ORIGINAL ARTICLE

The Use of Sustained Low-efficiency Dialysis in the Treatment of Sepsis-associated Acute Kidney Injury in a Low-income Country: A Prospective Cohort Study

Abdalla Kamal Abdalla Taha[1], Mazin Mohammed Taha Shigidi[2], Nazik Mahmoud Abdulfatah[3], Rajabia Khidir Alsayed[4]

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Abstract

Background: Limited data are available regarding the management and outcomes of patients with sepsis-associated acute kidney injury (SA-AKI) requiring dialysis in Sudan. Continuous renal replacement therapy (CRRT) is a highly favored treatment modality in such patients. However, it stays unavailable and expensive treatment in most low-income countries. We aimed to evaluate the use of sustained low-efficiency dialysis (SLED) in the treatment of hemodynamically unstable patients with SA-AKI admitted to the intensive care unit (ICU).

Materials and methods: A prospective cohort was conducted in Baraha Medical City, Khartoum, Sudan. Patients above 18 years of age, who were admitted to the ICU between January and September 2020 with SA-AKI, and required SLED or CRRT were enrolled. These were followed up till death or discharge from the ICU. They were observed regarding their dialysis tolerance, rate of renal recovery, ICU mortality, and cost of therapy. Data analysis was done using SPSS.

Results: Fifty-three adults were enrolled. Their mean age was 62 ± 11 years, and 56.6% were males. Thirty-one patients (58.5%) received SLED and 22 (41.5%) underwent CRRT. Patients in the two groups were age and sex matched and showed no significant differences in their comorbid conditions, source of sepsis, sequential organ failure assessment (SOFA) score, and their indications for dialysis ($p > 0.05$). Patients treated with SLED showed similar dialysis tolerance, rate of renal recovery, length of ICU admission, and risk of death compared to those treated with CRRT ($p > 0.05$). Moreover, SLED treatments were less expensive than CRRT, and the costs of ICU admission among the SLED group were significantly less ($p < 0.001$).

Conclusion: Our study shows that SLED is safe and effective. It is readily available and can be routinely performed in the treatment of hemodynamically unstable patients with SA-AKI at a significantly lower cost.

Keywords: Acute kidney injury, Dialysis, Intensive care unit, Prospective cohort, Sepsis.

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Highlights

- Continuous renal replacement therapy has always been recommended in the treatment of hemodynamically unstable AKI patients requiring dialysis although it remains expensive and mostly unavailable in most developing countries.
- The hemodynamically unstable patients with sepsis and AKI can be treated equally effective with SLED and at a lower cost.

Introduction

Sepsis remains a common cause of intensive care unit (ICU) admission with acute kidney injury (AKI), requiring renal replacement therapy (RRT).[1] The reported incidence of sepsis-associated acute kidney injury (SA-AKI) ranges from 14 to 87%. It had been associated with a mortality range of 11–77%. Such a wide mortality range is mostly due to the lack of a standardized definition for SA-AKI, the diversity of the clinical settings and populations studied as well as the inconsistency of the outcomes reported.[2]

Earlier reports from Sudan showed that AKI is mostly community-acquired, with sepsis and volume depletion being the commonest etiological causes. It had been reported that RRT is required in up to 19% of the AKI patients admitted to the hospital, with a mortality rate approaching 31.2%. Old age, the presence of sepsis, and the severity of AKI were reported as definitive predictors of increased mortality among these patients.[3,4]

Few reports are available from Sudan about the incidence, management, and outcomes of the patients with SA-AKI admitted to the ICU. Reports from low-income countries showed that the outcomes of these patients are often limited; mostly due to the absence of the appropriate medical setup required and the excessive costs of the services provided.[5,6]

[1,4]Intensive Care Unit, Baraha Medical City, Khartoum North, Sudan

[2]Department of Internal Medicine, College of Medicine, Jouf University, Al Jouf, Saudi Arabia; Department of Medicine, Baraha Medical City, Khartoum North, Sudan

[3]Department of Medicine, Baraha Medical City, Khartoum North, Sudan

Corresponding Author: Mazin Mohammed Taha Shigidi, Department of Internal Medicine, College of Medicine, Jouf University, Al Jouf, Saudi Arabia; Department of Medicine, Baraha Medical City, Khartoum North, Sudan, Phone: +00966543292625, e-mail: mmshigidi@ju.edu.sa.

