Original Article

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

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Abstract

Background: *Sustained low efficiency dialysis (SLED) has been evolved in recent years as technical hybrid of continuous renal replacement therapy and intermittent hemodialysis. It offers optimized hemodynamic stability of the critically ill patients with acute kidney injury (AKI). Our aim was to evaluate the hemodynamic tolerability of SLED in hemodynamically unstable patients with AKI.*

Methods: *This prospective experimental study was conducted in Intensive Care Unit of BIRDEM General Hospital, Dhaka over a period of one year.*

Results: *Forty three hemodynamically unstable patients with AKI were treated with one fifty three sessions of SLED. Mean arterial pressure of the patients before starting dialysis were 80.58±10.92 mmHg and 69.8% patients were on inotrope support. There were no significant differences (p>0.05) in mean arterial pressure during the procedure. No significant changes (p>0.05) occurred in pulse, respiratory rate and temperature during the sessions. Only thirty six out of 153 SLED sessions were associated with complications and hypotension was the commonest one (20.26%). Hypotensive episodes were effectively managed with addition or dose escalation of inotropes. No dialysis had to be discontinued because of hypotension/arrhythmia.*

Conclusion: *SLED is an effective renal replacement therapy for the critically ill patients with AKI which maintains their hemodynamic stability.*

Key words: *acute kidney injury; Intensive Care Unit; sustained low efficiency dialysis*

(BIRDEM Med J 2016; 6(2): 84-90)

Introduction

Acute kidney injury (AKI) is a frequent complication of critical illness. It may develop de novo in the setting of intact kidney function or can be superimposed on underlying chronic kidney disease (CKD).[1] AKI is associated with high mortality and morbidity and renal replacement therapy (RRT) is needed in 4-5% of AKI cases.[2]

RRT for AKI can be classified as intermittent or continuous, based on the duration of treatment. Duration of intermittent therapy like intermittent hemodialysis (iHD) and sustained low efficiency dialysis (SLED) is less than 24 hours. Continuous therapy like continuous renal replacement therapy (CRRT) and peritoneal dialysis (PD) is at least 24 hours or more. The optimal RRT modality in critically ill patients with AKI remains controversial. In the late 90's, SLED has emerged as an attractive form of CRRT for the hemodynamically unstable patients of intensive care unit (ICU). This dialysis modality is run for prolonged period using conventional hemodialysis machine with modification of blood and dialysate flows. Thus it combines the superior detoxification and hemodynamic stability of CRRT with the operational, reduced hemorrhagic risk

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Received: January 23, 2015 **Accepted:** May 30, 2016

and low cost of conventional iHD. Now-a-days it is also called prolonged intermittent renal replacement therapy (PIRRT).[1]

Many critically ill patients in ICU are either hypotensive or have some other cardiovascular problems which make them unsuitable for iHD. Though CRRT offers greater hemodynamic stability than iHD for ICU patients, the costly CRRT machine is not widely available in resource poor settings. Moreover, many patients find it very difficult to bear the cost of CRRT. The aim of the present study was to evaluate the hemodynamic tolerability of SLED in the critically ill patients of ICU suffering from AKI.

Methods

Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorder (BIRDEM) General Hospital is a tertiary care academic hospital in Dhaka, the capital of Bangladesh. It had an adult mixed (medical and surgical) ICU comprising of 10 beds. This Quasi-experimental study was conducted in this ICU after getting approval from the Ethical Review Committee of Bangladesh Diabetic Somiti. AKI patients who were admitted in this ICU or who developed AKI after admission from 1st June 2012 to 31st May 2013, were enrolled if they had hemodynamic instability.

Hemodynamic instability was defined as the composite of the following events: hypotension which needed treatment with inotropes/vasopressors and/or compromised cardiac function (left ventricular ejection fraction <35%). Hemodynamically unstable patients who were not fit for iHD were chosen for SLED and informed written consents were taken from individual patient or from their legal guardian for participation in the study. Exclusion criteria were patients suffering from end stage renal disease (ESRD) before ICU admission and consent denial.

SLED sessions were administered with the Dialog$^+$ B Braun hemodialysis machine without any additional hardware or software. F8 low flux polysulfone hemodialyzer was used with standard lines. As the minimum dialysate flow rate in Dialog$^+$ B Braun hemodialysis machine is 300 ml/min, this was set as the dialysate flow for every SLED session. The blood flow rates varied from 100 to 150 ml/min according to patients' blood pressure (BP) and/or dose of inotropes/vasopressors. The desired ultrafiltration volumes were prescribed by the intensivist.

Each SLED session was planned to deliver for 6 hours and was administered by ICU nurses. Hemodynamic monitoring and decisions regarding vasopressor dosing and anticoagulants were done by the ICU physicians.

