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Early Applicartion of Continuous Renal Replacement Therapy as Adjunctive Support in Pediatric Septic Shock: A Prospective Observational Study

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Responsible Party:

Principal Investigator, Vietnam National Children's Hospital

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STUDY PROTOCOL

Title: Early Application of Continuous Renal Replacement Therapy as Adjunctive Support in Pediatric Septic Shock: A Prospective Observational Study

1. Background and Rationale

Septic shock is a leading cause of morbidity and mortality in critically ill children. In addition to antimicrobial therapy and hemodynamic resuscitation, continuous renal replacement therapy (CRRT) has been increasingly used as adjunctive support to stabilize hemodynamics, modulate inflammatory mediators, and correct metabolic derangements in pediatric septic shock.

Despite growing clinical use, evidence regarding optimal timing, indications, and short-term outcomes of early CRRT initiation in children remains limited. This prospective observational study aims to generate real-world evidence on the association between early CRRT use and clinical, biological, and outcome measures in pediatric septic shock.

2. Study Objectives

2.1 Primary Objectives

- To evaluate time to shock reversal following initiation of early CRRT
- To assess changes in organ dysfunction severity after CRRT initiation

2.2 Secondary Objectives

- To assess changes in hemodynamic parameters after CRRT initiation
- To evaluate changes in inflammatory cytokine levels
- To evaluate changes in metabolic and inflammatory biomarkers
- To describe short-term mortality and ICU resource utilization

3. Study Design

- Study Type: Observational
- Observational Model: Prospective Cohort
- Time Perspective: Prospective
- Sampling Method: Consecutive sampling
- Estimated Enrollment: 50 pediatric patients

No randomization or intervention assignment is performed. CRRT is provided as part of routine clinical care.

4. Study Population

Pediatric patients with septic shock admitted to the Pediatric Intensive Care Unit (PICU) and receiving early CRRT as part of standard clinical management.

5. Eligibility Criteria

5.1 Inclusion Criteria

- Age 1 month to <18 years
- Diagnosis of septic shock according to Phoenix Sepsis Criteria
- At least one of the following:
    - Acute kidney injury KDIGO stage ≥2
    - Vasoactive-Inotropic Score (VIS) ≥50
- PICU admission
- Written informed consent from parent(s) or legal guardian(s)

5.2 Exclusion Criteria

- Expected survival <24 hours
- End-stage renal, liver, or heart disease
- Known immunosuppression (HIV or primary immunodeficiency)

- Emergency CRRT indications unrelated to septic shock
- PICU stay <24 hours or CRRT duration <6 hours

6. Study Procedures and Data Collection

Baseline data will be collected prior to CRRT initiation (T0), including:

- Clinical status and hemodynamic parameters
- Echocardiographic indices
- Laboratory and metabolic markers
- Serum cytokine levels

Follow-up assessments will be performed at predefined time points up to Day 28 after PICU admission.

7. Outcome Measures

7.1 Primary Outcomes

- Time to shock reversal
- Change in organ dysfunction scores (pSOFA, PELOD-2, PSS)

7.2 Secondary Outcomes

- Hemodynamic changes over time
- Cytokine level changes
- Metabolic and inflammatory biomarker changes
- Mortality at Day 7 and Day 28
- ICU-free days, ventilator-free days, vasopressor-free days

8. Ethical Considerations

The study is conducted in accordance with the Declaration of Helsinki. Approval has been obtained from the Institutional Review Board of Vietnam National Children's Hospital. Written informed consent is obtained prior to study participation.

STATISTICAL ANALYSIS PLAN

1. General principles

This is an exploratory, descriptive statistical analysis for a prospective observational study.

- Statistical analyses will be conducted using standard statistical software
- Significance testing will be exploratory in nature

2. Descriptive analysis

- Continuous variables: mean ± standard deviation or median (interquartile range)
- Categorical variables: counts and percentages

3. Primary Outcome Analysis

3.1 Time to Shock Reversal

- Analyzed using time-to-event methods
- Results reported as median time with interquartile range

3.2 Organ Dysfunction Scores

- Changes in pSOFA, PSS and PELOD-2 over time analyzed using repeated-measures methods

4. Secondary Outcome Analysis

- Hemodynamic, laboratory, cytokine, and metabolic parameters analyzed as changes from baseline
- Correlation analyses between cytokine changes and time to shock reversal
- Mortality outcomes reported descriptively
- ICU-free, ventilator-free, and vasopressor-free days summarized using standard definitions

5. Missing data

Missing data will be described and handled using available-case analysis without imputation.

6. Sample Size Considerations

No formal sample size calculation was performed due to the exploratory observational design.

7. Amendments

Any protocol or SAP amendments will be documented with version control and updated in ClinicalTrials.gov as required.