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Continuous renal replacement therapy has always been preferred over conventional intermittent hemodialysis (HD) in the management of hemodynamically unstable patients with AKI.[7–10] However, CRRT remains an overly expensive mode of RRT that is hardly available in most of the low-income countries.[11]

This study was conducted in Sudan, a low-income country, it aimed to evaluate the use of sustained low-efficiency dialysis (SLED) and CRRT in the treatment of hemodynamically unstable adult patients with sepsis and SA-AKI admitted to the ICU. It determines the patients' tolerance to dialysis, rate of renal recovery, ICU mortality, and the economic burden of the two therapeutic modalities.

Materials and Methods

Study Design and Setting

A hospital-based prospective cohort study was conducted in the ICU of Baraha Medical City (BMC) in Khartoum State, the capital city of Sudan. That BMC-ICU is an 18-bed capacity highly equipped ICU, specifically selected for this study due to the availability of a qualified full-time intensivist, a dedicated nephrologist, and the presence of a readily accessible bed-side dialysis facility in the form of intermittent HD, SLED therapy, as well as CRRT.

All patients above 18 years of age admitted to the BMC-ICU between January and September 2020 with sepsis, in septic shock, having SA-AKI, and requiring treatment with SLED or CRRT were included in the study. We excluded from the study all patients under 18 years of age at the time of admission, pregnant women, patients with chronic or acute on chronic kidney diseases, hemodynamically stable patients, those having AKI due to causes other than sepsis, patients on dialysis before enrollment, those who did not require ICU admission, patients treated with conventional intermittent HD or peritoneal dialysis, and those who refused to give consent for enrollment. Sample size calculation was not done, as all patients presented during the study period and fulfilled the study inclusion/exclusion criteria were targeted.

Throughout the study, the BMC-ICU protocols and admission criteria were followed.[12,13] Single verified criteria for diagnosing sepsis, septic shock, and SA-AKI were used.[2,14–16] Disease severity was assessed using the sequential organ failure assessment (SOFA) score.[17] The recognized Acute Kidney Injury Network (AKIN) definition for AKI was used, and the general indications for dialysis in AKI were applied.[10,16,18] Sustained low-efficiency dialysis was defined as "hemodialysis" or hemodiafiltration lasting for more than six but less than 24 hours per session, using a conventional HD machine. The protocol we implemented for SLED treatments aims for a blood flow of 200 mL/minute, dialysate flows of 300 mL/minute, a treatment duration of 8 hours per session, and sessions were to be delivered on a daily basis till otherwise indicated. All sessions were done at the bedside by well-trained ICU nurses.[19,20] On the contrary, CRRT was described as continuous HD or hemofiltration lasting for more than 24 hours. The CRRT sessions were operated entirely by the ICU nurses, using a PRISMA machine and its specified filter sets. The CRRT prescription includes a blood flow of 100–150 mL/minute, and an effluent dose of 25–30 mL/kg/hour aiming for a delivered dose of 20–25 mL/kg/hour. Heparin anticoagulation during SLED and CRRT treatments was decided jointly by the nephrologist and intensivist.[20,21]

The need for SLED or CRRT was decided by a single nephrologist. That was mostly based on the clinical judgment of the nephrologist as well as the financial affordability of the patient. Patients receiving SLED and CRRT treatments were followed up during their admission to the ICU. Their demographic features, clinical presentation, indications for RRT, number of dialysis sessions needed, complications during dialysis, duration of ICU admission, renal recovery, ICU mortality, costs of RRT, and cost of ICU admission were all recorded electronically using a pre-tested questionnaire. The relative costs of either dialysis modality were determined as the total costs of all dialysate and fluids, filters, tubing sets, concentrates, infusions, laboratory tests, medications, and disposables that are related to dialysis plus any extra payments done for the attending nurse and the dialysis technician.[20] Based on the official exchange rates, all costs were converted and expressed as United States Dollars (USD) throughout the study. Patients were followed up till discharged from the ICU, showed complete renal recovery, or death, swabbed from one dialysis modality to another, or withdrew their consent for enrollment.

