Steroid Use for Management of Vasoactive Resistant Shock in Pediatric Cardiac Intensive Care Patients

Experience of the Consortium of Congenital Cardiac Care–Measurement of Nursing Practice

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Background: Although a variety of doses and duration of hydrocortisone have been reported as a treatment modality for congenital heart surgery patients with refractory hypotension, there remains a lack of understanding of the clinical use in pediatric cardiac programs.

Objectives: The aim of this study was to describe the current practice of steroid use for refractory hypotension in postoperative congenital heart surgery patients.

Method: Survey participants were recruited from the Consortium of Congenital Cardiac Care–Measurement of Nursing Practice. The survey focused on 4 areas: diagnosis, intervention, duration of therapy, and clinical decision making. Data were summarized using descriptive statistics.

Results: Among the programs, 24 of 31 (77%) responded, with 21 (95%) using hydrocortisone as a treatment modality. Most, 20 (83%), reported no written clinical guideline for the use of hydrocortisone. Variation in dosing existed as 3 centers (14%) use 50 mg/m^2/d, 6 (29%) use 100 mg/m^2/d, and 8 (38%) indicated that dosing varies by provider.

Discussion: Nearly all centers reported using hydrocortisone for the treatment of hypotension refractory to fluid resuscitation and vasoactive medications. Substantial variation in practice exists in areas of diagnosis, dosing, and duration of hydrocortisone. More research is needed to develop a clinical practice guideline to standardize practice.

Keywords: Pediatric congenital heart surgery, Refractory hypotension, Steroid use

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Surgical repair of most congenital cardiac defects involves cardiopulmonary bypass (CPB), which has known consequences in the postoperative period including inflammatory response, low cardiac output syndrome (LCOS), and need for inotropic support to maintain hemodynamics.[1] In some patients, hypotension and LCOS are resistant to escalation of inotropes and fluid resuscitation. Hydrocortisone is one treatment option presuming the etiology of refractory hypotension to be a relative adrenal insufficiency.[2,3] Although the effect of CPB on the hypopituitary adrenal axis is not fully understood, there is literature supporting disruption of the adrenal axis secondary to CPB as evidenced by disruption of total cortisol levels.[4,5]

Hydrocortisone has been shown to be effective at improving hemodynamics and decreasing LCOS post CPB in pediatric patients, especially in the neonatal population.[3,6,7] Dosing and means of administration vary in the literature from 50 mg/m^2/d to 100 mg/m^2/d and are administered either with bolus dosing or q6 intermittent dosing.[2,6,7] Robert and colleagues[7] showed decrease in the severity of LCOS by using hydrocortisone infusions in postoperative patients. Additional studies have used retrospective review of bolus dosing to show the improvement of hemodynamics in the postoperative patient receiving hydrocortisone.[3,6]

Initiation of steroids is not without risk, as Mastropietro and colleagues[8] published that cumulative steroid exposure is positively associated with increase in infections. In contrast, Neunhoeffer et al's[6] study of 160 patients receiving hydrocortisone specifically showed no increase in infections. Flores and colleagues[9] conducted a survey confirming that a large percentage of physicians use hydrocortisone in practice to treat varying degrees of LCOS. There is a notable lack of systematic reviews and large randomized controlled trial evidence within the literature to guide practice, and there are important inconsistencies in the studies that have been completed, leading to difficulties in making a consensus statement on best practice.

AIMS

The aim of this study was to describe the state of practice regarding steroid use for vasoactive and fluid-resistant hypotension in postoperative congenital heart surgery patients in the United States.

METHODS

Survey Population

Survey participants were recruited from the Consortium of Congenital Cardiac Care–Measurement of Nursing Practice (C4-MNP). The C4-MNP is a national collaborative of 44 cardiovascular programs in freestanding children's hospitals established to identify nursing care actions for measurement in the pediatric cardiovascular environment and to test standardized measures representative of pediatric nursing care of the cardiovascular patient for benchmarking. Members of C4-MNP include advanced practice nurses, nurse administrators, clinical nurse specialists, researchers, and bedside clinicians. The development of state of practices begins with participating nurses and is sent out consortium-wide for feedback. The goal of these states of practices is to develop standardized, best practices within the field. Feedback is always summarized via aggregate report and disseminated to participating sites. One survey was requested from each center with the requirement that the respondent be a clinician taking direct care of cardiac intensive care unit (ICU) patients.

