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ORIGINAL ARTICLE

Sustained low-efficiency dialysis (SLED) in a referral hospital in Latin America

Diálisis sostenida de baja eficiencia (SLED) en un hospital de referencia en Latinoamérica

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What do we know about the subject matter of this study?

The best dialysis modality in pediatric critically ill patients is not well established. Sustained low-efficiency dialysis is a hybrid modality used in critically ill patients, although with little evidence in pediatrics and even more so in Latin America.

What does this study contribute to what is already known?

To describe the experience with the use of sustained low-efficiency dialysis (SLED) through a descriptive observational study in critically ill pediatric patients with acute renal failure admitted to critical care. We included 524 sessions, of which 11% were done in patients under 20 kilos. All laboratory tests showed improvement after therapy, with few intradialytic adverse effects (hypotension and catheter dysfunction) and few electrolyte alterations.

Abstract

Sustained Low-Efficiency Dialysis (SLED) is a hybrid modality of renal replacement therapy used in critically ill patients, although there is little evidence in pediatric patients. **Objective:** To describe the experience with the use of SLED in a critically ill pediatric population over five years in a hospital in Colombia. **Patients and Method:** Descriptive observational study. All patients < 17 years of age with acute kidney injury who required SLED therapy in the pediatric intensive care unit were included. A descriptive statistical analysis and an exploratory analysis were performed to evaluate the change in laboratory tests before and after dialysis. **Results:** 524 SLED sessions performed in 28 patients with acute kidney injury of different etiologies were included. The median age was 12 years (range 3-17 years), and 11% of the sessions were in patients under 20 kg. The main indication for SLED was fluid overload in 54% of sessions, followed by anuria in 37%. All laboratory tests showed a statistically significant improvement after SLED therapy. Complications occurred in 21% of sessions, with a predominance of intradialytic electrolyte imbalances (8%) and catheter dysfunction (5%). Mortality

Keywords:
Dialysis;
Pediatrics;
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Acute Kidney Injury;
Renal Replacement Therapy;
Sustained Low-Efficiency Dialysis (SLED);
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was 11%. **Conclusion:** SLED therapy in critically ill children is safe, with few intradialytic adverse effects such as hypotension and catheter dysfunction, and few post-dialysis complications (electrolyte imbalance). It is an effective modality for improving laboratory parameters (blood urea nitrogen, bicarbonate, and hyperkalemia).

Introduction

Acute kidney injury (AKI) is the abrupt loss of renal function generating a decrease in the glomerular filtration rate, with retention of urea and other nitrogenous products, loss of body water regulation, electrolytes, and acid-base status, with change in creatinine and diuresis in relation to a baseline measurement[1,2]. In critically ill patients, the development of AKI (based on the KDIGO classification) has been observed in 26.9%, and severe AKI in 11.6% during the first 7 days in the critical care unit [3]. The presence of AKI is associated with increased mortality in both general ward and intensive care unit hospitalized patients, with a direct relationship between the severity of AKI and mortality[3,4].

A small percentage (5.8%) of children with AKI require renal replacement therapy (RRT)[3]. There are several options for RRT in critically ill patients: peritoneal dialysis (PD), intermittent hemodialysis (IHD), and continuous RRT (CRRT), each with its benefits and adverse effects. The best modality in pediatric critically ill patients is not yet well established. PD is frequently used in low-income countries because of its cost-effectiveness, while CRRT is predominantly used in high-income countries because it is better tolerated in unstable critically ill patients since it allows a slower and more controlled decrease of fluids and solutes, but even so, it is not free of complications and is more expensive[5-8]. IHD in the pediatric population has not been very well tolerated, particularly in critically ill patients because it can aggravate hypotension and precipitate catastrophic events[9-11].

For some years now, a hybrid therapy has been evaluated in pediatrics, sustained low-efficiency dialysis (SLED), which combines technical aspects of IHD and CRRT, allowing longer dialysis-free time, efficient purification of solutes and greater hemodynamic stability, useful features in critically ill patients[12]. This therapy has been studied in adults with good clinical results in critically ill patients[13-15]. In 2012, the first descriptive study of SLED in the pediatric population was published describing 60 dialysis episodes with this modality, evidencing good tolerance, adequate pH control, hypervolemia, and fluid and electrolyte imbalance[16]. Subsequently, other studies have been published in India and Brazil[12,17,18].

The objective of this study was to describe the experience with the use of dialysis with the SLED modality in the critically ill pediatric population for 5 years.

