Haemodynamically Unstable Acute Kidney Injury Patients Treated with Sustained Low Efficiency Dialysis: Outcome in an ICU of Bangladesh

Fatema K[1], Faruq MO[2], Ahsan ASMA[1], Iqbal S[1], Ahmed F[1], Sultana MM[3]

[1]Department of Critical Care Medicine, BIRDEM General Hospital, Dhaka, Bangladesh
[2]Intensive Care Unit, Ibn Sina Hospital, Dhaka, Bangladesh
[3]Department of Nephrology, United Hospital Limited, Dhaka, Bangladesh

e-mail: drkanizfatemasb@gmail.com

Abstract

Acute kidney injury (AKI) is a risk factor for increased mortality in critically ill patients. Sustained low efficiency dialysis (SLED) is a new approach in renal replacement therapy (RRT) and it combines the advantages of continuous renal replacement therapy (CRRT) and intermittent haemodialysis (HD). The study was aimed to evaluate the outcome of the haemodynamically unstable patients with AKI in Bangladesh who were treated with SLED. So far this is the first reported study on SLED in intensive care unit (ICU) in Bangladesh. This quasi-experimental study was conducted in a 10-bed adult ICU of a tertiary care hospital in Bangladesh from June 2012 to May 2013. A total of 153 sessions of SLED were performed on 43 AKI patients. Mean age of the patients was 60.12 ± 15.57 years with male preponderance (67.4% were male). Mean APACHE II score was 26.88 ± 6.25. Fourteen patients (32.55%) had de novo AKI. Twenty nine patients (67.4%) had chronic kidney disease (CKD) with baseline mean serum creatinine 2.56 mg/dl, but did not require any RRT before admission in ICU. After giving SLED, AKI of the study patients were completely resolved in 27.9%. Some forty two percent patients became dialysis dependant and 30.23% patients died. Patients who had AKI on CKD became dialysis dependant more often than the patients with de novo AKI ($p < 0.01$). Mortality rate was significantly higher in patients who were on inotrope support ($p = 0.017$). Otherwise, there was no relation of 28 day mortality with age, prior renal function and mechanical ventilator requirement ($p > 0.05$). Thus, SLED is an excellent renal replacement therapy for the haemodynamically unstable AKI patients of ICU. It is also cost-effective compared to CRRT.

Keywords: Sustained Low Efficiency Dialysis, Acute Kidney Injury, Intensive Care Unit

Introduction

Acute Kidney Injury (AKI) is a common clinical syndrome with a broad aetiological profile. It complicates about 5% of hospital admissions and 30% of admissions to ICUs.[1] Patients with chronic kidney disease (CKD) also may present with superimposed AKI. As many as 70% of these critically ill patients require renal replacement therapy, making it an important outcome determinant in the management of acute renal failure in the ICU.[2] Various types of renal replacement therapy like peritoneal dialysis (PD), intermittent haemodialysis (HD) have been available for decades. But the critically ill patients of ICU often do not tolerate these RRT and often find them poorly effective. Though the

ICU patients usually tolerate continuous renal replacement therapy (CRRT) very well, it is very costly and available only in few centres in Bangladesh. In past few years, hybrid therapy that combines the benefits of intermittent HD and CRRT has emerged as RRT in ICU patients.[1] This modality is indicated in different literature with different terms such as 'sustained low efficiency dialysis' (SLED), 'extended daily dialysis' (EDD), 'slow low efficient daily dialysis' (SLEDD) or 'slow continuous dialysis' (SCD).[2] All have in common use of HD machines, but with blood pump speeds and dialysate flow rates intermediate between intermittent HD and CRRT. Treatment duration and frequency are greater than in intermittent HD.[2] In this study SLED on haemodynamically unstable ICU

patients aimed at assessing the outcome of these patients in an ICU of the   capital city of Bangladesh.

