Intensive Care Med (2016) 42:2037–2039
DOI 10.1007/s00134-016-4382-8

WHAT'S NEW IN INTENSIVE CARE

Pediatric sepsis and septic shock management in resource-limited settings

Ndidiamaka Musa[1], Srinivas Murthy[2*] and Niranjan Kissoon[2]

Introduction

Infectious diseases leading to septic shock remain a major cause of childhood mortality in all settings [1]. Recommendations in the Surviving Sepsis Campaign (SSC), guidelines for pediatric patients rely on evidence from resource-rich settings [2]. However, recommendations are context dependent, and published guidelines deriving evidence primarily from resource-rich settings may be less relevant in areas where resources are minimal and the epidemiology is very different [3]. Thus recommendations for the treatment of septic shock in children in intensive care units (ICUs) in resource-limited settings are sorely needed, where there is often lacking laboratory support, equipment, and trained staff, serving as a supplement to existing guidelines from the World Health Organization (WHO) that focus upon emergency triage and treatment in non-ICU contexts [4]. There is no standardized definition of ICU, but for the purposes of these recommendations, we are focusing on referral hospitals with the capability to continuously monitor critically ill children, ideally with the availability of some form of mechanical ventilation, acknowledging a lack of dedicated pediatric ICUs and that children are likely cared for by a variety of providers [5, 6]. A further discussion of defining resource-limited intensive care is forthcoming in this series.

The need for these recommendations is underlined by the surprising results from one large randomized controlled trial on fluid therapy in African children [7], suggesting that not all evidence for benefit in resource-rich settings guarantees benefit in resource-limited settings. Whether these different results are due to variability in the care provided, the patients' physiology or comorbidities, or altered pathogens remains unknown and deserves further research. These recommendations are not intended to be incorporated as a bundle or as formal guidelines, given the variability in resources available to care for critically ill children, even within countries, and the overall quality of the evidence base.

An international team of physicians with extensive clinical experience in resource-rich and resource-limited ICUs and systematic review methodology was formed under the auspices of the European Society of Intensive Care Medicine's Global Intensive Care Working Group and mandated with the task of evaluating the evidence for pediatric sepsis and septic shock in ICUs in resource-limited settings. The subgroup members formulated eight clearly defined questions following the principles of the GRADE process [2]. Quality of evidence was scored from high (grade A), moderate (B), low (C), or very low (D) and recommendations as strong (1) or weak (2). The factors influencing this classification are presented in the online supplement Table 1, with major attention given to several other contextual factors relevant to delivery of care in resource-limited settings, such as the availability, affordability, feasibility and safety of care interventions in resource-limited ICUs. A strong recommendation was worded as "*we recommend*" and a weak recommendation as "*we suggest*". One recommendation remained "ungraded" (UG) as it was not conducive to the process described above. A full explanation of methodology, group composition and selection, and overview of findings is available in the online supplement, as well as a complete list of relevant articles.

*Correspondence: Srinivas.murthy@cw.bc.ca
[2] Department of Pediatrics, BC Children's Hospital, University of British Columbia, 4500 Oak Street, Vancouver, BC, Canada
Full author information is available at the end of the article

For the European Society of Intensive Care Medicine (ESICM) Global Intensive Care Working Group and the Mahidol–Oxford Research Unit (MORU) in Bangkok, Thailand.Members of the Sepsis in Resource-Limited Settings—Expert Consensus Recommendations Group are listed in the online supplement.

Springer

Results and recommendations

Key recommendations are provided in Table 1 and more detailed scoring details are available in the online supplement. A major challenge is early identification of children who are critically ill. The most important interventions to reduce sepsis morbidity and mortality must be made generically, often before the definitive diagnosis. Rapidly identifying which children have evidence of organ dysfunction or impaired circulation due to infections is vital. We *recommend* that severely ill children in ICUs with signs of infection be identified through observing for a combination of danger signs of end-organ dysfunction or impaired circulation. More studies are required to determine better definitions and scoring systems for risk stratification in these settings.

We recognize that rapid vascular access is critical and usually a rate-limiting step in the early resuscitation of children. We *suggest* that in children with septic shock in resource-limited settings, the placement of an intraosseous line can be considered for vascular access after a short period of time for intravenous access attempts. Further studies are required to document its role in resource-limited settings, including maintaining training of practitioners.

We *recommend* a very careful and individualized approach to fluid administration in children with sepsis in ICUs in resource-limited settings. For children with severe acute malnutrition without signs of severe shock, we do *suggest* against rapid intravenous fluid administration. Children with severe acute malnutrition and signs of septic shock have very high levels of baseline mortality, and we *suggest* careful administration of intravenous fluids at an initial rate of 10–15 ml/kg/h [4]. For well-nourished children who do not have evidence of severely impaired circulation (see online supplement), we *recommend* administration of maintenance fluids only. For well-nourished children who have evidence of severely impaired circulation, we *suggest* very careful administration of 10–15 ml/kg of crystalloids over 30–60 min. This may be repeated if the shock is persistent and there are no signs of fluid overload, with careful titration following repeated observations. We could not make a recommendation regarding incorporating early goal-directed therapy for children with septic shock in resource-limited settings. Further studies are urgently required to clarify the definitions of septic shock in children in resource-limited settings.