A preformed data sheet was used for collecting data from each patient. Demographic informations like age, gender etc, diagnoses at the time of ICU admission and reason for giving SLED were documented on the day of SLED initiation. Blood tests like complete blood count, coagulation screening, blood urea, serum creatinine, serum electrolytes and arterial blood gas analyses were recorded on admission to ICU, on day of RRT initiation and after each RRT session. Systolic and diastolic BP, mean arterial pressure (MAP), pulse, temperature, respiratory rate and vasopressor/inotrope requirements were recorded at the beginning of SLED, during SLED sessions and at the end of the therapy. Vasopressor/inotropes included norepinephrine, dopamine, vasopressin, epinephrine and/or dobutamine. Data were collected for 1st seven days after initiation of SLED and patients were followed up for 28 days for outcome. Outcomes were documented as resolution of AKI or continuation of RRT or death within 28-days of initiation of SLED.

Hemodynamic instability was decided when any patient developed any form of arrhythmia during SLED sessions or intra-therapy drop in MAP from the pre-SLED value or need to escalate the dose of vasopressor/inotrope or addition of a vasopressor/inotrope. If hypotension or arrhythmia persisted for more than half an hour after giving adequate treatment or if MAP dropped more than 20% from pre-SLED MAP, RRT was discontinued and that SLED session was marked as 'treatment failure'.

Statistical analyses were done by SPSS 17 for Windows. Comparison was performed using t-test, and anova. P less than 0.05 was considered as significant.

Results

During the study period, 43(including 29 male) hemodynamically unstable patients with AKI received SLED in the study ICU. Mean age of the patients was 60.12±14.57 years. The commonest diagnosis during ICU admission was pneumonia (46.5%) followed by acute myocardial infarction (AMI, 41.9%). Indications of choosing SLED were cardiogenic shock and ischemic heart disease (IHD) with compromised cardiac function (n=20, 46.5%) and septic shock (n=18, 41.9%). One patient had chronic liver disease with low BP (Systolic BP <90 mmHg) and another patient had severe hyponatremia (serum sodium <120 mmol/L). So, SLED was given to treat AKI in these two patients also. Three patients were suffering from both cardiogenic and septic shock.

Thirty out of 43 patients required inotrope/vasopressor before initiation of SLED to maintain their BP. Twenty five patients were put on mechanical ventilator (MV) support after ICU admission. Other baseline variables are shown in table I.

Table I. Baseline variables of study subjects (n = 43)

Mean arterial pressure (mmHg)	80.58±10.9
Pulse (per minute)	105.40±17.9
Respiratory rate (breathe per minute)	20.07±3.9
Temperature (p F)	99.51±1.3
Serum creatinine (mg/dl)	7.096±2.3
Blood urea (mg/dl)	194.5±63.1

Total 153 sessions of SLED were performed in 43 study patients in seven days of data collection. Blood flows were adjusted based on patients' BP and inotrope requirements and ranged from 80-180ml/min. Dialysate flow was 300 ml/min in all sessions. Ultrafiltrate (UF) volumes ranged from 1-4.2 L and were determined according to patients' volume status, BP and inotrope requirements.

Table II. SLED parameters

Total SLED sessions	153
Blood flow (ml/min)	119.67±22.0
Dialysate flow (ml/min)	300
Anticoagulation with heparin	77 (50.32%)
Duration of dialysis (hours)	5.75±1.204
UF volume (L)	2.16±0.5

The following table (Table III) show the MAP of the patients' which were recorded before initiation of each session of SLED, during SLED and after completion of the treatment. There were no significant changes of MAP during the procedure.

There were no significant changes in pulse, R/R and temperature during and after SLED sessions.

One hundred and seventeen sessions of SLED could be performed without any complication. Only thirty six (23.52%) sessions were associated with complications shown in figure 1. The commonest complication was hypotension (n=31 sessions) which required increase in dosage of inotrope or addition of inotrope. But no

Table III. Comparison of Mean Arterial Pressure changes during SLED

	MAP before SLED	MAP during SLED	MAP after SLED	*p*-value
1st session (n=43)	80.58 ± 10.92	81.46 ± 13.69	83.67 ± 15.81	0.55
2nd session (n=43)	84.54 ± 14.65	84.61 ± 13.31	84.33 ± 12.55	0.99
3rd session (n=41)	84.49 ± 14.29	84.05 ± 10.81	86.54 ± 13.23	0.64
4th session (n=26)	81.9 ± 11.74	82.47 ± 9.33	81.71 ± 10.65	0.96

Table IV. Comparison of pulse, respiratory rate and temperature before and after SLED

	Before SLED	After SLED	*p*-value
Pulse (per minute)	20.07 ± 3.942	20.09 ± 3.702	0.965
Respiratory rate (breath/minute)	20.07 ± 3.94	20.09 ± 3.7	0.96
Temperature (°F)	98.94 ± 0.91	98.71 ± 0.77	0.13

dialysis had to be discontinued for any of the complications. No complication due to heparin occurred in any of the dialysis sessions which were done with heparin (n=77).