Patients and Method

Study design

Retrospective, longitudinal, observational study. Information was collected on RRT sessions with the SLED modality in pediatric patients with AKI in a high-complexity hospital (*Hospital Pablo Tobón Uribe*) in Medellín, Colombia, between 2012 and 2017. The institution has 27 pediatric and neonatal intensive care beds and a pediatric nephrologist. All patients under 17 years of age with acute renal failure who required SLED therapy in the Pediatric Intensive Care Unit (PICU) were included. The decision to initiate SLED and its duration between 6 to 12 hours was made jointly between the pediatric intensivist and the nephrologist according to indications such as oliguria, positive fluid balance, fluid overload > 20%, persistent metabolic acidosis, or electrolyte imbalance that did not respond to other treatments. Patients with non-decompensated stage V chronic kidney disease on IHD treatment were excluded.

Demographic and clinical variables such as indication for therapy, weight, etiology of AKI, laboratory tests such as renal function, electrolytes (potassium, phosphate, magnesium), pH, and bicarbonate before and after dialysis were collected. In addition, dialysis data such as filter, blood flow, dialysis fluids, ultrafiltration, and heparin dose were recorded. Therapy-related complications and mortality at PICU discharge were evaluated. The study was approved by the institution's ethics committee (11/2017).

Definitions

- SLED: defined as sessions performed with blood flows ≤ 5 ml/kg/min and dialysate flow less than twice the blood flow, with a duration > 6 hours.
- Acute kidney injury according to KDIGO criteria [2].
- Hypotension: defined as systolic blood pressure below the 5th percentile for age.
- Fluid overload: the percentage was calculated as (fluid intake-fluid output) / weight upon PICU admission x 100. Fluid overload was defined as a percentage > 20%.

- Hypokalemia was defined as serum potassium < 3.0 mEq/L and hypophosphatemia as serum phosphate < 2 mg/dL.
- Severe hyperkalemia: potassium > 7 mEq/L.
- Uremia: blood urea nitrogen between 80 and 100 mg/dl.
- Anuria: decrease in diuresis < 50 mL/24 hours.

SLED therapy components

The Genius® 90 Therapy System (Fresenius Medical Care, Bad Homburg, Germany) was used for all sessions, with the Fresenius Fx 40 high-flux dialyzer for children with body surface area between 0.6 and 1.6 m^2 and the Fx 60 between 1.6 and 1.9 m^2. In the sessions in which heparin was used, the dose was 5 units/kg/hour. Three types of dialyzing fluid were used (Table 1).

Statistical analysis

For categorical variables, absolute frequencies and proportions were calculated. For quantitative variables, the normality of each variable was evaluated (Shapiro-Wilk test) and according to this they are reported as the median or interquartile range (IQR) or mean and standard deviation (SD). An exploratory analysis was performed to evaluate the change in laboratory tests before and after dialysis, using the Student t-test for normal variables and the Wilcoxon test for those that were not. A $p < 0.05$ value was considered statistically significant. Data were processed using SPSS software, version 20 (IBM statistics).

Results

We included 524 SLED sessions performed in 28 patients, 15 females and 13 males. The age ranged from 3 to 17 years and weight between 16 and 78 kg. Tables 2 and 3 summarize demographic data and the prescription characteristics, respectively.

Of the 524 sessions analyzed, the main indication for SLED was fluid overload (n = 285, 54%), followed by anuria (n = 193, 37%), uremia (n = 78, 15%), severe hyperkalemia (n = 29, 6%), and less frequently severe metabolic acidosis (n = 3, 1%) and hypertensive emergency (n = 3, 1%).

Laboratory tests

All laboratory tests showed statistically significant improvement after SLED therapy (Table 4).

Complications

Complications occurred in 109 sessions (21%), with electrolyte imbalances predominating at the end of 37 dialysis sessions (7%), the most frequent were hypophosphatemia in 15 patients (3%) and hypokalemia

Table 1. Characteristics of dialysate solutions used in SLED therapy (Sustained Low Efficiency Dialysis)

Content	Number 2	Number 3	Number 6
Sodium	140	135	140
Bicarbonate	35	35	35
Potassium	1	3	3
Calcium	1.5	1	1.25
Magnesium	0.5	0.5	0.5
Chloride	112	108	113.5
Hydrogen	2.3	2.2	2.25
Citrate	0.101	0.07	0.08
Glucose (g/l)	1	1	1

Table 2. Basal characteristics of the study population with SLED therapy (Sustained Low Efficiency Dialysis)

Characteristic	Value
Age (years), median (IQR)	12 (7 - 14)
Weight (kg), median (IQR)	32 (24 - 56)
Cardiovascular dysfunction, n (%)	8 (28)
Mechanical ventilation, n (%)	11 (39)
Causes of acute kidney njury, n (%))	
Sepsis	8 (28,5)
Vasculitis	4 (14,2)
Hypovolemic shock	4 (14,2)
Hemolytic uremic syndrome	2 (7,1)
Nephrotic syndrome	2 (7,1)
Kidney transplant rejection	2 (7,1)
Severe malaria	1 (3,5)
Bilateral Wilms Tumor	1 (3,5)
Obstructive uropathy	1 (3,5)
Others	3 (10,7)

IQR: interquartile range; [a]Inotropes/Vasopressors.

