Hemodynamic Considerations for Children

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Children with acute COVID-19 infrequently experience shock requiring hemodynamic support. However, similar to children with sepsis or septic shock from other causes, children with COVID-19 and shock should be evaluated and managed per the *Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children*.[1,2]

Shock occurs in approximately half of the patients with multisystem inflammatory syndrome in children (MIS-C); reported prevalence ranges from 35% to 80%.[3-5] Limited data inform optimal hemodynamic management for MIS-C. Given that the physiology observed in patients with MIS-C results from a combination of distributive, cardiogenic, and, occasionally, hypovolemic shock, the COVID-19 Treatment Guidelines Panel (the Panel) suggests that clinicians use the management principles outlined in the Surviving Sepsis Campaign's guidelines for children, as well as the principles for clinical management of heart failure and general critical care, as appropriate. The Panel's recommendations apply to the care of children and infants >37 weeks gestational age.

Recommendation

- For children with COVID-19 or MIS-C and shock, the COVID-19 Treatment Guidelines Panel (the Panel) recommends a target mean arterial pressure (MAP) between the fifth and fiftieth, or greater than the fiftieth, percentiles for age **(AIII)**.

Rationale

There are no clinical trials that support specific hemodynamic targets for children with septic shock due to COVID-19, MIS-C, or any other etiology. The panel members for the pediatric Surviving Sepsis Campaign guidelines were divided on the most appropriate MAP target and made no specific recommendation for a target MAP. Therefore, for children with COVID-19 or MIS-C, clinicians should use the same approach used for children without COVID-19 and target a MAP between the fifth and fiftieth, or greater than the fiftieth, percentiles for age. When MAP cannot be reliably measured, systolic blood pressure is a reasonable alternative.[2]

Recommendation

- The Panel recommends that, when available, a combination of serial clinical assessments; cardiac ultrasound or echocardiography; and/or laboratory markers, including lactate levels, should be used to monitor the response to resuscitation in children with COVID-19 or MIS-C and shock **(BIII)**.

Rationale

Observational data from children with non-COVID-19-related sepsis suggest that using clinical assessment alone limits the ability to classify patients with sepsis as having "warm" (i.e., likely to require fluid or vasopressors) or "cold" (i.e., likely to require inotropes) shock, when compared with assessments that include objective measures of cardiac output/index or systemic vascular resistance.[6,7] Cardiac ultrasonography can be performed at the bedside and serially, and it may provide additional clinical data on volume responsiveness and cardiac function.[8] Data from studies evaluating use of cardiac ultrasound in children with COVID-19 and MIS-C are limited to reports from case series.[9]

However, given the spectrum of hemodynamic perturbations observed and because approximately a third of children with MIS-C exhibit left ventricular dysfunction, cardiac ultrasonography may have particular value in MIS-C.[4]

Elevated lactate level is associated with worse outcomes in children with non-COVID-19-related sepsis, although the specific threshold is unknown and has varied from 2 mmol/L to 4 mmol/L across studies.[10,11] Data on serial lactate measures are limited to a single observational study demonstrating an association between normalization in lactate and a decreased risk of persistent organ dysfunction in children with non-COVID-19-related sepsis (adjusted relative risk 0.47; 95% CI, 0.29–0.78).[12] The role of serial lactate measures has not been systematically evaluated for COVID-19 or MIS-C. An observational study of 1,080 children with MIS-C demonstrated an association between elevated markers of inflammation (e.g., C-reactive protein, procalcitonin), brain natriuretic peptide (BNP) or N-terminal proBNP (NT-proBNP), and troponin and the presence of cardiac dysfunction, shock, and the need for intensive care unit admission. However, the timing of the laboratory values in the study was not available, so the elevated markers may reflect, rather than predict, severe illness.[3]

Recommendation

- The Panel recommends administration of balanced **crystalloids** rather than 0.9% saline for the initial resuscitation of children with shock due to COVID-19 or MIS-C **(CIIb)**.

