



## EDITORIAL

## Sedation and subglottic stenosis in critically ill children<sup>☆,☆☆</sup>



### Sedação e estenose subglótica em crianças gravemente doentes

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As mortality rates have decreased over the past few decades, the focus of contemporary pediatric critical care has shifted toward minimizing long-term morbidity. Children requiring endotracheal intubation and mechanical ventilation are at risk for a number of lasting sequelae, including chronic respiratory failure, neuropathy/myopathy, and cognitive impairment.<sup>1</sup> Risk factors for individual complications have been described, and actions to avoid these risk factors should be considered. However, avoiding one action invariably causes a reaction that may confer its own adverse effects. For example, a dry lung strategy shortens the duration of mechanical ventilation in the acute respiratory distress syndrome (ARDS), but may worsen long-term neurologic status.<sup>2,3</sup> A lung-protective strategy may reduce ventilator-associated lung injury and the risk of chronic respiratory failure, but the resultant acidosis and elevated intrathoracic pressures can be poorly tolerated in children with fluid-refractory shock, pulmonary hypertension, and/or intracranial hypertension.<sup>4</sup> When faced with multiple therapeutic options, pediatric intensivists must be cognizant of the risks and benefits of all possible paths.

Another risk of endotracheal intubation is the development of subglottic stenosis. Investigators from Hospital de Clínicas de Porto Alegre have established themselves

at the forefront of research into this important condition. They have previously shown that subglottic stenosis is a common problem among their intubated patients, occurring in approximately 10% of cases.<sup>5,6</sup> In this issue of the *Jornal de Pediatria*, they aimed to take an important next step – identifying risk factors associated with the development of subglottic stenosis.<sup>7</sup> Understanding risk factors for developing subglottic stenosis may allow a reduction in its occurrence, which may in turn reduce extubation failure, the need for diagnostic procedures and therapeutic interventions. However, if risk factors are identified, one must be cautious to think of the possible reactions, in order to avoid them.

Before considering any identified risk factors, one must evaluate the validity of the study and its applicability to one's own patient population. Schweiger et al.<sup>7</sup> should be commended for the several strengths of their methods, including the subglottic stenosis assessment, which was prospective and uniformly thorough the study, and the use of a validated and widely used sedation assessment score (COMFORT-B).<sup>8</sup> However, their sample size was small ( $n=36$ ), which limited the power of their statistical analysis. This small sample size also likely influenced the distribution of the COMFORT-B scores, which were presumably not normally distributed (as they were evaluated using a non-parametric test) but were reported in the style typically used for normally-distributed data (mean and standard deviation), which limits our ability to fully interpret their findings. We look forward to their future work, which will hopefully evaluate for risk factors in a larger cohort.

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There are several factors worth considering regarding the applicability of their findings to your patient population. First, given that the authors conclude that undersedation is a key risk factor for developing subglottic stenosis (see below), it is important to compare their sedation practices with your own. The authors report that the infusion rates for fentanyl (2 µg/kg/h) and midazolam (0.2 mg/kg/h) were not titrated to effect, but supplemented as needed with “additional doses of sedation.” This reactive protocol may limit the generalizability of their data to centers that practice a more proactive style, in which infusion rates are adjusted and in which comfort levels may be more consistent. Second, most of their cohort (72.2%) was ventilated through uncuffed endotracheal tubes. In the 2010 and 2015 editions, the American Heart Association guidelines stated that cuffed endotracheal tubes “may be preferable” for situations that are commonly seen in the pediatric intensive care unit (PICU), such as poor lung compliance and high airway resistance, and it is our general practice to use cuffed endotracheal tubes in children of all ages.<sup>9,10</sup> The use of cuffed endotracheal tubes is associated with a low side effect profile, likely influenced by recent improvements in cuff design to better fit the pediatric airway and create a sufficient seal at low pressures, with minimal pressure points.<sup>11</sup> Regarding subglottic stenosis, there are possible benefits of using a cuffed tube. For any given patient, the recommended diameter of an uncuffed tube is larger than that recommended for a cuffed tube. Larger endotracheal tubes lead to increased tissue injury, including by direct mucosal compression at several sites along the airway by the side of the endotracheal tube.<sup>12</sup> Tracheal damage can also be caused by pressure from the distal edge of the tube against the airway. A properly inflated cuff may keep the edge of the endotracheal tube more centrally situated within the lumen of the airway and away from the mucosa. Moreover, the use of uncuffed tubes often prompts reintubation – during which the edge of the endotracheal tube may irritate the pharynx, larynx, and trachea – for an increased tube size if a significant leak develops. In one randomized study of children undergoing surgery, the insertion of an uncuffed tube required reintubation for a properly sized tube in 347 out of 1127 subjects (30.8%), a significantly higher rate than what was observed with cuffed tube placement (24/1119 [2.1%]).<sup>13</sup> The number of reintubations has been previously shown to be associated with increased airway injury.<sup>14</sup> Reintubation due to an incorrectly sized uncuffed endotracheal tube was needed in the current study cohort (exact number not reported), and the use of cuffed tubes may avoid unnecessary additional airway trauma. Finally, it is important to note that the approximately 10% rate of subglottic stenosis reported in multiple studies by this research group is higher than those reported by other groups (6/215 [2.8%] by Gomes Cordiero et al., 6/144 [4.2%] by Jorgensen et al.), but this may actually reflect a more sensitive and thorough evaluation rather than a true increased local incidence.<sup>14,15</sup>

Those issues notwithstanding, the authors report that children in their cohort who developed subglottic stenosis spent much more time (15.8%) undersedated with a COMFORT-B score of 23–30 when compared with those who did not develop subglottic stenosis (3.7%). Taking this at face value, one could postulate that avoiding periods of

undersedation may reduce the risk of subglottic stenosis. But what is the reaction to aiming to avoid undersedation? Obviously, it will be a predilection toward oversedation. Oversedation and increased use of sedative/analgesic drugs come with a litany of possible adverse effects. Increased drug usage is associated with increased risks of drug withdrawal syndrome and extubation failure.<sup>16,17</sup> Opiates and benzodiazepines have been associated with dose- and time-dependent neurodegeneration in pediatric animal models, and increased usage of particular drugs may worsen cognitive outcomes in children.<sup>18,19</sup> The most commonly used sedative/analgesic drugs can prompt hypotension, which itself is a risk factor for unfavorable outcomes in many common PICU conditions.<sup>20,21</sup> More specifically to the topic at hand, the authors themselves note in their introduction that excessive sedation can lead to airway hypoperfusion and local ischemia, which may then contribute to subglottic stenosis.

So where does this leave the practicing pediatric intensivist? As is often the case, we now have more data to incorporate into our clinical decision-making, but we are also left with many more questions. These data support the intuitive practice that keeping a child “well-sedated” may reduce trauma to the airway, but is that worth the risks of oversedation? What is the impact of sedation on subglottic stenosis in children with a properly inflated cuffed endotracheal tube? Further work is needed to answer these questions and more, and we look forward to the next contribution from this prolific research group.

## Conflicts of interest

The authors declare no conflicts of interest.

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