overall ANOVA, \(P = .002\); adjusted \(R^2 = -.231\)). Both polypharmacy (Figure 3; \(P = .008\); 95% CI, 0.109 to 0.699) and younger age (Figure 4; \(P = .030\); 95% CI, −0.087 to −0.005) were independently correlated with longer hospital stays after extubation.

**Discussion**

Postoperative management of children with reconstructed airways remains a challenge in balancing the intended sedative effects of a variety of medications with the negative consequences such as withdrawal and tolerance. Dexmedetomidine is a promising sedative agent that has gained increased interest in the pediatric surgical and intensive care communities over the past decade.\(^\text{12,13,15-23}\)

The current study is the largest study to date to evaluate the outcomes of dexmedetomidine use after single-stage airway surgery. Children receiving dexmedetomidine as a primary sedative agent were compared with children who received a more traditional sedation regimen. There were no differences in the complications or hospitalization lengths between the 2 groups. It is critical to note that the use of dexmedetomidine did not reduce the need for additional pharmacologic agents in this study. This finding is contrary to 1 prior study that showed a decreased need for opioids in patients receiving dexmedetomidine.\(^\text{24}\) Another recent study showed a decreased need for analgesic, anxiolytic, and sedative medications in children receiving dexmedetomidine for less than 7 days after single-stage airway reconstruction; however, the reverse was true in those children who received dexmedetomidine for more than 7 days.\(^\text{21}\) The current study did not examine the effect of intubation length on outcomes or polypharmacy needs.

On multivariate analysis, polypharmacy was subsequently identified to be independently correlated with both complications and longer hospital stays after extubation. One possible explanation for this finding would be that withdrawal may be more common in children receiving more medications, thereby prolonging postextubation hospitalizations. However, this did not prove true in the multivariate analysis of withdrawal. Another explanation could lie in the known side effects and complications of

### Table 2. Complications and Admission Lengths

<table>
<thead>
<tr>
<th></th>
<th>Dex (n = 30)</th>
<th>No Dex (n = 20)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall complications</td>
<td>73.3</td>
<td>60.0</td>
<td>.322</td>
</tr>
<tr>
<td>Reintubation</td>
<td>13.3</td>
<td>20.0</td>
<td>.529</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>50.0</td>
<td>45.0</td>
<td>.729</td>
</tr>
<tr>
<td>Pneumonia/tracheitis</td>
<td>36.7</td>
<td>25.0</td>
<td>.386</td>
</tr>
<tr>
<td>Accidental extubation</td>
<td>6.7</td>
<td>0</td>
<td>.239</td>
</tr>
<tr>
<td>Cardiac events</td>
<td>40.0</td>
<td>35.0</td>
<td>.721</td>
</tr>
<tr>
<td>Other complications</td>
<td>10.0</td>
<td>20.0</td>
<td>.318</td>
</tr>
<tr>
<td>Intubation length, d</td>
<td>9 ± 3.65</td>
<td>8 ± 2.78</td>
<td>.429</td>
</tr>
<tr>
<td>Postextubation PICU, d</td>
<td>4 ± 3.67</td>
<td>3.5 ± 4.17</td>
<td>.847</td>
</tr>
<tr>
<td>Postextubation hospital, d</td>
<td>7 ± 3.75</td>
<td>7.5 ± 4.68</td>
<td>.142</td>
</tr>
<tr>
<td>Polypharmacy, d</td>
<td>7.0 ± 3.59</td>
<td>5.5 ± 3.54</td>
<td>.069</td>
</tr>
<tr>
<td>Polypharmacy (% of intubation)</td>
<td>81.6</td>
<td>64.6</td>
<td>.152</td>
</tr>
</tbody>
</table>

Values are presented as median ± SD or as a percentage. Abbreviations: Dex, dexmedetomidine; PICU, pediatric intensive care unit.