Rationale

No published clinical trials directly compare balanced/buffered crystalloids with 0.9% saline administered to children with sepsis of any etiology, although an international randomized trial is underway (ClinicalTrials.gov Identifier NCT04102371). Two observational studies using administrative data compared the use of balanced/buffered crystalloids to 0.9% saline in propensity-matched cohorts of children with non-COVID-19-related severe sepsis or septic shock. One of the studies compared patients who received any or only Ringer's lactate solution in the first 3 days of admission with patients who received only normal saline. The study demonstrated no differences between the arms for 30-day mortality or frequency of acute kidney injury.[13]

The other study compared patients receiving only balanced fluids with those receiving only 0.9% saline. The study demonstrated that the balanced-fluid arm had lower mortality (12.5% vs. 15.9%; OR 0.76; 95% CI, 0.62–0.93; $P = 0.007$), reduced acute kidney injury (16.0% vs. 19.2%; OR 0.82; 95% CI, 0.68–0.98; $P = 0.028$), and fewer days on vasoactive infusions (3.0 days vs. 3.3 days; $P < 0.001$) than the saline arm.[14] No published studies focused on patients with COVID-19 or MIS-C, although hyponatremia is common in patients with MIS-C, and decisions about the type of fluid therapy used should be individualized for this population.

Recommendations

- The Panel recommends the use of **epinephrine** or **norepinephrine** rather than dopamine in children with COVID-19 or MIS-C and shock **(BIIa)**.
- There is insufficient evidence to differentiate between norepinephrine or epinephrine as a first-line vasoactive drug in children with COVID-19 or MIS-C. The choice of vasoactive agent should be individualized and based on clinical examination, laboratory data, and data from cardiac ultrasound or echocardiography.

Rationale

Use of vasoactive infusions should be considered for children with shock due to COVID-19 if signs of

shock persist after resuscitation with 40 mL/kg to 60 mL/kg of fluid, or sooner if there is evidence of cardiac dysfunction or signs of fluid overload (e.g., tachypnea, hepatomegaly). Similar principles may be applied to patients with MIS-C, particularly because their clinical presentation overlaps significantly with the clinical presentation of children with septic shock due to other causes. However, given the high prevalence of cardiac dysfunction in patients with MIS-C, clinicians should consider performing echocardiography or cardiac ultrasound early in the initial resuscitation if MIS-C is suspected and consider initiating a vasoactive infusion if cardiac dysfunction is identified.

Data from pediatric studies comparing vasopressors are limited, and there are no data specific to patients with COVID-19 or MIS-C. Two small pediatric trials compared epinephrine with dopamine in patients with non-COVID-19-related fluid-refractory septic shock.[15,16] One study randomized 63 children to receive dopamine 5 µg/kg/min to 10 µg/kg/min and 57 children to receive epinephrine 0.1 µg/kg/min to 0.3 µg/kg/min. Mortality by Day 28 was 14.2% in the dopamine arm and 7% in the epinephrine arm (OR 6.5; 95% CI, 1.1–37.8; $P = 0.03$). In the other study, 31 children were randomized to receive incremental doses of dopamine 10 µg/kg/min to 20 µg/kg/min, and 29 children were randomized to receive incremental doses of epinephrine 0.1 to 0.3 µg/kg/min. The primary outcome of shock resolution within 1 hour occurred in 4 children (13%) receiving dopamine and 12 children (41%) receiving epinephrine (OR 4.8; 95% CI, 1.3–17.2; $P = 0.019$).

No pediatric trials have compared norepinephrine to other vasoactive agents in patients with sepsis, but based on data from studies of adults, the pharmacologic properties of norepinephrine and dopamine (see Hemodynamics for Adults), and the 2020 Surviving Sepsis Campaign guidelines for children, norepinephrine is suggested over dopamine.[2]

Collectively, this evidence is insufficient to recommend norepinephrine versus epinephrine as a first-line vasoactive agent in children with COVID-19 or MIS-C. Further, given the varied physiology observed with MIS-C in particular, decisions about which vasopressor to use should be individualized based on clinical and laboratory data and findings from bedside cardiac ultrasound or echocardiography.

Recommendation

- There is insufficient evidence for the Panel to recommend either for or against the use of inodilators (including dobutamine or milrinone) in children with COVID-19 or MIS-C who show evidence of cardiac dysfunction and persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents.

Rationale

Data from studies evaluating use of inodilators in children with COVID-19, MIS-C, and non-COVID-19-related sepsis are limited to reports from case series. However, the majority of the pediatric Surviving Sepsis Campaign guidelines panel (77%) would use an inodilator at least some of the time for patients with non-COVID-19-related sepsis, cardiac dysfunction, and persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents.[2] Expert consultation from specialists in pediatric cardiology and critical care medicine is recommended in this scenario.