Survey Development and Administration

Development of the survey began with presentation of the idea and background literature to the C4-MNP members. An electronic survey was developed that included 26 multiple-choice questions, with the option for further open-ended explanation for some of the questions. Survey questions were developed based on input from a variety of experienced providers throughout the C4-MNP. Content consisted of 4 demographic questions, 6 questions related to diagnostics, 8 questions related to the intervention, 3 related to duration of therapy, and 5 related to clinical decision making. Several versions of the survey were reviewed and edited by members of the consortium for clarity, accuracy, and redundancy. The survey was trialed with content experts to ensure readability and clarity of questions. The survey took approximately 10 minutes to complete. The survey was administered via REDCap (Research Electronic Data Capture). REDCap is a secure, Web-based application designed to support data capture for research and quality improvement.[10] A link was sent to each consortium representative requesting that 1 survey be completed per center.

ANALYSIS

Survey data were collected and managed using REDCap electronic data capture tools hosted at Boston Children's Hospital. Deidentified survey data were exported from REDCap into Microsoft Excel and were cleaned and assessed by a data analyst to ensure accuracy of data before analysis. Quantitative data were summarized in Microsoft Excel using descriptive statistics, frequencies, and proportions. Qualitative data were summarized into accompanying tables. Results were then synthesized into a report to describe the current state of practice in pediatric critical care units regarding steroid use for refractory hypotension.

RESULTS

At the time of the survey, 31 sites were participating in C4-MNP programs and were invited to participate in

the electronic survey. A total of 24 sites responded, for a response rate of 77%.

Demographics

Most, 19 (91%), of the respondents were providers, 8 (38%) were physicians, 10 (48%) were nurse practitioners, and one (5%) was a physician assistant, with the remainder 10% of respondents being certified nurse specialists or registered nurses. Of the respondents, 19 (91%) worked in a cardiac or pediatric ICU setting, whereas the remaining 2 respondents worked in cardiothoracic surgery service. Of the respondents, 12 (57%) had greater than 10 years of clinical experience, 4 (19%) had 5 to 10 years of experience, and another 4 (19%) had 3 to 5 years of experience. The centers represented a majority of high-volume cases, with 20 (95%) doing greater than 200 CPB cases per year (Table 1).

TABLE 1 Demographic Characteristics of Participants/Centers

Characteristic (N = 21)	n (%)
Clinical role	
PA	1 (4.8)
NP	10 (47.6)
Physician	8 (38.1)
Other (CNS, RN)	2 (9.5)
Area of practice	
Inpatient cardiac floor or step-down	0 (0.0)
CICU or pediatric ICU	19 (90.5)
Outpatient care area	0 (0.0)
Other (CT surgical service line, preoperative/postoperative clinics, CTICU, CV, acute ward)	2 (9.5)
Years of clinical experience	
0-2	1 (4.8)
3-5	4 (19.1)
5-10	4 (19.1)
>10	12 (57.0)
CPB cases per year	
0-50	0 (0.0)
5-100	1 (4.8)
101-200	0 (0.0)
201-400	13 (61.9)
401-600	4 (19.1)
>600	3 (14.2)

Abbreviations: CICU, cardiac intensive care unit; CNS, clinical nurse specialist; CPB, cardiopulmonary bypass; CT, Cardiothoracic; CTICU, Cardiothoracic Intensive Care Unit; CV, Cardiovascular; ICU, intensive care unit; NP, nurse practitioner; PA, physician assistant; RN, registered nurse.

Diagnosis of Postoperative Adrenal Insufficiency

Twenty centers (83%) reported that there was no written or clinical guideline in place for diagnosis of relative adrenal insufficiency or critical illness–related adrenal insufficiency in cardiac patients. Variations in practice existed in the diagnostic process: 7 centers (29%) always include baseline cortisol levels for diagnosis of postoperative adrenal insufficiency, 5 (21%) responded often, 10 (42%) responded sometimes, and 2 (8%) responded they never use cortisol levels as part of diagnosis. For postoperative adrenal insufficiency, 13 (54%) responded they sometimes use adrenocorticotropin hormone (ACTH) stimulation test for diagnosis, whereas 8 (33%) never use ACTH testing for diagnosis. Knowing there is variation in laboratory diagnostics, which correlates with variation in literature on this topic,[11] clinical diagnostic factors were also assessed. All centers included hypotension refractory to vasoactive medication and fluid resuscitation as clinical factors for postoperative adrenal insufficiency diagnosis, whereas 23 (96%) responded increased inotropic requirement, 6 (25%) included tachycardia, and 6 (25%) included relative bradycardia for diagnosis (Table 2).