We *recommend* incorporation of quality assurance protocols for timely antibiotic administration, oxygen and respiratory support, and fluid management protocols into resource-limited settings for the management of pediatric sepsis. We also *recommend* transfusing children with severe anemia and malaria only if there are signs such as respiratory distress or shock. Children in

Table 1 Recommendations and suggestions on pediatric sepsis or septic shock management in resource-limited settings (with grading)

1	Identification	Observe for a combination of danger signs of end-organ dysfunction, such as altered mental status and poor peripheral perfusion, and including lactic acid levels if available (1C)
2	Intraosseous access	Placement of an intraosseous line must be considered for vascular access after 3–5 min of intravenous access attempts (2B)
3	Resuscitation of malnourished children	Children with severe acute malnutrition without signs of severe shock should not receive rapid intravenous fluids as bolus therapy (2C); children with severe acute malnutrition and signs of septic shock have high levels of mortality and we suggest that they should be given intravenous rehydration with either half-strength Darrow's solution with 5 % dextrose or Ringer's lactate solution with 5 % dextrose at a rate of 10–15 ml/kg/h with avoidance of rapid bolus therapy (2C)
4	Bolus fluid resuscitation	Use a careful but foremost individualized approach to fluid administration in children with sepsis in resource-poor settings (1B); for those who do not have evidence of severely impaired circulation, administer maintenance fluids only (1B); for those who do have evidence of severely impaired circulation, very carefully administer 10–15 ml/kg of crystalloid over 30–60 min, which may be repeated if there are no signs of improvement and no signs of fluid overload (2C)
5	Goal-directed fluid resuscitation	No recommendation can be made regarding incorporating early goal-directed therapy for children with septic shock in resource-limited ICUs, specifically pertaining to using $ScvO_2$, lactate, or central venous pressure to guide resuscitation (UG); incorporate quality assurance protocols for timely antibiotic administration, oxygen and respiratory support, and fluid management protocols into resource-limited settings for the management of pediatric sepsis (1D)
6	Transfusion in severe malaria and sepsis	Transfuse children with severe anemia and malaria only if there are signs of severe sepsis such as respiratory distress or shock (1C); transfuse children with severe anemia <4 g/dl (1D); there is no evidence to support a specific transfusion threshold for children with anemia and sepsis in resource-limited settings
7	Noninvasive ventilation	Children with severe respiratory distress and hypoxemia from sepsis related to pneumonia would benefit from bubble CPAP (1B)
8	Low tidal volume ventilation	Use a tidal volume of 5–8 ml/kg predicted body weight in all mechanically ventilated children with sepsis-induced acute lung injury in resource-limited settings (1D)

resource-limited settings with severe respiratory distress and hypoxemia from sepsis could benefit from bubble continuous positive airway pressure (CPAP). Research is needed to clarify the upper age limit for effectiveness of bubble CPAP and to clarify the role of high-flow nasal cannula. Finally, we *recommend* using a tidal volume of 5–8 ml/kg predicted body weight in all mechanically ventilated children with sepsis-induced lung injury, but further research is urgently needed to better define the management of pediatrics ARDS in resource-limited settings.

Conclusion

Most of the available evidence is from resource-rich settings, suggesting an urgent need for further studies in resource-limited settings. We present a set of recommendations, based upon varying degrees of evidence, that can be adapted to specific circumstances and resources available and can form the basis of a research agenda in this rapidly changing field. These recommendations are in line with existing recommendations from the WHO and SSC, which are focused on different contexts.

Electronic supplementary material

The online version of this article (doi:10.1007/s00134-016-4382-8) contains supplementary material, which is available to authorized users.

Group members of the Pediatric Considerations Subgroup

(Heads) Ndidiamaka Musa (Seattle Children's Hospital, Seattle, USA), Srinivas Murthy (BC Children's Hospital, Vancouver, Canada), Niranjan Kissoon (BC Children's Hospital, Vancouver, Canada). Other members, in alphabetic order: Rakesh Lodha (All India Institute of Medical Sciences, Delhi, India), Suchitra Ranjit (Apollo Hospital, Chennai, India).

Author details

[1] Department of Pediatrics, Seattle Children's Hospital, University of Washington, Seattle, USA. [2] Department of Pediatrics, BC Children's Hospital, University of British Columbia, 4500 Oak Street, Vancouver, BC, Canada.

Received: 31 March 2016 Accepted: 10 May 2016
Published online: 23 May 2016

References

1. Global Burden of Disease Pediatrics Committee, Kyu HH, Pinho C, Wagner JA, Brown JC, Bertozzi-Villa A, Charlson FJ, Coffeng LE, Dandona L, Erskine HE et al (2016) Global and national burden of diseases and injuries among children and adolescents between 1990 and 2013: findings from the global burden of disease 2013 study. JAMA Pediatr 170(3):267–287
2. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R et al (2013) Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med 39(2):165–228
3. Khilnani P, Singhi S, Lodha R, Santhanam I, Sachdev A, Chugh K, Jaishree M, Ranjit S, Ramachandran B, Ali U et al (2010) Pediatric sepsis guidelines: summary for resource-limited countries. Indian J Crit Care Med 14(1):41–52
4. World Health Organization (2016) Paediatric emergency triage, assessment and treatment: care of critically-ill children. http://who.int/maternal_child_adolescent/documents/paediatric-emergency-triage-update/en/. Accessed 21 Apr 2016
5. Murthy S, Leligdowicz A, Adhikari NK (2015) Intensive care unit capacity in low-income countries: a systematic review. PLoS One 10(1):e0116949
6. Basnet S, Adhikari N, Koirala J (2011) Challenges in setting up pediatric and neonatal intensive care units in a resource-limited country. Pediatrics 128(4):e986–e992
7. Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akech SO, Nyeko R, Mtove G, Reyburn H, Lang T et al (2011) Mortality after fluid bolus in African children with severe infection. N Engl J Med 364(26):2483–2495