**Figure 1.** Intubation length and hospital length of stay (LOS). There were no differences between the dexmedetomidine (Dex) and no Dex groups when comparing intubation length (\(P = .429\)), pediatric intensive care unit (PICU) stay after extubation (\(P = .847\)), and hospital stay after extubation (\(P = .142\)).
For example, decreased post-operative paralytic use has been shown to decrease complications and hospitalization lengths after single-stage laryngotraceoplasty. Younger age was also independently correlated with an increase in hospital stay after extubation. To our knowledge, no prior studies have specifically examined this relationship. It has been shown that younger children, especially those younger than 3 years, often require more pharmacological and physical restraint and, as such, are at a higher risk for withdrawal. Therefore, a longer length of stay in younger children can in some ways be expected. Another potential explanation of this finding is the existence of a smaller airway in younger children, even after augmentation. This anatomical difference could make these children more susceptible to edema and stridor, which may discourage earlier discharge. This latter explanation would also explain why younger children did not experience more complications despite the longer hospitalizations.

The current study is not without its limitations. Children were not randomized to a particular treatment but were rather divided according to how much dexmedetomidine they received, thereby creating a selection bias. The retrospective nature of the study often involved synthesizing data from handwritten progress notes, nursing records, and medication administration reconciliations. This approach can provide only a limited answer to the problem of postoperative sedation after single-stage airway surgery. In addition, it is difficult to control

Table 3. Overall Complications

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>Standard Error</th>
<th>P Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.461</td>
<td>0.152</td>
<td>.004</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>0.077</td>
<td>0.137</td>
<td>.577</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>0.041</td>
<td>0.019</td>
<td>.035</td>
</tr>
<tr>
<td>Age</td>
<td>-0.003</td>
<td>0.003</td>
<td>.300</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

Overall analysis of variance, P = .044; adjusted $R^2 = 0.105$.

Figure 2. Polypharmacy and complications. Multivariate regression of complications identified polypharmacy to be independently correlated with an increase in complications ($P = .035$).

Table 4. Length of Stay after Extubation

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>Standard Error</th>
<th>P Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>8.647</td>
<td>1.190</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>-0.993</td>
<td>1.068</td>
<td>.358</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>0.404</td>
<td>0.146</td>
<td>.008</td>
</tr>
<tr>
<td>Age</td>
<td>-0.046</td>
<td>0.021</td>
<td>.030</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

Overall analysis of variance, P = .002; adjusted $R^2 = -0.231$. 

Figure 3. Polypharmacy and length of stay (LOS) after extubation. Polypharmacy independently correlated with an increased length of stay after extubation on multivariate regression analysis ($P = .008$).
for variations in practice patterns among providers. An example of this is the administration of as-needed medications in the intensive care unit. Furthermore, because of the limited sample size, it is still possible that we have made a type II statistical error; there still could exist a difference in outcomes with the use of dexmedetomidine after single-stage airway reconstruction. As more data are collected and as more studies emerge from other institutions, we hope to gain further insight into this clinical problem.

Future studies include the continuing prospective collection of data for inclusion in the analysis. We are also attempting to better compare withdrawal in these patients using the Withdrawal Assessment Tool–1 (WAT-1), a validated tool for monitoring withdrawal in pediatric patients. Randomized trials are needed to better elucidate the effect of dexmedetomidine on outcomes in these children.

In conclusion, the use of dexmedetomidine in children after single-stage airway reconstruction appears safe but does not seem to produce improved immediate postoperative outcomes when compared with more traditional regimens. The avoidance of polypharmacy continues to be a safe and pragmatic approach to the management of these children.

Author Contributions

Michael E. McCormick, data collection and analysis, manuscript drafting and revision; Yewande J. Johnson, study design, manuscript revision and approval; Maria Pena, study design, manuscript revision and approval; Angela T. Wratney, study design, manuscript revision and approval; Sophie R. Pestieau, study design, manuscript revision and approval; George H. Zalzal, study design, manuscript revision and approval; Diego A. Preciado, study design, data collection and analysis, manuscript preparation, revision, and approval.

Disclosures

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Funding source: None.

References


Figure 4. Age and length of stay (LOS) after extubation. On multivariate regression analysis, younger age was independently correlated with a longer length of stay after extubation (P = .030).