Intervention

Of the centers, 21 (96%) responded that hydrocortisone therapy was used as a treatment modality for LCOS refractory to vasoactive medication and fluid resuscitation, and 19 centers responded that hydrocortisone was routinely used as a treatment. Nineteen centers responded no to having a written guideline for indication to start hydrocortisone therapy. Initial dosing of hydrocortisone was variable for each center, with 8 (38%) reporting dosing varied by provider within their center, 3 (14%) selecting 50 mg/m^2/d, and 6 (29%) reporting that 100 mg/m^2/d was used. In addition, there was also variation in practice regarding hydrocortisone use across patients (initiation, dosing, duration); of the centers, 1 (5%) responded always, 7 (33%) responded often, 10 (48%) responded sometimes, and 3 (14%) said never (Table 2).

Duration of Therapy

Weaning of hydrocortisone therapy was reportedly driven by clinical guideline in only 1 center. Timing of initiation of weaning and average duration of therapy were variable within centers. Of the centers, 6 providers (25%) begin weaning hydrocortisone between 24 and 48 hours, another 6 (25%) begin between 3 and 5 days, 1 (5%) begins between 7 and 10 days, 5 (24%) begin when patient tolerates wean of inotropes, and 3 (14%) chose other and listed specific scenarios. As for the duration of hydrocortisone therapy, of the 13 respondents, most (69%) recorded 5

TABLE 2 Diagnosis, Intervention, and Duration

	n (%)
Diagnosis of postoperative adrenal insufficiency (N = 24)	
Baseline cortisol levels	
Always	7 (29.2)
Often	5 (20.8)
Sometimes	10 (41.7)
Never	2 (8.3)
Adrenocorticoid stimulation test	
Always	1 (4.2)
Often	2 (8.3)
Sometimes	13 (54.2)
Never	8 (33.3)
Clinical factors included in diagnosis	
Hypotension refractory to vasoactive medication and fluid resuscitation	24 (100.0)
Tachycardia	6 (25.0)
Increased inotropic requirements	23 (95.8)
Relative bradycardia	6 (25.0)
Other	3 (12.5)
Intervention (N = 21)	
Initial dose of hydrocortisone	
50 mg/m^2/d	3 (14.3)
100 mg/m^2/d	6 (28.6)
Varies by provider	8 (38.1)
Other	4 (19.0)
Variation in practice regarding hydrocortisone across patients (initiation, dosing, duration, etc)	
Always	1 (4.8)
Often	7 (33.3)
Sometimes	10 (47.6)
Never	3 (14.3)
Duration of therapy (N = 21)	
Time to wean hydrocortisone	
24-48 h	6 (28.6)
3-5 d	6 (28.6)
7-10 d	1 (4.8)
When patient tolerates wean of inotropes	5 (23.8)
Other	3 (14.3)
Average duration of hydrocortisone therapy, d	
0-2	2 (15.4)
3-4	2 (15.4)
5-7	9 (69.2)
Clinical decision making (N = 20)	
Cortisone level: tool for dosing/duration of steroid therapy	
Always	3 (15.0)
Often	7 (35.0)
Sometimes	7 (35.0)
Never	3 (15.0)
Endocrine consult	
Always	0 (0.0)
Often	0 (0.0)
Sometimes	13 (65.0)
Never	7 (35.0)
Steroid initiation by provider	
Upon return from OR	0 (0.0)
At the time patient appears clinically symptomatic/labile	7 (35.0)
Variable depending on procedure/patient characteristics	8 (40.0)
Other	5 (25.0)

Abbreviation: OR, Operating Room.

to 7 days, whereas the remainder of respondents (31%) responded between 0 and 4 days (Table 2).