Data Analysis

Data analysis was done using statistical package for social sciences (SPSS), version 20, computer software. Numerical variables were expressed as means ± standard deviation (SD) or medians ± standard error of the mean (SEM). Categorical variables were represented as numerical values and their percentages. Univariate analysis of data was done to compare variables between the SLED and CRRT groups, with the unpaired t-test being applied for the numerical variables, and the Chi-square test for the categorical variables. Statistical significance was defined as a *p*-value of less than 0.05.

Results

During the study period, a total of 68 adult Sudanese patients were admitted to the BMC-ICU hemodynamically unstable, having AKI, and were scheduled for SLED or CRRT. Among these, AKI was due to acute coronary syndrome in 9 patients (13.2%), exposure to iodinated contrast in two patients (2.9%), active systemic lupus erythematosus in one patient (1.5%), pregnancy-related conditions in two patients (2.9%), and one patient (1.5%) refused to give consent for enrollment; these were all excluded from the study, whereas a total of 53 hemodynamically unstable adult patients with sepsis and SA-AKI (77.9%) fulfilled the study inclusion/exclusion criteria and were enrolled.

The study population included 30 male (56.6%) and 23 female patients (43.4%). All patients were admitted to the ICU *via* the emergency department. Their mean age was 62 ± 11 years, 34 patients (64.2%) were hypertensives and 29 (54.7%) were diabetics. All patients were diagnosed as having sepsis and septic shock. The primary sites of the infection were the lungs and the urinary system in most patients, 62.3%. The mean SOFA score was 11.3 ± 2.5. Forty-two patients (79.2%) required ventilatory support. All patients were on inotropes for blood pressure support since admission. Out of the 53 patients enrolled, 31 patients (58.5%) were treated with SLED and 22 patients (41.5%) were put on CRRT for their AKI. The characteristics of the study cohort are summarized in Table 1.

Dialysis was mostly indicated by the presence of resistant pulmonary edema, highly elevated blood urea levels, and severe metabolic acidosis; however, a combination of these had always been present. A total of 91 SLED sessions were delivered, compared to 34 sessions in the CRRT group ($p < 0.001$). The mean duration of dialysis was 6.9 ± 1.6 hour/session and 41.6 ± 6.9 hour/session in the SLED and CRRT groups, respectively ($p < 0.001$). Most of the patients

Table 1: Characteristic features of the ICU patients with SA-AKI studied

Characteristic features	*SLED group (n = 31)*	*CRRT group (n = 22)*	*Total (n = 53)*	*p-value*
Male/female ratio	17/14 (54.8%/45.2%)	13/9 (59.1%/40.9%)	30/23 (56.6%/43.4%)	0.76
Mean age (years)	63 ± 12	61 ± 9	62 ± 11	0.51
Comorbid conditions				0.33
Hypertension	18 (58.1%)	16 (73%)	34 (64.2%)	
Diabetes mellitus	16 (51.6%)	15 (68.2%)	29 (54.7%)	
Coronary artery disease	4 (12.9%)	11 (50%)	15 (28.3%)	
Autoimmune disease	0 (0.0%)	2 (9.1%)	2 (3.8%)	
Cause of sepsis				0.64
Pneumonia	9 (29.0%)	10 (45.4%)	19 (35.9%)	
Urinary tract infection	8 (25.8%)	6 (27.3%)	14 (26.4%)	
Abdominal	5 (16.1%)	3 (13.6%)	8 (15.1%)	
Skin and soft tissue	3 (9.7%)	0 (0.0%)	3 (5.7%)	
Other sites	2 (6.4%)	1 (4.5%)	3 (5.7%)	
Unknown focus	4 (12.9%)	2 (9.1%)	6 (11.3%)	
Illness severity				
Mean SOFA score	10.8 ± 2.9	12 ± 1.6	11.3 ± 2.5	0.09
On ventilatory support	23 (74.2%)	19 (86.4%)	42 (79.2%)	0.29
Blood pressure support				0.47
1 vasopressor drug	20 (64.5%)	12 (54.5%)	32 (60.4%)	
≥2 vasopressor drugs	11 (35.5%)	10 (45.5%)	21 (39.6%)	

