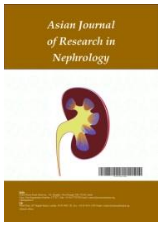

Asian Journal of Research in Nephrology

3(1): 24-32, 2020; Article no.AJRN.58330

Feasibility and Hemodynamic Tolerability of Sustained Low- Efficiency Dialysis in Critically Ill Patients with Acute Kidney Injury

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Authors' contributions

This work was carried out in collaboration among all authors. Author MR conceived, designed, collected the data and authored the first manuscript of the study. He is the guarantor of the study. Authors SB and PM designed, monitored the progress of the study & edited the final manuscript and revised it for important intellectual content. All authors helped with final approval of the version to be published.

Article Information

Editor(s):
(1) Dr. P. Kiranmayi, GITAM University, India.
Reviewers:
(1) Amir Mostafa, Cairo University, Egypt.
(2) Mohsen Zhaleh, Kermanshah University of Medical Sciences, Iran.
(3) Esther Kesewa Amfo, University of Texas at El Paso, USA.
Complete Peer review History: http://www.sdiarticle4.com/review-history/58330

Original Research Article

Received 20 April 2020
Accepted 27 June 2020
Published 06 July 2020

ABSTRACT

Introduction: AKI is a common complication of critical illness. Management of AKI may require the initiation of RRT to correct metabolic and fluid derangements. CRRT does have some advantages over conventional intermittent dialysis in critical care settings. The main disadvantage of CRRT is its exorbitant cost. SLED is a hybrid technique between CRRT and IHD, done using conventional HD machines and dialyzers.

Materials and Methods: The primary objective of the study was to determine the hemodynamic tolerability & feasibility of SLED in critically ill patients with AKI. All patients admitted to the ICU; who was started on SLED was included in this study. Data on demographic information, pre-dialysis Biochemical & Hematological parameters were collected. BP and vasopressor requirements during the SLED sessions were recorded. Survival predictors were described using a SOFA score at the time of initiation of the first SLED session.

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Results: 427 SLED sessions were conducted in 148 patients. Two patients suffered from cardiac arrest during the SLED session. There was an increased requirement of inotropic support in 56 sessions which was labeled as a hemodynamically unstable session. Hypotension refractory to inotropic medication, requiring SLED discontinuation occurred in 14 sessions. 97.7% of the prescribed duration of treatment and 89.07% of the ultrafiltration goal was achieved with SLED in this study.

Conclusion: SLED is a well-tolerated, feasible, cost-effective RRT modality in resource-limited settings for critically ill patients with AKI.

Keywords: Sustained low-efficiency dialysis (SLED); acute kidney injury (AKI); continuous renal replacement therapy (CRRT); renal replacement therapy (RRT).

1. INTRODUCTION

Acute Kidney Injury (AKI) has emerged as a major public health problem that affects millions of patients worldwide and leads to decreased survival and increased progression of underlying Chronic Kidney Disease (CKD). AKI is a frequent complication of critical illness. Studies describe AKI based on serum creatinine changes, changes in Blood Urea Nitrogen levels, urine output, or the need for dialysis. The currently accepted definition of AKI is the one suggested by Kidney Disease: Improving Global Outcomes (KDIGO). KDIGO has defined AKI as an increase in serum Creatinine by ≥ 0.3 mg/dl (≥26.5 μmol/l) within 48 hours, or increase in serum Creatinine to ≥ 1.5 times baseline, which has occurred within the prior 7 days; or Urine volume < 0.5 ml/kg/h for 6 hours [1]. The above criteria include both an absolute and a percentage change in creatinine to accommodate variations related to age, gender, and body mass index and to reduce the need for a baseline creatinine. The diagnosis of AKI based on the urine output criterion alone will require exclusion of urinary tract obstructions that reduce urine output or other easily reversible causes of reduced urine output.