Clinical Decision Making

The use of cortisol levels as a tool for dosing or duration of therapy of hydrocortisone was also assessed. Of the centers, 3 (15%) responded always, 7 (35%) responded often, 7 (35%) responded sometimes, and 3 (15%) responded never. Follow-up services for patients receiving hydrocortisone were also assessed. Of the centers, 13 (65%) responded that endocrine service is sometimes consulted for patients receiving hydrocortisone, whereas the remaining 7 (35%) responded endocrine service is never consulted. Two centers (10%) reported they have long-term follow-up for patients who received stress steroids in the ICU, which included repeat ACTH stimulation testing after long periods of steroid use and outpatient follow-up for patients with proven insufficiency. In addition to follow-up, there was a question assessing how clinicians approached patients who had previously received steroids and when they would initiate steroids in that patient. Of the centers, 7 (35%) initiated steroid use at the time patient appears clinically symptomatic/labile, 8 (40%) responded initiation was variable depending on procedure or patient characteristics, and the remaining 5 (25%) described other times of steroid initiation that included intraoperatively, before operation, or not done (Table 2).

DISCUSSION

This assessment of the current practice of steroid use for postoperative congenital heart surgery with vasoactive resistant shock revealed a number of findings and important

opportunities. Although there were some similarities, there were also variations found in areas of diagnosis, intervention, duration, and clinical decision making in the use of hydrocortisone both within and across centers.

Most respondents used hypotension refractory to vasoactive medications and fluid resuscitation as a diagnostic factor in the decision to start hydrocortisone. There were no consistencies for laboratory diagnostics such as ACTH stimulation tests or cortisol levels reported across programs. Cortisol levels were also not consistently used in determination for duration of therapy or weaning of hydrocortisone, although a percentage of centers did report using them for this purpose. This is consistent with findings that cortisol levels may not be sufficient to predict response to hydrocortisone.[11,12]

Most centers also reported using hydrocortisone for low cardiac output refractory to inotropes and fluid resuscitation, but there were variations in the dosing both across and within centers. Findings in variation of hydrocortisone dosing used by the provider in this survey were consistent with findings of variation of dosing reported by Flores and colleagues,[9] which reported 28% of respondents used 50 mg/m^2/d and 26% used 100 mg/m^2/d. However, there was a surprising variation of practice related to the intervention dosing within centers not reported in previous surveys.

In regard to the weaning of hydrocortisone therapy, respondents were fairly evenly spread into 3 different responses: 24 to 48 hours, 7 to 10 days, and when the patient is tolerating wean of inotropes. Sixty-nine percent of respondents reported total duration of hydrocortisone to be in the range of 5 to 7 days. Again, there was a lack of guideline for weaning hydrocortisone reported across most centers. Variation in practice existed in all facets of hydrocortisone administration from dosing used to the weaning process used.

One area of further study is looking into why the variation exists. Patients undergoing congenital heart surgery may vary greatly in comorbidities and complexity particularly in the postoperative period.[13,14] These variables may be factors in the lack of consistency in diagnosis, dosing, and duration of hydrocortisone in pediatric congenital heart patients. An important area of future work for the C4-MNP collaborative is to understand factors that are important in developing standardized practices. The variation within centers is perhaps more surprising, with only 10% of centers using a written guideline for hydrocortisone therapy. Retrospective reviews of center practices related to hydrocortisone use would be useful in determining whether there are improved outcomes related to a specific dose or timing of initiation of hydrocortisone. Standardization of practice in regard to medication practices has been successful in regard to other areas of pediatric cardiac ICU care such as sedation practices.[15,16] More data are needed to support the development of a standardized guideline for hydrocortisone use in this population.

LIMITATIONS

Although this survey captured the current practice of steroid use for postoperative congenital heart surgery patients, the outcomes of these centers were not studied and will be an opportunity of future research. We also recognize that although we were able to describe the practice across a number of centers, these are not all the centers that provide postoperative care for congenital heart surgery patients and most responding centers provide a high volume of CPB cases.

CONCLUSION

These findings support the need for further research on optimal dosing and weaning of hydrocortisone in postoperative congenital heart surgery patients. Existing studies in many pediatric centers have determined that hydrocortisone has positive hemodynamic effects in this population; however, varied approaches to dosing, duration, and initiation are used. Collaboration can guide the development of a clinical practice guideline to standardize practice both within institutions and between institutions, which has the potential to improve outcomes.