Table 3. Characteristics of SLED prescription (Sustained Low Efficiency Dialysis)

Characteristic	Value
Number of sessions by patient, median (IQR)	10 (2.5-25.5)
FFilter, n (%)	
Fx60	266 (51)
Fx40	258 (49)
Filtration rate (cc/hour), mean (SD)	230 (± 150)
Heparin anticoagulation, n (%)	257 (49%)
Heparin dose, median (IQR)	3.8 units/kg/hour (2.8-5)
Qb (mL/kg/min), mean (SD)	5 (± 2.3)
Dialysate solution used, n (%)	
2	141 (27)
3	5 (1)
6	378 (72)
Premature session termination, n (%)	56 (11)

IQR: interquartile range; SD: Standard deviation

Table 4. Lab results pre and post-SLED therapy (Sustained Low Efficiency Dialysis)

Lab	n	Pre dialysis	n	Post dialysis	p value
Creatinine (mg/dL)*	273	3.5 (2.1-5.5)	190	2.6 (1.6-4)	0.01[a]
Blood urea nitrogen (mg/dL)*	292	46 (29-69.9)	203	35.6 (23-54)	0.01[a]
Potassium (mEq/L)*	379	4.4 (3.7-5.2)	308	4.2 (3.6-4.9)	0.01[a]
Phosphorus (mg/dL)*	206	4.0 (3-5)	169	3.7 (2.8-4.8)	0.01[a]
pH§	236	7.3 (± 0.09)	223	7.4 (± 0.08)	0.01[b]
Bicarbonate (mEq/L)§	136	24.2 (± 5.7)	221	25.4 (± 3.5)	0.01[b]

[a]Wilcoxon. [b] T Student. *Median (Interquartile range). §Median (Standard deviation)-

Table 5. Complications related to SLED therapy (Sustained Low Efficiency Dialysis)

Complications	All sessions N = 524 N (%)	Sessions in patients under de 20 k N = 56 N (%)
Electrolyte abnormality	37 (7)	8 (14)
Catheter dysfunction	27 (5)	3 (5)
Intradialytic hypotension	24 (5)	3 (5)
Bleeding	9 (2)	0 (0)
Catheter-related bloodstream infection	5 (1)	1 (2)

Values correspond to sessions.

in 13 patients (2.5%), followed by hyponatremia in 6 patients (1%) and hypocalcemia in 3 patients (1%). Table 5 describes the frequency of complications. Catheter replacement was necessary on 26 occasions (5%). In the sessions in which bleeding occurred, all of them involved the use of heparin as anticoagulation. Three patients (11%) died during the PICU stay.

SLED in children under 20 kg

When analyzing separately the events of SLED in children under 20 kilograms, 56 sessions were performed (11%), with a median age of 3 years (3-6), the most frequent indication for SLED was fluid overload in 30 patients (54%), followed by anuria in 16 patients (29%), uremia in 9 patients (16%), and severe hyperkalemia in one patient (1%). Electrolyte imbalances were the most frequent complications in 8 patients (14%), with hypokalemia predominating in 4 patients (50%) and hypophosphatemia in 3 severe hyperkalemia (40%) and less frequently hyponatremia in one patient (10%).

Discussion

To our knowledge, this study is the only one that describes the use of SLED therapy in 524 sessions in a pediatric population in Latin America. In our study, the main indication for therapy was fluid overload in 54% of the sessions, followed by anuria in 37%, with 11% of the sessions in children under 20 kilos. All laboratory tests showed statistically significant improvement after SLED therapy. Complications occurred in 21% of the sessions, predominantly intra-dialysis electrolyte imbalances (8%) and catheter dysfunction (5%), with 11% of mortality.

Although SLED therapy has shown promising results in adults when compared to other RRT modalities, there are few studies evaluating this modality in pediatrics[12,16,18,19]. Previously, it had not been used in the pediatric population due to technical difficulties such as the size of the extracorporeal circuit, the flow to be circulated through it, and the size of the catheter and filter, among others.