AKI is well recognized for its adverse impact on patient outcome, especially in Critical Care Units (CCU), world-wide [2-5]. AKI is seen in 13-18% of all people admitted to the hospital. AKI affects 20-60% of critically ill patients. In patients with severe AKI requiring Renal Replacement Therapy (RRT), mortality is to the tune of 50% to 70% [5]. AKI not only increases morbidity and mortality rates but also utilizes considerable health care resources. Thus prevention and management of AKI in the CCU are critically important to patient survival.

The etiology of AKI in CCU patients is multifactorial and can be due to sepsis, hypovolemia, or even due to drugs. Different etiologies are classified as pre-renal, intrinsic renal, and post-renal due to obstruction. Since many times the cause of AKI is multifactorial, the focus should be mainly on prevention.

Management of AKI may require the initiation of RRT to correct metabolic and fluid derangements. RRT is the treatment modality that replaces the normal filtering function of the Kidneys. It is used for the management of compromised Renal function in both acute and chronic Kidney diseases when the need arises. Several options of RRT are available, which include Intermittent Hemodialysis (IHD), Peritoneal Dialysis (PD), Continuous Renal Replacement Therapy (CRRT) and Sustained low-efficiency Dialysis (SLED).

CRRT is a type of Renal replacement therapy that is intended to be applied for 24 hours per day in CCU. Solute removal with CRRT is achieved either by convection (hemofiltration), diffusion (hemodialysis), or a combination of both these methods (hemodiafiltration). CRRT does have some advantages over conventional intermittent dialysis, in terms of improved cardiovascular stability, improved tolerance to ultrafiltration allowing correction of fluid overload, and the ability to maintain solute control, especially in a catabolic patient. The main disadvantage of this form of treatment is its exorbitant cost, the requirement of specialized pre-manufactured solutions, technical expertise, and continuous anticoagulation for prolonged periods [6,7]. Another option is IHD which allows greater volume removal in shorter periods, but when high ultrafiltration (UF) rates are required it may lead to hemodynamic instability in critically ill patients. Besides, aggressive dialysis may lead to sudden osmotic changes in the patient which will be poorly tolerated. Experience with PD in AKI is limited in adult settings.

SLED is a hybrid technique between CRRT and IHD with advantages like low UF rates with better hemodynamic stability, prolonged solute removal with fewer hemodynamic imbalances, and can be done using conventional HD machines & dialyzers. This therapy can be applied to all patients with AKI requiring dialytic support, who cannot tolerate regular Haemodialysis [8,9]. Few studies from the Western world have suggested comparable clinical outcomes and lower costs, in patients treated with SLED as compared to CRRT [10-15]. The choice about the type of RRT finally depends upon the availability, expertise, hemodynamic stability, indication for therapy, and cost of treatment. In developing countries like India, the most important hindrance in the delivery of optimal care is the cost factor.

There is an unresolved controversy about the optimal modality for the delivery of RRT to critically ill patients with AKI. Many Nephrologists and Intensivists prefer CRRT because of the availability of extensive literature on the use of CRRT techniques in hemodynamically unstable patients. On the other hand, the data on the experience of SLED in CCU settings has been comparatively sparse. So, this study was designed with a primary objective to determine the hemodynamic tolerability & feasibility of SLED in critically ill patients with AKI.

2. MATERIALS AND METHODS

2.1 Study Design & Population

This prospective observational study was conducted at a Tertiary level multi-specialty hospital in the State of Kerala, India, after the approval of the Institutional Ethical Committee. The primary study population was the patients admitted to CCU, who was started on SLED for AKI, above the age of 18 years.

Patients who were already on maintenance HD, patient discharged from CCU against medical advice, and those cases subject to change in dialysis modality or use of more than one type of modality for dialysis were excluded from the study.

2.2 Method of Measurement of the Outcome of Interest

All patient admitted to CCU was considered as critically ill and was included in the study. The patient was assigned a Sequential Organ Failure Assessment (SOFA) score [16-18] before the initiation of the first dialysis, to describe the severity of acute illness.