Data are presented as means ± SD or *n* (%). CRRT, continuous renal replacement therapy; ICU, intensive care unit; SLED, sustained low-efficiency dialysis; SOFA, sequential organ failure assessment

were dialyzed using heparin, 94.3%. Persistent hypotension despite the use of vasopressors, and recurrent episodes of hypoglycemia were the most common intradialytic complications necessitating withholding of dialysis (Table 2).

Patients with SA-AKI who underwent SLED required an average of 4.7 ± 2.1 sessions/patient, while those who were scheduled for CRRT required an average of 2.0 ± 1.6 sessions/patient ($p < 0.001$). None of the patients studied were swabbed from one dialysis modality to another during their ICU admission.

The mean cost of the SLED was 96 ± 43 USD, which was significantly less expensive than CRRT ($p < 0.001$). Furthermore, the other costs of ICU admission were found to be significantly less in the SLED group compared to the CRRT group ($p < 0.001$). Among the population studied, 18 patients (34%) had no medical insurance coverage for their ICU admission or dialysis. Two-thirds of patients had partial or complete insurance coverage for their ICU admission. Only 20 patients (37.7%) were able to have partial or complete medical insurance coverage for the cost of SLED or CRRT. The cost of the SLED treatments was more likely to be covered by medical insurance ($p = 0.01$). Twenty-eight patients with SA-AKI (52.8%) died during their ICU admission, 17 patients (32.1%) showed partial or complete renal recovery and were weaned off dialysis, whereas eight patients (15.1%) required to be on intermittent HD after discharge from the ICU (Table 3).

Discussion

Numerous studies compared the use of SLED and CRRT in the treatment of hemodynamically unstable adult patients admitted to the ICU with AKI. Most of these studies were limited by their different methodologies, heterogeneous populations enrolled, substantial risk of bias, and poor description of the outcomes measured, and thus labeled as having reduced validity and utility of the results obtained. These facts have led to the absence of firm conclusions so far about the use of SLED or CRRT in the ICU.[6]

In the current study, we compared the use of SLED and CRRT in the hemodynamically unstable adult patients admitted to the ICU with SA-AKI. All patients were followed prospectively till death or discharge from the ICU. Their tolerance to the modality of RRT provided, renal recovery, ICU mortality, and cost of therapy were observed. The two groups were age and sex matched, showing no significant differences regarding their comorbid conditions, source of sepsis as well as the determinants of the severity of their illness. The SOFA score applied in our study is a recognized, widely accepted prognostic marker in the ICU.[22] Patients enrolled for CRRT tend to be more ill with a higher mean SOFA score; however, on statistical analysis, the difference between the two groups was not statistically significant ($p = 0.09$).

Throughout the study, SLED and CRRT were entirely performed by the same ICU team. Persistent hypotension and recurrent hypoglycemia were the most common intradialytic complications seen during dialysis. Recurrent hypoglycemia during dialysis was seen much more often in the SLED group; that finding was not statistically significant. Our patients showed similar hemodynamic effects when treated with SLED or CRRT.[23] Saline flushes/heparin-free dialysis were prescribed in only 5.7% of sessions due to increased risks of bleeding. Whereas heparin anticoagulation was given in most treatments with no significant bleeding complications in either group.[20] Overall, patients in the two groups were able to tolerate the two dialysis modalities in a similar fashion ($p = 0.19$).