In relation to age, this was similar to those of the study by Lee et al. and the two studies by Sethi et al., but in relation to weight, in the study by Lee et al., they excluded patients under 20 kg due to technical difficulties inherent to the therapy. Another study carried out in India which included 49 sessions in patients under 10 kg found that this dialysis modality was effective and safe[17].

The most important indication for RRT in this study was fluid overload followed by anuria, being

consistent with reports of AKI in pediatrics in low- and middle-income countries[8] and similar to other studies where fluid overload and metabolic acidosis were the main indications for SLED therapy[12,18], probably because they were performed in countries with similar economic conditions. The dialysis prescription parameters were similar to those used by other authors and to those recommended by the literature[12,16,18].

The use of heparin in this dialysis modality is still not very clear, even its absence is proposed as an advantage that can reduce bleeding and thus morbidity and mortality[18]. Most studies in pediatrics with this therapy used heparin in dialysis in a significant percentage of sessions[12,16,17], except in the study by Sethi et al., where it was not used in any session, with a very low rate of extracorporeal circuit obstruction (0.8%)[11,18].

Regarding laboratory results, we found that they all presented statistically significant improvement when compared before and after dialysis, similar to other studies with the same dialysis modality[12,16,18].

The most frequent complication was electrolyte imbalances. Post-dialysis hypokalemia was lower than other reports (7%-28%)[12,18]. Post-dialysis hypophosphatemia was similar to another study[12] but higher than in another report[18], except that the definitions between the studies were different. Electrolyte imbalances were higher in those under 20 kg, similar to that reported in the 49 sessions of Ali et al. where hypokalemia was 24.4% and hypophosphatemia was 12.2%[17].

In the sessions where bleeding occurred, all were with the use of heparin as an anticoagulant, and none presented a fatal outcome. In a study where the use of heparin was higher than in our study, no bleeding was reported in any session[16]. Another study reported a higher frequency of bleeding, but this was not related to early discontinuation of SLED[20].

Hypotension occurred in 5% of all sessions, a lower value than those reported by other studies which are between 8.6% and 20.4%, but similar to the study by Lee et al.[12,16-18,21]. These differences may be explained by the fact that in these studies the patients had a high frequency of multiple organ dysfunction (43-94%) and sepsis (41-55%), with high rates of ventilatory support (65-84%) and vasopressor use (63%). A recent study in hemodynamically unstable patients, predominantly with sepsis (94%), concluded that SLED is safe and effective in this population[19].

Regarding mortality in our study, it was lower than in other reports ranging from 29% to 77.8%[12,16,18,19], which is possibly explained by the etiology of renal failure, since there was a higher proportion of patients with sepsis and multiple organ failure.

The only comparative studies of SLED therapy with other RRT modalities are in adults. It has been compared with IHD and peritoneal dialysis, showing better metabolic and volume control in patients undergoing SLED therapy, with lower rates of hypotension when compared to IHD, and no significant differences in mortality[13-15]. Additionally, this modality has an intermediate cost between IHD and continuous hemodialysis, with less need for nursing staff, which for countries with similar incomes to ours may be an advantage[11].

It is striking the few studies in pediatrics and high-income countries, considering that in these countries SLED is available and its prescription rate is higher[8]. In relation to this, the results of a European study published in 2019, do not report SLED as a dialysis modality used in this continent[22], unlike another similar study in India in 2012, which reported the availability of SLED in 23% of participating centers, with the use of this in 10%[23].

In our center, this type of therapy constitutes a useful alternative since it allows dialysis-free times that facilitate patient mobility to diagnostic studies or procedures and has a lower cost than continuous slow therapies. In other centers, the use of SLED has been proposed as a modality used for the transition between CRRT and IHD in patients with multiple organ dysfunction[21].

The limitations of our study are inherent to the retrospective design since not all the data for the analysis were obtained for some variables. In addition, due to the low rate of septic patients or patients with multiorgan failure, it is not possible to extrapolate the results and conclusions to other centers with a higher percentage of patients with sepsis and hemodynamic instability.

Conclusions

Our results show that SLED therapy in critically ill children is a safe RRT modality, with few intradialytic adverse effects such as hypotension and CVC dysfunction and few post-dialysis complications such as electrolyte imbalances, although these are slightly more frequent in children weighing less than 20 kg. It is an effective modality, with improvement of laboratory parameters such as urea nitrogen, pH, bicarbonate, and hyperkalemia.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

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