A session was defined as a minimum of 6 hours' treatment with SLED. A session was assigned as a 'hemodynamic unstable SLED session' if there was an intradialytic mean arterial pressure (MAP) drop by more than 20% from pre-treatment value [19] or if there was an increase in Vasopressor escalation or new inotropic addition or if the patient died during or within one hour of completion of the SLED session.

Treatment Interruption was defined as the session which had not achieved at least 90% of Nephrologist prescribed time due to any reason including machine malfunction, clotting of blood in the circuit, hemodynamic instability, nursing or patient-related issues, etc. [19]. The factor responsible for treatment interruption was documented and was used for determining the feasibility of administration of SLED in critically ill patients.

SLED was administered by trained dialysis staff, using Fresenius Medical Care 4008 S dialysis machine and Hemoflow F6HPS Fresenius 1.3m [2] Polysulfone dialyzer. Dialysate composition, frequency of sessions, blood flow, and dialysis flow rates were individualized to patient requirements and the desired ultrafiltration volume was prescribed by the Nephrologist. Each SLED session was a minimum of 6 hours duration. Hemodynamic monitoring was done by the CCU team and decision regarding vasopressor dosing was at the discretion of the Intensivist.

Data on Demographic information, predialysis serum Biochemical & Hematological parameters including serum electrolyte and Renal function tests were collected. Systolic and diastolic blood pressure, MAP, and vasopressor requirements were recorded at the beginning, every 3 hours, and the end of each session. Nadir BP during the session was also recorded.

Clinical outcomes in terms of mortality and survivorship and survival predictors were described using a SOFA scoring system done at the time of initiation of the first SLED.

All data were entered into MS Excel and were analyzed using the statistical software SPSS version 16.0. Descriptive statistics were summarized using means with standard deviations (SDs) or medians with interquartile ranges (IQR) for continuous variables; percentiles and rates for categorical variables. The distributions were examined using histograms. The Chi-square test was used for qualitative outcomes of the independent samples, *t*-test, or *U* Mann Whitney test for quantitative outcomes. Significance was set at $p < 0.05$.

3. RESULTS AND DISCUSSION

427 SLED sessions conducted in 148 patients were analyzed. The mean age of the study group was 52.09 + 13.424 years, comprising of 103 males and 45 females. They had a mean SOFA score of 8.79 and the majority of cases were in the middle age group (45 to 65).

Table 1. Baseline characteristics

Parameter	Mean + SD
Age (years)	52.09 + 13.424
S Creatinine (mg/dL)	3.06 + 1.564
BUN (mg/dL)	53.36 + 23.059
S. Sodium (mmol/L)	135.08 +6.802
S. Potassium (mmol/L)	4.79 +0.970
Hemoglobin (g/dL)	10.08 + 1.220
SOFA score at SLED initiation	8.79 + 2.881
Systolic BP (mm of Hg)	100.49 + 11.792
Diastolic BP (mm of Hg)	67.10 + 10.263
Blood Flow Rate (Qb) (ml/ minute)	163.23 + 29.580
Dialysate Flow rate (Qd) (ml/ minute)	334.66 + 76.714

Table 2. Dialysis parameters of SLED sessions

Parameter	Value + SD
Mean duration of HD prescribed (hours)	6.20 + 0.729
Mean Duration of HD achieved (hours)	6.06 + 0.867
Percent time delivered / time prescribed	97.74 %
Mean Ultrafiltration prescribed (ml/session)	2567.05 + 195.31
Mean Ultrafiltration achieved (ml/session)	2286.56 + 528.94
Percentage of Ultrafiltration achieved	89.07 %
Number of sessions with hemodynamic instability	72 (16.86%)