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References

1. Hoffman TM, Wernovsky G, Atz AM, et al. Efficacy and safety of milrinone in preventing low cardiac output syndrome in infants and children after corrective surgery for congenital heart disease. *Circulation*. 2003;107(7):996-1002. doi:10.1161/01.CIR.0000051365.81920.28.
2. Ando M, Park I-S, Wada N, Takahashi Y. Steroid supplementation: a legitimate pharmacotherapy after neonatal open heart surgery. *Ann Thorac Surg*. 2005;80(5):1672-1678. doi:10.1016/j.athoracsur.2005.04.035.
3. Suominen PK, Dickerson HA, Moffett BS, et al. Hemodynamic effects of rescue protocol hydrocortisone in neonates with low cardiac output syndrome after cardiac surgery. *Pediatr Crit Care Med*. 2005;6(6):655-659. doi:10.1097/01.PCC.0000185487.69215.29.
4. Wald EL, Preze E, Eickhoff JC, Backer CL. The effect of cardiopulmonary bypass on the hypothalamic-pituitary-adrenal axis in children. *Pediatr Crit Care Med*. 2011;12(2):190-196. doi:10.1097/PCC.0b013e3181f36d17.
5. Wald EL, Backer CL, Dearani JA, Li Z, Oliver WC, Crow SS. Total and free cortisol responses and their relation to outcomes after cardiopulmonary bypass in infants. *J Thorac Cardiovasc Surg*. 2017;153(5):1155-1163. doi:10.1016/j.jtcvs.2016.11.030.
6. Neunhoeffer F, Renk H, Hofbeck M, et al. Safety, efficacy and response to a hydrocortisone rescue therapy protocol in children with refractory hypotension after cardiopulmonal bypass. *Pediatr Cardiol*. 2015;36(3):640-645. doi:10.1007/s00246-014-1059-3.
7. Robert SM, Borasino S, Dabal RJ, Cleveland DC, Hock KM, Alten JA. Postoperative hydrocortisone infusion reduces the prevalence of low cardiac output syndrome after neonatal cardiopulmonary bypass. *Pediatr Crit Care Med*. 2015;16(7):629-636. doi:10.1097/PCC.0000000000000426.

8. Mastropietro CW, Barrett R, Davalos MC, et al. Cumulative corticosteroid exposure and infection risk after complex pediatric cardiac surgery. *Ann Thorac Surg*. 2013;95(6):2133-2139. doi:10.1016/j.athoracsur.2013.02.026.
9. Flores S, FitzGerald MR, Iliopoulos I, et al. An international survey of corticosteroid use for the management of low cardiac output syndrome. *Pediatr Crit Care Med*. 2017;18(7):630-637. doi:10.1097/PCC.0000000000001180.
10. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010.
11. Green ML, Koch J. Adrenocortical function in the postoperative pediatric cardiac surgical patient. *Curr Opin Pediatr*. 2012;24(3):285-290. doi:10.1097/MOP.0b013e3283532d12.
12. Fernandez EF, Montman R, Watterberg KL. ACTH and cortisol response to critical illness in term and late preterm newborns. *J Perinatol*. 2008;28(12):797-802. doi:10.1038/jp.2008.190.
13. Jacobs JP, Jacobs ML, Lacour-Gayet FG, et al. Stratification of complexity improves the utility and accuracy of outcomes analysis in a multi-institutional congenital heart surgery database: application of the risk adjustment in congenital heart surgery (RACHS-1) and Aristotle Systems in the Society of Thoracic Surgeons (STS) congenital heart surgery database. *Pediatr Cardiol*. 2009;30(8):1117-1130. doi:10.1007/s00246-009-9496-0.
14. Jenkins KJ, Gauvreau K, Newburger JW, Spray TL, Moller JH, Iezzoni LI. Consensus-based method for risk adjustment for surgery for congenital heart disease. *J Thorac Cardiovasc Surg*. 2002;123(1):110-118. doi:10.1067/mtc.2002.119064.
15. Donnellan A, Sawyer J, Peach A, Staveski S, Nelson DP, Pratap JN. Reducing exposure to opioid and benzodiazepine medications for pediatric cardiac intensive care patients: a quality improvement project. *Pediatr Crit Care Med*. 2019;20(4):340-349. doi:10.1097/PCC.0000000000001870.
16. Curley MA, Wypij D, Watson RS, et al, RESTORE Study Investigators and the Pediatric Acute Lung Injury and Sepsis Investigators Network. Protocolized sedation vs usual care in pediatric patients mechanically ventilated for acute respiratory failure: a randomized clinical trial. *JAMA*. 2015;313(4):379-389. doi:10.1001/jama.2014.18399.

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