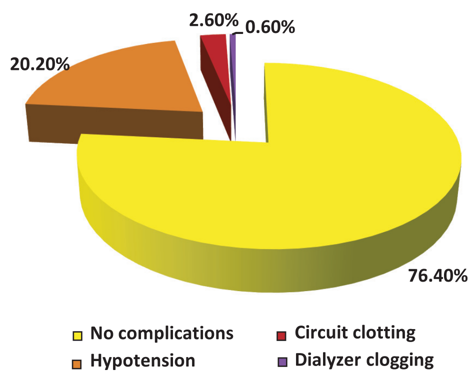

Figure-1: *Pie chart showing percentage of SLED sessions associated with and without complications*

Nearly seventy percent patients required inotrope prior to SLED and inotropes/vasopressors were employed at 85 sessions of SLED out of 153. Though 31 sessions required increasing the dose of vasopressor/inotrope during dialysis, none of the treatment session had to be discontinued because of hypotension (Table V). Inotrope dose could be decreased only in 6 sessions out of 153 SLED.

TableV. Hemodynamic tolerability of SLED

MAP prior to treatment session (mmHg)	80.58±10.9
Vasopressor requirement prior to RRT session (%)	85 (55.55%)
Sessions associated with reduction in MAP (%)	31 (20.26%)
Sessions with vasopressor escalation (%) *	31 (20.26%)
Unstable sessions (%) †	0
Sessions associated with development of arrhythmia	0
Sessions associated with premature termination of treatment because of hypotension/arrhythmia (Treatment failure)	0

*Includes any increase in pressor dosage, as well as initiation of pressors
†Defined as a treatment associated with >20% intra-dialysis reduction in MAP

Significant reduction of blood urea and serum creatinine were achieved with SLED ($p < 0.05$).

At 28 day after initiation of SLED, 17 patients became dialysis dependent and AKI resolved completely in twelve patients. Fourteen patients died within this period.

Discussion

RRT for the AKI patients in ICU can be offered in several different formats. Among them, CRRT has been advocated for hemodynamically unstable patients as a mean of mitigating the blood pressure liability that may occur with conventional iHD. However, randomized controlled trials have not demonstrated superior survival in patients treated with CRRT.[3,4] Moreover, implementation of a CRRT program is expensive because of costs related to specialized machinery, filters, lines and filtrate replacement fluid. More recently, newer hybrid techniques i.e. SLED combining several advantages of CRRT and iHD have been introduced in clinical practice across the world as a RRT for the critically ill patients. Cardiovascular tolerability associated with SLED is similar to that associated with CRRT, even in severely ill patients.[5] Though solute and fluid removal are slower than conventional iHD, but faster than CRRT; several prospective controlled studies have shown that SLED clears small solutes with an efficacy comparable to that of iHD and CRRT. At the same time it is less expensive than CRRT.[6,7] So, SLED combines the therapeutic advantages of CRRT with the logistic and cost advantages of iHD. Our study aimed to investigate the hemodynamic stability in critically ill patients with AKI treated with SLED. This is the first study of SLED done on ICU patients of Bangladesh.

All of our patients showed excellent hemodynamic stability with SLED treatment. Changes in MAP before SLED, during treatment and after dialysis were not significant ($p > 0.05$ in all sessions). This maintained hemodynamic stability might be the result of the extended duration of the SLED treatment (5.75 ± 1.2 hours) along with low dialysate flow (300ml/min). None of our treatment had to be discontinued because of hypotension as the hypotensive sessions were managed with increasing the dose of inotropes or adding another inotrope/vasopressor. Our findings contribute to an expanding literature supporting the use of SLED in critically ill patients in circumstances where CRRT would typically be considered.[1,5]