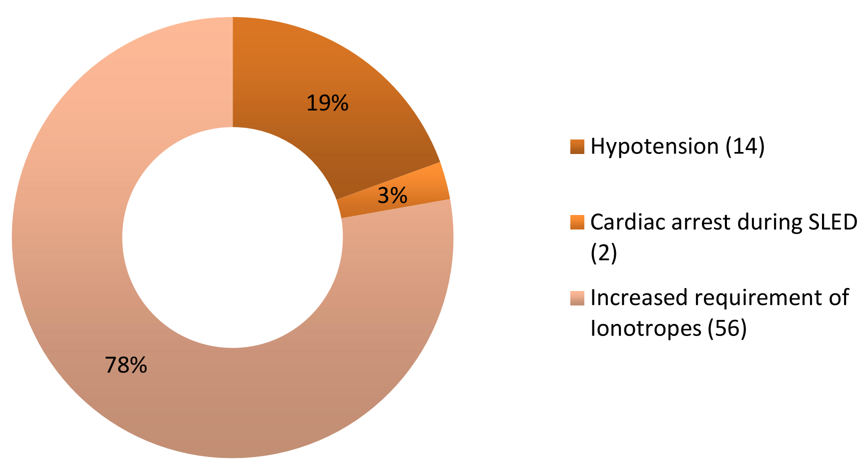

Fig. 1. Cause for Hemodynamic Instability

We were able to achieve 97.74% of the prescribed duration of treatment and 89.07% of the ultrafiltrate goal in our cases. There were 21 sessions with filter clotting, as most of the cases were done heparin free for non-renal indications. This resulted in transient treatment interruption but the session was continued with a fresh dialyzer to achieve the prescribed duration of treatment. Since the sessions were continued with a new filter and patient hemodynamics was not altered, the same group was considered for intention to treat analysis and not excluded. Two patients suffered from cardiac arrest during a SLED session in this study group.

The hemodynamically unstable sessions were higher in those age groups with mean SOFA score of 9 or above. There was an increased requirement of inotropic support in 56 sessions which was labeled as hemodynamically unstable SLED sessions. This may be partially due to the fact that inotropic titration was independently done by CCU nursing staff and Intensivists, who were blind to this study methodology and were trained to react immediately to hypotensive episodes in CCU patients. Hypotension refractory to inotropic medication, requiring SLED discontinuation occurred in 14 sessions. Excluding these 72 (16.9%) sessions, SLED was successfully completed in the majority of critically ill patients with AKI.

The mortality in our study is 14%(20). We analyzed various patient parameters that predict a worse outcome for SLED therapy. Statistically, a significant association was found between the mean creatinine value at the time of initiation of SLED and the SOFA score at RRT initiation. The mean duration of SLED was higher in the very elderly group, mainly because of their frailty. A statistically significant difference in outcome in terms of survival was detected among those with a SOFA score above and below 9. The odds of death in a SOFA score of 9 and above, is nearly 30 times than of those with lower scores.

Table 3. Age-wise distribution of hemodynamically unstable cases with relation to SOFA score

Age group	Mean SOFA Score	Standard deviation	Hemodynamic stability Number of cases		Total
			Unstable	Stable	
< 35	8.68	2.968	1 4%	24 96%	25 100
36-45	9.42	3.453	5 25%	15 75%	20 100%
46-55	8.21	2.256	4 10.53%	34 89.47%	38 100%
56-65	8.75	2.562	1 2.27%	43 97.73%	44 100%
66-75	10	3.873	4 23.53%	13 76.47%	17 100%
76-85	9.25	3.403	1 25%	3 75%	4 100%

Table 4. Mortality and SOFA score

SOFA Score	n (Cases)	n (Death)	Death rate (percentage)	Overall Mortality rate in the study
< 6	26	0	0	0
7-8	65	1	1.54	6.71
9-10	27	2	7.40	13.4
11-12	13	3	23.07	20.13
13-14	8	5	62.5	33.6
15-16	6	6	100	40.3
17-18	2	2	100	13.43
>18	1	1	100	6.71

