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Editorial

Do Children With Down Syndrome Require More Opioids During Cardiac Surgery?

THE ASSOCIATION between Down syndrome (DS) and congenital heart disease (CHD) is well- documented, with many of these patients requiring surgical intervention in early childhood.[1] Although DS does not convey an increased risk of mortality after congenital heart surgery, children with DS have an increased risk for postoperative complications, including increased length of stay (LOS), heart block requiring permanent pacemaker placement after ventricular septal defect (VSD) repair, respiratory complications, and complications related to pulmonary hypertension.[2]

In the past, it was common to hear that pediatric intensivists adhered to the belief that children with DS needed more (or less) sedation and/or analgesics than other children, and this tenet infused clinical practice. The phrase "a sedation nightmare" was a hackneyed expression with regard to management of a child with DS after undergoing cardiac surgery. It is important to remember that children with DS also are disproportionately affected by obstructive sleep apnea and chronic upper airway obstruction, which not only increase their risk of respiratory complications after congenital heart surgery, but also are associated with an increased sensitivity to opioids.[2,3] Additionally, poor pain control can precipitate or worsen pulmonary hypertension postoperatively in DS children.[4]

However, in the last ten years, there have been significant contributions toward understanding whether DS confers differences in both processing and metabolizing opioids and benzodiazepines, as well as differences in pain interpretation and expression in this population.[5-9] Dr Vogel and her colleagues provided a strong addition to this literature with their article in this edition of the *Journal of Cardiothoracic and Vascular Anesthesia.* The authors reported on the dosing of opioid and concluded that children with DS do not have an increased requirement for opioids and nonopioid analgesia after cardiovascular surgery compared with their non-DS cohorts.[10] The strength of Dr Vogel's study was the size of the cohort, the homogeneity of the cardiac defect afflicting the patients, and the consideration of adjunct medications such as dexmedetomidine, ketamine, and nonsteroidal anti-inflammatory drugs (NSAIDs). Prior studies have been small, heterogeneous, and lacking in consideration of adjunct nonopioid medications.[5,11] This last point is important; the recognition that delirium occurs frequently in pediatric critical illness and that delirium's deleterious effects (that for years have been well-understood in the adult intensive care unit [ICU]) also can have clinical significance only recently has gained a foothold in pediatric ICUs.[12-14] The relationship between developing delirium and use of medications, such as benzodiazepines in particular, but also opioids, argue for the use of adjunct medications. The presence of often fierce and difficult-to-manage opioid and benzodiazepine withdrawal syndrome, also is a common occurrence in the pediatric cardiac ICU.

Vogel and colleagues tested the hypothesis that children with DS receive higher doses of opioids compared with children without DS after single-stage, surgical repair of complete atrioventricular canal (CAVC) defects. Additionally, they analyzed the effect of intraoperative and postoperative administration of opioid-adjunct medications: acetaminophen, dexmedetomidine, ketamine, ketorolac, and midazolam. This is especially important given the recent trend toward inclusion of these medications in minimizing opioid exposure in children. Primary outcomes were oral morphine equivalents (OME) postoperatively received in the first 24 and 48 hours. Please see Table 1 for the OME conversion chart.[15] Pain scores, length-of-stay (LOS), and incidence of complications including endotracheal reintubation, the need for permanent pacemaker placement, and 30-day mortality also were evaluated. These complications described are a thoughtful assessment of the common postoperative complications in this patient population. The major critique of this retrospective study is that the DS group (n = 131 children) was much larger than the control group (n = 24 children) due to the increased incidence of balanced CAVC in children with DS compared with the general population. However, a post-hoc power calculation was done and indicated that the sample sizes of n = 24 and n = 131 provided 80% power for detecting moderate differences (standardized effect size = 0.70) between the two

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Table 1
Oral Morphine-Equivalent Conversions[15]

Drug (Unit, Route)	Conversion Factor
Fentanyl (mcg, IV)	0.2
Hydromorphone (mg, IV)	17.5
Morphine (mg, IV)	3
Oxycodone (mg, PO)	1.5

Abbreviations: IV, intravenous; PO, postoperative.

groups based on the nonparametric Wilcoxon rank sum test and assuming a Bonferroni-adjusted two-tailed 2.5% alpha.[10]

No significant differences in preoperative respiratory status, surgical times, and intraoperative medication administration were detected between the two groups. There also were no differences in administration of nonopioid adjuncts (dexmedetomidine and acetaminophen), pain scores, LOS, and respiratory complications. Importantly, no difference in OME administration was found in the first 24 hours postoperatively; however, median OME administration was lower in the DS group for the second two postoperative days.[10]

The clinical observation that children with DS do not have increased postoperative opioid requirements is consistent with pharmacokinetic studies in children with DS reported by Goot et al. In this prospective study, patients with DS undergoing congenital heart surgery (n = 20) received morphine infusions for the first 24 hours postoperatively after receiving a morphine-free cardiac anesthetic. A control group (n = 22) was matched by age and cardiac lesion. No difference in pharmacokinetics of morphine metabolism was detected between the two groups.[9]

The report by Vogel and colleagues strengthens reconsideration of caregiver bias regarding Down syndrome and postoperative pain and pharmacologic metabolism. That there is a closer alliance of perception and reality is important. That is not to say that there may not be an altered mechanism of pain interpretation and expression in children with Down syndrome. This still is not clear. We hope that the work of Vogel and colleagues will spur efforts to look prospectively at challenges such as pain scoring in the pediatric postoperative cardiac surgical patient. However, for now, their study adds to our current understanding of the perceived differences and similarities in the opioid requirements in children with DS and those without.

Conflict of Interest

None.

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