Are Current Prophylactic Antibiotic Dosing Regimens in Pediatric Cardiac Surgery Sufficient to Prevent Surgical-Site Infections?

The reported prevalence of congenital heart disease (CHD) has continued to increase globally with a recent estimate of 9.41 cases for every 1000 live births.[1] Approximately 25% of the 40,000 children born in the United States annually with CHD will require surgical intervention within the first year of life.[2] However, surgical-site infections (SSI) still remain a rare but potentially devastating complication with significant impact on patient mortality, morbidity, and health-care costs.[3,4]

The use of perioperative antibiotic prophylaxis has been the cornerstone in SSI prevention.[5] However, no standard guidelines regarding the optimal antibiotic dosing regimens in pediatric cardiac surgery have been published. The challenges in establishing a standard guideline for this group of cardiac surgical patients stem from variabilities in pharmacokinetics of the antibiotics in different age groups of patients, population characteristics, complexity of the operations, and protocols for cardiopulmonary bypass (CPB). Much of the research in this area has been directed toward measuring plasma antibiotic concentrations at various points during surgery to ensure adequate levels above the minimum inhibitory concentrations (MICs) for the common causative organisms responsible for SSI[6,7] as well as constructing pharmacokinetic models to support specific dosing guidelines.[8]

In this issue of *Annals of Cardiac Anaesthesia,* Lapmahapaisan *et al.*[9] have demonstrated that an intravenous infusion of cefazolin 25 mg kg^{-1} within 1 h of skin incision followed by a similar infusion administered to the CPB prime volume in uncomplicated pediatric surgery achieved plasma concentrations 4 times above the MICs for Methicillin-sensitive *Staphylococcus aureus* (MSSA) and *Staphylococcus epidermidis* in most patients, but not for *Enterobacter* and *Escherichia coli*. Since approximately 75% of SSI in infants after cardiac surgery are caused by gram-positive bacteria, with MSSA responsible for 63% in particular,[10] this would seem like a perfectly reasonable dosing regimen.

However, there are several limitations of this study that we must bear in mind while interpreting the results. First, plasma antibiotic concentrations may not be reflective of actual tissue concentrations as demonstrated by Himebauch *et al.*, who reported that subjects with the highest plasma cefazolin concentrations did not necessarily have the highest concentrations of unbound cefazolin in skeletal muscles.[11] This observation highlights the limitation of using plasma concentrations as surrogate markers for tissue antibiotic concentrations. Second, cefazolin is extensively bound to plasma proteins and the unbound cefazolin concentrations in this study were calculated assuming 80% protein binding. Alterations in protein binding can occur as a result of hemodilution, hypothermia, or drug displacement, which can result in incorrect inference. Finally, this study was conducted in pediatric patients with simple cardiac diseases and uncomplicated surgeries with CPB time less than 3 h. The results from this study should not be extrapolated to complex patients undergoing complicated surgeries involving deep hypothermic circulatory arrest and long CPB durations due to the different pharmacokinetic and pharmacodynamic alterations involved.

While have provided additional data on the pharmacokinetics and adequacy of cefazolin dosing in a specific population, more research is still needed to develop pharmacokinetic models to predict and guide dosing of antibiotics in pediatric cardiac surgery.

Priscilla Hui Yi Phoon[1,2], Nian Chih Hwang[1,2]

[1]Department of Anaesthesiology, Singapore General Hospital, [2]Department of Cardiothoracic Anaesthesia, National Heart Centre, Singapore

Address for correspondence: Prof. Nian Chih Hwang
Department of Anaesthesiology, Singapore General Hospital, Outram Road, 169608, Singapore.
E-mail: hwang.nian.chih@singhealth.com.sg

Submitted: 20-Oct-2019
Accepted: 05-Nov-2019 **Published:** 19-Apr-2021

REFERENCES

1. Liu Y, Chen S, Zühlke L, Black GC, Choy MK, Li N, *et al.* Global birth prevalence of congenital heart defects 1970-2017: Updated systematic review and meta-analysis of 260 studies. Int J Epidemiol

2019;48:455-63.
2. Triedman JK, Newburger JW. Trends in congenital heart disease: The next decade. Circulation 2016;133:2716-33.
3. Cannon M, Hersey D, Harrison S, Joy B, Naguib A, Galantowicz M, *et al*. Improving surveillance and prevention of surgical site infection in pediatric cardiac surgery. Am J Crit Care 2016;25:e30-7.
4. Sochet AA, Cartron AM, Nyhan A, Spaeder MC, Song X, Brown AT, *et al*. Surgical site infection after pediatric cardiothoracic surgery. World J Pediatr Congenit Heart Surg 2017;8:7-12.
5. Abu-Omar Y, Kocher GJ, Bosco P, Barbero C, Waller D, Gudbjartsson T, *et al*. European association for cardiothoracic surgery expert consensus statement on the prevention and management of mediastinitis. Eur J Cardiothorac Surg 2017;51:10-29.
6. Haessler D, Reverdy M-E, Neidecker J, Brûlé P, Ninet J, Lehot JJ. Antibiotic prophylaxis with cefazolin and gentamicin in cardiac surgery for children less than ten kilograms. J Cardiothorac Vasc Anesth 2003;17:221-5.
7. Himebauch AS, Nicolson SC, Sisko M, Moorthy G, Fuller S, Gaynor JW, *et al*. Skeletal muscle and plasma concentrations of cefazolin during cardiac surgery in infants. J Thorac Cardiovasc Surg 2014;148:2634-41.
8. Ingrande J, Gutierrez K, Lemmens HJ, Verma A, Nicolau DP, Sutherland CA, *et al*. Pharmacokinetics of cefazolin and vancomycin in infants undergoing open-heart surgery with cardiopulmonary bypass. Anesth Analg 2019;128:935-43.
9. Lapmahapaisan S, Maisat W, Tantiwongkosri K, Jutasompakorn P, Sisan W. Plasma concentrations of cefazolin in pediatric patients undergoing cardiac surgery. Ann Card Anaesth 2021;24:149-54.
10. Murray MT, Krishnamurthy G, Corda R, Turcotte RF, Jia H, Bacha E, *et al*. Surgical site infections and bloodstream infections in infants after cardiac surgery. J Thorac Cardiovasc Surg 2014;148:259-65.
11. Himebauch AS, Nicolson SC, Sisko M, Moorthy G, Fuller S, Gaynor JW, *et al*. Skeletal muscle and plasma concentrations of cefazolin during cardiac surgery in infants. J Thorac Cardiovasc Surg 2014;148:2634-41.

Access this article online

Quick Response Code:

Website: www.annals.in

DOI: 10.4103/aca.ACA_156_19

How to cite this article: Phoon PH, Hwang NC. Are current prophylactic antibiotic dosing regimens in pediatric cardiac surgery sufficient to prevent surgical-site infections? Ann Card Anaesth 2021;24:129-30.