Table 5. Effect of various parameters on patient outcome

Parameter	Outcome	N(Patients)	Mean	Std. deviation	p-Value
Age (years)	Expired	20	55.30	13.712	0.278
	Survived	128	51.65	13.399	
SerumCreatinine(mg/dL)	Expired	20	4.26	2.018	<0.001
	Survived	128	2.87	1.404	
BUN(mg/dL)	Expired	20	64.85	29.003	0.060
	Survived	128	51.48	21.638	
Hb(g/dL)	Expired	20	9.51	1.074	0.010
	Survived	128	10.24	1.224	
Systolic BP(mm of Hg)	Expired	20	97.10	11.801	0.135
	Survived	128	101.48	11.750	
Diastolic BP(mm of Hg)	Expired	20	65.00	12.260	0.472
	Survived	128	67.10	9.685	
SOFA score	Expired	20	14.15	3.031	<0.001
	Survived	128	8.00	1.757	

A cost analysis revealed that the expense for CRRT in this study group for the same duration of SLED would be 72 times that of SLED therapy in our setting.

The minimization of hemodynamic instability during RRT in critically ill patients is often demanding. Many studies have been done worldwide with various modalities of RRT; but to date, no specific modality is recommended for all patients in CCU settings.

Several studies [10,19,20,21,22] compared the feasibility of SLED administration with that of CRRT and IHD in AKI patients. Most of them concluded that there is no added advantage to CRRT in terms of hemodynamic stability in critically ill patients with AKI. We were also able to achieve nearly 87% of the UF goal and 97% of dialysis time without major hemodynamic instability. Robert LL etal [22] in their multicentre prospective randomized controlled trial observed no difference in duration of hospital stay, mortality rates, or time for Renal recovery in IHD cases.

Few studies [23,24] do have some conflicting observations suggesting that CRRT cases had better hemodynamic parameters than SLED, especially on blood pressure. Abhijat K et al. [25] demonstrated lower mortality at 30 days among SLED when compared with CRRT treated patients. Accepting the limitations of our trial, it's not possible to conclude that SLED therapy will reduce mortality when compared to CRRT.

Schwenger et al. [26] in a Prospective, randomized, interventional, clinical study demonstrated reduced nursing time and lower costs for SLED compared to CRRT with similar patient outcomes. Even our study showed a considerable cost difference between SLED & CRRT. The financial implication to the patient is of due importance in the developing world where most of the population has to pay themselves, as the health system is not completely insurance covered. SLED has some practical advantages over CRRT as it can be performed with minimal or no systemic anticoagulation [10,15,27,28]. The fixed duration of SLED allows patients to be transported outside the critical care unit for imaging and procedures, without the apprehension of disrupting the RRT session. Moreover, recent evidence supports the fact that neither the modality nor the dose of RRT has any impact on patient survival or outcome [21,29,30, 31].

Our study is not without limitations. Given the observational nature of this study, we cannot rule out confounding factors that increase illness severity and alters patient hemodynamics. Pre-admission comorbidities were not similar in this study group. The study has taken into account the severity of illness at the time of initiation of RRT but the effect of pre-existing comorbidities onoutcome and hemodynamics of patients was not considered. Moreover, our study revolved around hemodynamic instability aspect in patients on SLED, which is a surrogate endpoint and may not be predictive of patient outcomes such as mortality and persistent dialysis dependence.

This is a prospective observational study on the outcome and feasibility of SLED in AKI patients at CCU. The findings of the study should be verified by larger randomized control prospective trials to determine long-term outcome There is no head to head direct comparison with CRRT technique in our study, as this kind of RCT requires a larger sample size, long follow-up periods, more logistic and financial support. This is a single-center study and our results may not be readily applicable to other settings. But despite these limitations, our findings support the use of SLED as a feasible option in critically ill patients with AKI requiring some form of RRT support.

4. CONCLUSION

We conclude that SLED is a well-tolerated RRT modality in the majority of critically ill patients with AKI and is a feasible alternative to CRRT in resource-limited settings.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication and use of case data.

ETHICAL APPROVAL

This observational study was approved by an Institutional Review Board (IRB), Ethical Committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/58330