Sedation Practices in Pediatric Cardiac ICUs After Cardiopulmonary Bypass*

Luc L. Mertens, MD, PhD
Department of Paediatrics
The Labatt Family Heart Centre
The Hospital for Sick Children
University of Toronto
Toronto, ON, Canada

Steven M. Schwartz, MD
Departments of Critical Care Medicine and Paediatrics
The Labatt Family Heart Centre
The Hospital for Sick Children
University of Toronto
Toronto, ON, Canada

After cardiopulmonary bypass (CPB), significant cardiovascular instability can occur, especially within the first 12–24 hours after surgery. This is a period during which cardiac function decreases, whereas oxygen consumption and metabolic demands are increased partially related to the inflammatory response to CPB (1). This effect is less significant after short bypass runs and less extensive surgery, such as after closure of atrial or ventricular septal defects. In the less complex cases, when patients are hemodynamically stable, fast weaning from ventilation with good pain control allows for early extubation in a significant number of cases without prolonged use of sedatives (2). For more complex cases, such as after the arterial switch operation or Norwood operation, the effect of the longer bypass and more extensive surgery is more significant and often requires prolonged ventilation with sedation and analgesia to reduce metabolic demands and to cope with the reality of safely maintaining invasive instrumentation in a baby or a small child. Different cardiac ICUs (CICUs) use different sedation and analgesia strategies, and few comparative studies are available.

In this issue of *Pediatric Critical Care Medicine*, Kleiber et al (3) compare two sedation strategies after complex cardiac surgeries in infants less than 6 months old requiring prolonged CPB (defined as longer than 150 min) in a single CICU in Australia. The authors compared a historical preemptive strategy of using continuous infusion of midazolam with a targeted on-demand sedation strategy of using intermittent sedation dosages of clonidine followed by midazolam boluses and continuous infusions. The on-demand treatment is based on intermittent patient evaluations (every 4 hr) aiming for a COMFORT-Behavior (COMFORT-B) score between 10 and 20 (4). In both groups, analgesia was provided using a continuous infusion of morphine with intermittent dosages of morphine or fentanyl. The study design is a retrospective case-control study whereby the preemptive patients were matched with the on-demand sedation patients for the type of surgery and CPB duration. The authors found no significant differences in the prevalence of cardiovascular instability defined by administration of two or more inotropic infusions or administration of volume boluses above 60 mL/kg (68.8% in the preemptive group vs 62.5% in the targeted group). Also other variables of cardiovascular outcomes, including mixed venous saturations, vasoactive inotropic score, and lactate, were not significantly different between the two groups. Although the total amount of morphine used was similar between the two groups, a lower cumulative dose of sedatives was given in the targeted group. The authors also tried to retrospectively compare the prevalence of oversedation between the two groups, but this was proven difficult as the COMFORT-B score was only introduced in their unit together with the new on-demand sedation protocol. The use of different assessment protocols makes direct comparisons between the two groups extremely difficult. The authors still claim that the preemptive strategy was associated with more frequent oversedation (90% of all patients vs 61% in the on-demand group), but this has to be interpreted with caution. The higher reported incidence of oversedation did not seem to influence the duration of mechanical ventilation, ICU stay, or any other adverse events.

Overall, the outcomes between the two strategies are not significantly different although with a relatively small sample size of 33 patients per group, and both approaches seem to result in comparable outcomes. This type of study provides objective data on which the impact of different sedation strategies can be evaluated. It is interesting to note that in the on-demand group, about one-third of the patients still were started on a midazolam infusion mainly because of a concern about the bradycardia and hypotension that can be associated with boluses of clonidine. Especially, in the more unstable children, physicians deviated from the sedation protocol. This reflects good medical practice that drives the management based on a variety of sources of information, including individual patient condition and understanding of the specific physiologic situation at hand, which has been recognized as preferable to strictly applying population-derived evidence across the board in the critical care unit (5, 6). This approach also may have influenced the results in the on-demand group as it seems that physicians more commonly deviated from the protocol in the case of hemodynamic instability and avoided

*See also p. 321.