Additional Recommendations

- For the acute resuscitation of children with COVID-19 or MIS-C and shock, the Panel recommends the use of **crystalloids** rather than albumin **(AIIb)**.
- The Panel **recommends against** using **hydroxyethyl starches** for intravascular volume replacement in children with COVID-19 or MIS-C and sepsis or septic shock **(AIII)**.

- For children with refractory shock who have recently completed a course of corticosteroids to treat COVID-19, the Panel recommends using low-dose corticosteroid therapy ("shock-reversal") over no corticosteroid therapy **(CIII)**.
  - Children who are currently receiving corticosteroids for COVID-19 or MIS-C are generally receiving sufficient glucocorticoid replacement therapy and do not require additional hydrocortisone for refractory shock.

References

1. Weiss SL, Peters MJ, Agus MSD, et al. Perspective of the Surviving Sepsis Campaign on the management of pediatric sepsis in the era of coronavirus disease 2019. *Pediatr Crit Care Med*. 2020;21(11):e1031-e1037. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32886460.
2. Weiss SL, Peters MJ, Alhazzani W, et al. Surviving Sepsis Campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. *Pediatr Crit Care Med*. 2020;21(2):e52-e106. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32032273.
3. Abrams JY, Oster ME, Godfred-Cato SE, et al. Factors linked to severe outcomes in multisystem inflammatory syndrome in children (MIS-C) in the USA: a retrospective surveillance study. *Lancet Child Adolesc Health*. 2021;5(5):323-331. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33711293.
4. Feldstein LR, Tenforde MW, Friedman KG, et al. Characteristics and outcomes of US children and adolescents with multisystem inflammatory syndrome in children (MIS-C) compared with severe acute COVID-19. *JAMA*. 2021;325(11):1074-1087. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33625505.
5. Godfred-Cato S, Bryant B, Leung J, et al. COVID-19-associated multisystem inflammatory syndrome in children—United States, March–July 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(32):1074-1080. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32790663.
6. Egan JR, Festa M, Cole AD, et al. Clinical assessment of cardiac performance in infants and children following cardiac surgery. *Intensive Care Med*. 2005;31(4):568-573. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15711976.
7. Razavi A, Newth CJL, Khemani RG, Beltramo F, Ross PA. Cardiac output and systemic vascular resistance: clinical assessment compared with a noninvasive objective measurement in children with shock. *J Crit Care*. 2017;39:6-10. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28088009.
8. Ranjit S, Aram G, Kissoon N, et al. Multimodal monitoring for hemodynamic categorization and management of pediatric septic shock: a pilot observational study. *Pediatr Crit Care Med*. 2014;15(1):e17-26. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24196006.
9. Kennedy TM, Dessie A, Kessler DO, et al. Point-of-care ultrasound findings in multisystem inflammatory syndrome in children: a cross-sectional study. *Pediatr Emerg Care*. 2021;37(6):334-339. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33871226.
10. Scott HF, Brou L, Deakyne SJ, et al. Association between early lactate levels and 30-day mortality in clinically suspected sepsis in children. *JAMA Pediatr.* 2017;171(3):249-255. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28068437.
11. Bai Z, Zhu X, Li M, et al. Effectiveness of predicting in-hospital mortality in critically ill children by assessing blood lactate levels at admission. *BMC Pediatr*. 2014;14:83. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24673817.
12. Scott HF, Brou L, Deakyne SJ, et al. Lactate clearance and normalization and prolonged organ dysfunction in pediatric sepsis. *J Pediatr*. 2016;170:149-155 e141-144. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26711848.
13. Weiss SL, Keele L, Balamuth F, et al. Crystalloid fluid choice and clinical outcomes in pediatric sepsis: a matched retrospective cohort study. *J Pediatr*. 2017;182:304-310 e310. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28063688.

14. Emrath ET, Fortenberry JD, Travers C, McCracken CE, Hebbar KB. Resuscitation with balanced fluids is associated with improved survival in pediatric severe sepsis. *Crit Care Med*. 2017;45(7):1177-1183. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28437373.
15. Ventura AM, Shieh HH, Bousso A, et al. Double-blind prospective randomized controlled trial of dopamine versus epinephrine as first-line vasoactive drugs in pediatric septic shock. *Crit Care Med*. 2015;43(11):2292-2302. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26323041.
16. Ramaswamy KN, Singhi S, Jayashree M, Bansal A, Nallasamy K. Double-blind randomized clinical trial comparing dopamine and epinephrine in pediatric fluid-refractory hypotensive septic shock. *Pediatr Crit Care Med*. 2016;17(11):e502-e512. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27673385.