Table 2: Details of the dialysis treatments for the patients with SA-AKI studied

Characteristic features	*SLED group (n = 31)*	*CRRT group (n = 22)*	*Total (n = 53)*	*p-value*
*Main indications for dialysis				0.34
Pulmonary edema	18 (58.1%)	6 (27.3%)	24 (45.3%)	
Urea levels > 250 mg/dL	14 (45.2%)	8 (36.4%)	22 (41.5%)	
Severe metabolic acidosis	8 (25.8%)	10 (45.5%)	18 (34%)	
Anuria	10 (32.3%)	6 (27.3%)	16 (30.2%)	
Resistant hyperkalemia	4 (12.9%)	4 (18.2%)	8 (15.1%)	
Delivered dialysis therapy				
Total number of sessions delivered	91 (72.8%)	34 (27.2%)	125 (100%)	<0.001
Mean dialysis duration (hour/session)	6.9 ± 1.6	41.6 ± 6.9	–	<0.001
Mean blood flow (mL/minute)	209.4 ± 32.7	98.3 ± 51.2	–	<0.001
Mean dialysate flow (mL/minute)	218.4 ± 31.8	–	–	–
Mean effluent flow (m/kg/hour)	–	26.4 ± 13.2	–	–
Mean net ultrafiltration (L/session)	1.4 ± 0.7	3.5 ± 0.9	–	<0.001
Heparin anticoagulation given	29 (93.5%)	21 (95.5%)	50 (94.3%)	0.77
*Dialysis complications necessitated withholding of therapy				0.19
Persistent hypotension	16 (51.6%)	12 (54.5%)	28 (52.8%)	
Persistent hypoglycemia	10 (32.3%)	4 (18.2%)	14 (26.4%)	
Cardiac arrest	3 (9.7%)	5 (22.7%)	8 (15.1%)	
Cardiac arrhythmias	1 (3.2%)	3 (13.6%)	4 (7.5%)	
Bleeding	0 (0%)	1 (4.5%)	1 (1.9%)	
Recurrent hypokalemia	0 (0%)	2 (9.1%)	2 (3.8%)	

Data are presented as means ± SD or *n* (%). *An overlap in these features does occur. CRRT, continuous renal replacement therapy; SLED, sustained low-efficiency dialysis

Table 3: Outcomes of the patients with SA-AKI required SLED or CRRT

Details	*SLED group (n = 31)*	*CRRT group (n = 22)*	*Total (n = 53)*	*p-value*
Duration of ICU admission (days)	7 ± 2.7	6.8 ± 2.9	–	0.8
Dialysis sessions per patient	4.7 ± 2.1	2.0 ± 1.6	–	<0.001
Cost of a single dialysis session (USD)	96 ± 43	645 ± 256	–	<0.001
Cost of dialysis per patient (USD)	451 ± 90	2580 ± 410	–	<0.001
*Cost of ICU admission per patient (USD)	661 ± 257	1192 ± 480	–	<0.001
Medical insurance coverage	21 (67.7%)	14 (63.6%)	35 (66%)	0.76
Dialysis insurance coverage	16 (51.6%)	4 (18.2%)	20 (37.7%)	0.01
Overall patient outcome				0.2
Died during the ICU admission	15 (48.4%)	13 (59.1%)	28 (52.8%)	
Recovered renal function in the ICU	9 (29%)	8 (36.4%)	17 (32.1%)	
Required to be on intermittent dialysis after discharge from the ICU	7 (22.6%)	1 (4.5%)	8 (15.1%)	

Data are presented as means ± SD or *n* (%). *Intensive care unit costs other than that of dialysis. CRRT, continuous renal replacement therapy; SLED, sustained low-efficiency dialysis