There is a concern that hypotension during RRT may be detrimental to renal recovery.[8] In a study done by Marshall et al, SLED was hemodynamically tolerated in most patients (MAP pre-SLED 69.1 mmHg and post-SLED 68.9 mmHg, p=0.26) though hypotension did occur during treatment and necessitated discontinuation in 7.6% sessions.[9] But there was significant intradialytic decrease in MAP in the study by Kumar N. (MAP pre-SLED 103.3 mmHg and post-SLED 78.6 mmHg, p=<0.001).[10] In our study, 31 (20.26%) SLED sessions were associated with one or more episodes of hypotension defined as MAP less than 65 mmHg. So, these sessions required an increase in vasopressor dose or addition of another inotrope. But, none of the dialysis had to be discontinued because of hypotension and there was no significant differences in pre-, during and post-SLED MAP (p>0.05). The hypotensive episodes may be explained by the rapid removal of water and solutes during dialysis. The fluid and solute removal in iHD occurs over a short period of time (4 hours every alternate day), but over a longer period in CRRT (at least 24 hours, commonly 3-5 days). So, the hemodynamically unstable patients cannot tolerate iHD. In case of SLED, fluid and solutes are removed over 6-12 hours time, which is longer than iHD but shorter than CRRT. The decline in blood pressure in our ICU patients is explained by this relatively rapid removal of water and solutes. It is pertinent to note that in some previous studies, the SLED was found to be hemodynamically well tolerated even by the critically ill patients on inotropic support and its effect on hemodynamic variables was found to be comparable with continuous veno-venous hemodiafiltration (CVVH).[9,11] Kielstein et al. had to increase the dose of inotropes in 25% study subjects, the dose remained unchanged in 25% and could be reduced in 50%.[12].

Vital signs of the patients were monitored meticulously through the course of dialysis. There were no significant differences in pre- and post-SLED pulse rate and respiratory rate which strongly support in favor of hemodynamic tolerability of SLED. Fliser reported significant reduction in core temperature (37.4 ± 0.3p C to 36.7 ± 0.2p C, p<0.05) while performing SLED in septic patients.[13] This decrease in core temperature could actually be advantageous as it increases peripheral resistance and improves cardiovascular stability. But we did not find any significant change in temperature among our patients. It may be explained by the fact that we included not only septic patients but also other patients. Twenty one out of 43 patients had severe sepsis and the rest did not have any infection. The mean temperature of the study subjects before initiation of SLED was 99.51 ± 1.335 °F and ranged from 98° to 103°F. This indicates that all patients with sepsis did not have hyperthermia. Antimicrobials were started as soon as possible in patients with septic shock which also explains the reason behind the mean temperature of 99.5°F.

A potentially complicating factor is the more intensified anticoagulation for CRRT due to longer treatment time required to prevent clotting of the extracorporeal circuit. SLED can be performed without the need for systemic anticoagulation. Earlier studies by Kumar, Kielstein and Berbece demonstrated a significantly lower need for anticoagulation in SLED-treated patients.[11,12,14]In our study, we conducted 76 (49.6%) sessions without heparin as the patients had coagulopathy. Though dialyzer and circuit clotting occurred in 5 of these sessions, dialysis treatments could be re-started after clearing the circuits and filter. So, it is an additive advantage of SLED for the critically ill patients with severe bleeding diathesis.

An important aspect, especially in the developing countries, might be the cost. There is a markedly lesser cost of the circuit tubing, membranes and the machines used in SLED than those used in CRRT. In fact, all centers across the world offering SLED use various standard iHD machines without adding or altering any software or hardware.[15] In our ICU, we also used the hemodialysis machine which resulted in substantial cost reduction.

Overall, SLED was tolerated well by the critically ill patients and widely accepted by our ICU staff. SLED has been adopted worldwide on a significant scale.[1]
[6]Recent data demonstrate that neither the technique of RRT[4,17] nor the dose of RRT[18,19] had an impact on patient survival. In the light of markedly higher costs of CRRT, it was therefore suggested that, in the absence of a survival benefit of CRRT, slow continuous therapy like SLED should be the preferred treatment modality for AKI in ICU.[1,20,21] In Bangladesh, hemodialysis machines are available in many places. As SLED can be given with iHD machine, this new RRT can be safely conducted in ICU for management of AKI of the critically ill patients.

Limitations

Sample size in this study was small; so the findings derived from the study cannot be generalized to reference population and the data should be interpreted with utmost caution. As all the ICU patients are critically ill requiring RRT, we could neither have any control group who could be treated without RRT, nor any control group who could be treated with CRRT due to financial problem. There was only one HD machine in ICU, BIRDEM. So, it was not technically possible to treat the study subjects with daily SLED. It was also difficult to treat the study subjects with SLED sessions consisting of 8 hours or more due to same reason.

Conclusion

SLED is a slower dialytic modality which is ran for prolonged periods using conventional hemodialysis machines with modification of blood and dialysate flows. This study concludes that SLED maintains hemodynamic stability in the critically ill patients of ICU. In a country like Bangladesh with limited health care resources, SLED is a practical and attractive RRT for the AKI patients who are hemodynamically unstable. As hemodialysis machines are now available in many parts of our country, SLED appears to be a promising technique for the critically ill patients of ICUs suffering from renal failure.

Acknowledgement: We express our gratitude to all the ICU staff of BIRDEM hospital for their technical support.

Conflict of interest: None

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