Key Words: cardiopulmonary bypass; infants; sedation

Dr. Schwartz received funding from Novartis AG and from Health Outcomes International and disclosed other support (the relationships above are not related to the current work in any way). Dr. Mertens has disclosed that he does not have any potential conflicts of interest.

DOI: 10.1097/PCC.0000000000000693

the use of clonidine, which could have resulted in more favorable hemodynamic outcomes in this group. Thus, the results may not really reflect a full practice change within the unit as physicians tended to fall back on the more familiar continuous infusion strategy in the more unstable patients. Outside of the 12-hour study window, the number of patients in which continuous sedation was used increased to about 47%. This also demonstrates how difficult it is to change strategies especially when management is more challenging. We would suggest the authors to perform a follow-up study to look at evolution of protocol adherence over time and further monitor the impact on outcomes.

A positive potential benefit of the proposed protocol that is difficult to study was the introduction of the targeted protocol may have resulted in more conscious attention of the entire team to sedation, which could have contributed to prevention of oversedation and resulted in a more rational systematic approach. Using a standardized scoring system contributes to more objective decisions and careful use of medication only when indicated. Overall, the project could be seen as a quality improvement effort without immediate demonstrable effects on clinical outcomes. The systematic evaluation of patient comfort and sedation could, however, have more qualitative impact on patient care that is more difficult to measure by just looking at outcome variables.

The authors motivated the study based on the hypothesis that sedation is potentially bad for patients, and especially, the use of benzodiazepines may be neurotoxic. Much of the work done with regard to this question in the pediatric cardiac population has focused on repeated dosing over longer periods (7). Therefore, it remains questionable whether the relative small differences in cumulative sedation dose between the two groups would have any significant impact on long-term neurologic outcomes in this high-risk population because sedative infusions were ultimately started in almost half the targeted patients after the conclusion of the study period. A change from midazolam to clonidine as the preferred sedative would only complicate any attempts to understand sedative use compared with sedative agent in this particular study group. Factors such as fetal brain circulation and its effect on brain growth, the impact of CPB and hemodynamic instability in the postoperative period, and the impact of inflammatory response on the brain and brain perfusion all seem more likely determinants for long-term neurocognitive outcome. The basic hypothesis of the study that the use of sedative drugs is to be avoided as much as possible because of potential negative effects on the brain remains controversial and is currently under study by a number of groups. In the end though, targeting the use of these agents to individual patient need within the context of an overall systematic approach seems wise.

REFERENCES

1. Floh AA, Nakada M, La Rotta G, et al: Systemic inflammation increases energy expenditure following pediatric cardiopulmonary bypass. *Pediatr Crit Care Med* 2015; 16:343–351
2. Gaies M, Tabbutt S, Schwartz SM, et al: Clinical epidemiology of extubation failure in the pediatric cardiac ICU: A report from the pediatric cardiac critical care consortium. *Pediatr Crit Care Med* 2015; 16:837–845
3. Kleiber N, de Wildt SN, Cortina G, et al: Comparative Analysis of Preemptive Versus Targeted Sedation on Cardiovascular Stability After High-Risk Cardiac Surgery in Infants. *Pediatr Crit Care Med* 2016; 17:321–331
4. Ista E, van Dijk M, Tibboel D, et al: Assessment of sedation levels in pediatric intensive care patients can be improved by using the COMFORT "behavior" scale. *Pediatr Crit Care Med* 2005; 6:58–63
5. Tonelli MR: The limits of evidence-based medicine. *Respir Care* 2001; 46:1435–1440
6. Tonelli MR, Curtis JR, Guntupalli KK, et al; ACCP/ATS/SCCM Working Group: An official multi-society statement: The role of clinical research results in the practice of critical care medicine. *Am J Respir Crit Care Med* 2012; 185:1117–1124
7. Guerra GG, Robertson CM, Alton GY, et al; Western Canadian Complex Pediatric Therapies Follow-up Group: Neurodevelopmental outcome following exposure to sedative and analgesic drugs for complex cardiac surgery in infancy. *Paediatr Anaesth* 2011; 21:932–941