Throughout the study, the basic prescriptions of SLED and CRRT had to be much more dynamic and required various modifications to suit our patients' medical conditions.[20,21] To attain adequate dialysis, significantly more frequent SLED sessions were needed compared to CRRT ($p < 0.001$). Our study showed that SA-AKI patients treated with SLED had a similar risk of death when compared to those treated with CRRT. Similarly, there were no significant differences in the rates of renal recovery, dialysis dependence, and the length of ICU admission on comparing the two groups ($p > 0.05$). However, we realized that patients undergoing SLED were more likely to be on intermittent HD following discharge from the ICU. That finding was not statistically significant, but it remains to be consistent with the results obtained from earlier reports.[6,20]

The government of Sudan runs a community-based health insurance system in addition to numerous private medical insurance companies operating in the country. Most of these tend to provide pre-defined insurance coverage limited to specific illnesses, with the amount of coverage being restricted to a fixed budget.[24]

Despite the high frequency of SLED treatment sessions needed per patient, it remained significantly less expensive compared to CRRT and more likely to be covered by medical insurance.[20,25,26] However, neither the government-run community-based health insurance nor most private medical insurance companies support the prohibitive cost of CRRT. The majority of our CRRT patients had their treatment expenses covered by the patients' and family's own resources.[24,27,28] The high costs of the replacement fluids, filter, and lines of the CRRT machine made the CRRT treatment a very expensive therapeutic modality in Sudan, with most of the insurance companies refraining from supporting its expenses. These facts made SLED a more appropriate and cost-effective therapeutic option for our patients.[6,25,26] In addition to the fact that SLED is often readily available and requires less expertise to operate.[6,20,22]

Our study was reinforced by its prospective nature, the adherence to standardized definitions for the diagnosis of sepsis, AKI, SA-AKI, SLED, and CRRT throughout the study, and the implementation of a unified enrollment strategy by a single intensivist and a nephrologist regarding admission, requirement for dialysis, dialysis modality selection, withhold of dialysis and discharge from the ICU. All these facts make the study having a focused research question, clearly defined population evaluation and standardized interventions. Furthermore, no significant differences were seen between the SLED and CRRT groups regarding their demographic feature, comorbid conditions, and indications for dialysis. These facts tend to reduce the risk of confounding errors in our study. On the contrary, our study was limited by an increased risk of selection bias being an open labeled single center study. Again, it included a relatively small number of patients, which was mostly due to the strict inclusion/exclusion criteria implemented throughout the study.[6]

Conclusion

In low-income countries, establishing an appropriate ICU setup is often hindered by the lack of infrastructure, trained manpower, the presence of the necessary equipment, and adequate financial funds. These facts make CRRT an expensive and inaccessible therapeutic modality in most of these countries.[29] Our study supports the results from earlier reports, which found SLED to be a safe and effective treatment for hemodynamically unstable patients with SA-AKI admitted to the ICU. The study provides added information about the cost of SLED and CRRT in a low-income African country. It supports the fact that SLED can be routinely performed in patients with SA-AKI, with a significantly lower cost than CRRT, and an overall similar outcome.[6] These facts encourage its use in low-income countries; however, a larger sample size, multicenter, randomized controlled trial remains essential.

Ethical Approval

Ethical approval was obtained from the Ethical Committee of the Sudan Medical Specialization Board. Ethical clearance was obtained from BMC-ICU. An informed consent was obtained from all participants or the next of kin before enrollment.

Authors' Contributions

Conception: AT and MS. Design: RA and MS. Acquisition of data: AT, NA, and RA. Analysis of data: MS and AT. Interpretation of data: AT, NA, and MS. Draft manuscript: MS and NA. Revised manuscript: AT, MS, RA. All authors read and approved the final manuscript.

Availability of Data and Materilas

The data used and analyzed in the current study are available from the corresponding author upon reasonable request.

Orcid

Abdalla Kamal Abdalla Taha https://orcid.org/0009-0009-1042-7239

Mazin Mohammed Taha Shigidi https://orcid.org/0000-0003-3697-0941

Nazik Mahmoud Abdulfatah https://orcid.org/0009-0006-2927-8702

Rajabia Khidir Alsayed https://orcid.org/0009-0008-9615-4720

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