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Original Article

Pathogens and outcomes in pediatric septic shock patients supported by extracorporeal membrane oxygenation

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Abstract *Background:* Refractory septic shock is the leading cause of mortality in children. There is limited evidence to support extracorporeal membrane oxygenation (ECMO) use in pediatric septic shock. We described the etiology and outcomes of septic patients in our institution and attempted to find predictive factors.
Methods: We retrospectively reviewed 55 pediatric patients with septic shock who required ECMO support in a tertiary medical center from 2008 to 2015. Septic shock was defined as culture proved or clinical suspected sepsis with hypotension or end-organ hypoperfusion. ECMO would be applied when pediatric advanced life support steps were performed thoroughly without clinical response. Patient's demographics, laboratory parameters before and after ECMO, and outcomes were analyzed.
Results: Among 55 children with ECMO support, 31% of them survived on discharge. For 25 immunocompromised patients, causal pathogens were found in 17 patients: 7 due to bacteremia, 9 with preexisting virus infections and one with invasive fungal infection. Among 30 previously healthy patients, causal pathogens were found in 18 patients: 10 due to bacteremia

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(the most common was *pneumococcus*), 7 with preexisting virus infections including influenza (n = 4), adenovirus (n = 2), RSV, and 1 patient had mixed virus and bacterial infections. Predictive factors associated with death were arterial blood gas pH, CO_2 and Glasgow Coma Scale ($p < 0.05$). SOFA score was a valuable predictive scoring system for outcome prediction ($p < 0.05$).

Conclusions: Pediatric patients with refractory septic shock had high mortality rate and ECMO could be used as a rescue modality, and SOFA score could be applied to predict outcomes.

Background

Severe sepsis or septic shock is one of the major causes of pediatric death. It accounted for about 8% pediatric intensive care unit (PICU) admission and the proportion varied across regions from 6.2 to 23.1%.[1] The overall mortality rate was 24%, ranging from 21% in North America and 40% in Africa.[1–3] Extracorporeal membrane oxygenation (ECMO) had first been introduced in cardiopulmonary support during surgery in 1970 by Thomas G. Baffes.[4] In 1976, Robert H. Bartlett reported the first case of neonatal ECMO survivors.[5] Since then, ECMO had become an important modality for the transition during the critical condition such as neonatal respiratory distress syndrome or cardiac surgery. However, sepsis or septic shock had been considered as a contraindication for ECMO before 1990. Previous concerns included secondary contamination of the circuit (later reports refuted this assumption),[6] disseminated intravascular coagulation or risk of hemorrhage, and poor prognosis.[7] After 1990, strict heparin management and improvement of circuit care lead to fewer complications. In the sequentially published guidelines,[8,9] for septic shock unresponsive to fluid resuscitation and inotropic agents, ECMO could be considered. In contrast, there were limited studies to analyze the outcomes and prognostic factors of these patients. We thus initiated this study to investigate the etiology and outcomes of septic patients in our institution and attempted to find predictive factors.

Patients and methods

We retrospectively reviewed 55 pediatric septic patients (age from 0 to 18 years old) with ECMO support in National Taiwan University Children's Hospital from 2008 to 2015. They fulfilled the definition of sepsis which included systemic infections with culture-proven microorganisms or systemic inflammatory response syndrome (SIRS) with highly clinical suspicion of sepsis. Refractory shock was defined as persistent hypotension with poor end-organ perfusion even under fluid resuscitation and the use of inotropic agents. Generally, we used 20 mL/kg of isotonic crystalloid solution for fluid challenge. pH < 7.2, PaO_2/FiO_2 < 200, serum lactate > 5 mM/L, inotropic equivalent >25 and ejection fraction <40% were parameters for poor perfusion. Traumatic, cardiogenic, post-cardiac surgery or acute myocarditis related ECMO supports were excluded.

Patient's demography, medical history, laboratory data during hospitalization, ECMO indication, mode, duration of ECMO support and discharge status were collected. For causal agents of sepsis, bacteria found in blood culture before or on the day of ECMO were considered as related pathogens. Viral or fungal infections were diagnosed based on isolation, serology titers or antigen tests. All pathogen isolation results were correlated with medical charts and clinical presentations.

The data collections and medical chart reviews were approved by the National Taiwan University Hospital's IRB (Institutional Review Board for Human Subject Research) with IRB number of 201701062RINC.

ECMO indication

According to 2012 Surviving sepsis campaign,[9] ECMO could be a rescue modality for refractory septic shock. There was no worldwide consensus for definite parameters or clinical conditions that ECMO should be initiated. In our hospital, ECMO will be considered when PALS (Pediatric advanced life support) steps are performed thoroughly without clinical response, such as the development of adult respiratory distress syndrome (ARDS) or failure to maintain adequate end-organ perfusion even under the use of high-dose inotropic agents. Prematurity with gestational age less than 34 weeks, body weight less than 2 kg, irreversible pulmonary or cardiovascular disease, obvious intracranial hemorrhage, severe hypoxic-ischemic encephalopathy or malignant end stage disease are contraindicated.

Data analysis

All analyses were performed with commercially available statistical software (SPSS v22.0). Patients were categorized into two groups, survivors and nonsurvivors. Continuous data were analyzed with Mann–Whitney test or *t*-test, and categorical data were compared with the chi-square test. The receiver operating characteristic curve analysis was applied to determine the best cut-off-point for each parameter which was significant in univariate analysis, and then multiple logistic regressions were applied to perform multivariate analysis for predicting the most significant factors associated with mortality. p Value less than 0.05 by two-tailed test was considered statistical significance in both tests.

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