Materials and Methods

A quasi-experimental prospective study was conducted in a 10-bed adult mixed (medical and surgical) ICU in BIRDEM (Bangladesh Institute of Research in Diabetes, Endocrine and Metabolic Disorders) General Hospital, a teaching hospital in the capital city of Bangladesh. This ICU has access to bedside intermittent HD, CRRT, SLED and peritoneal dialysis (PD). Both acute PD with rigid catheter and continuous PD with flexible catheter (Tenckhoff catheter) were done here. Ethical clearance was obtained from the Institutional Ethical Review Committee prior to study. Data were collected using a structured datasheet from the case notes and hospital documents by the on duty physicians during the 1st 7days after initiation of SLED. Patients were followed-up upto 28 days period after the initiation of SLED, or until their death whichever came first.

Patient selection: Haemodynamically unstable patients were included if they had been suffering from AKI (according to RIFLE criteria)[3] requiring RRT. Patients with either mean arterial pressure (MAP) less than 65 mmHg, or cardiac arrhythmia with haemodynamic compromise, or left ventricular ejection fraction (LVEF) $\leq$ 35% with systolic BP <100 mmHg were categorized as haemodynamically unstable. Patients with acute myocardial infarction (AMI) with AKI were potentially haemodynamically unstable, and so were included. Patients meeting these criteria who were admitted in the ICU from June 2012 to May 2013 were enrolled for the study. Informed written consents were taken from the patients' or their legal guardians. Patients were excluded if they were younger than 18 years of age, or declining consent, or suffering from pre-admission chronic kidney disease (CKD) stage IV or V according to Kidney Disease Outcome Quality Initiative (KDOQI)[4] or end stage renal disease (ESRD).

Demographic information including age, gender and date of admission were recorded. APACHE (Acute Physiology and Chronic Health Evaluation) II score was calculated before starting SLED. Data on kidney function included blood urea, serum creatinine, serum electrolytes, arterial blood gas (ABG) analyses and daily urine output were collected. Clinical data also included the primary diagnosis, and presence of comorbidities.

Patients were considered as improved if their serum creatinine came down to normal (<1.2 mg/dl) in de novo AKI group or came down to previous level (prior to ICU admission) in CKD group. If they required any form of RRT at 28 days after initiation of SLED, they are categorized as 'dialysis dependant'.

Technical consideration: The Dialog+ (B Braun) haemodialysis machine was utilized without additional software or hardware with standard lines and F8 low flux polysulfone haemodialyzers. Angioaccess was established with double lumen central venous haemodialysis catheters, either in femoral vein or in internal jugular vein.

Default dialysate flow rate was set at 300 ml/min which is the minimum dialysate flow in the Dialog+ haemodialysis machine. The blood flow rates were adjusted according to patients' MAP and dose of inotropes, and usually ranged from 100-150 ml/min. To avoid dialysis disequilibrium syndrome, 1st session of SLED was given 2.5 hours if that was patient's 1st RRT ever. Subsequent sessions were of 4 to 6 hours duration. In the absence of coagulopathy or active   bleeding, unfractionated heparin was given to prevent extracorporeal circuit clotting.

All study patients were treated with SLED for 6 to 8 hours duration in every alternate day. So, each patient received at least 4 sessions of SLED in 7 days of data collection period for an individual patient.

Statistical analyses: Data were presented as mean values $\pm$ SD, or percentage (%). Means were compared by the Student *t* test, and percentages are compared by Z-test of proportion. Chi-square test is used for qualitative variables. All statistical analyses were performed using the SPSS for windows software version 17. $p \leq 0.05$ was considered significant.

Results

One hundred fifty three sessions of SLED were performed in 43 haemodynamically unstable AKI patients admitted in ICU over one year of study period. The demographic and clinical variables of the study populations are summarized in table I.

Table I: Baseline variables of study patients

Gender	Male	29 (67.4%)
	Female	14 (32.6%)
Age in years		60.12 ± 14.57
Inotrope/vasopressor requirement		30 (69.8%)
Mechanical ventilation requirement		25 (58.1%)
APACHE II score at SLED initiation		26.88 ± 6.25
Blood Urea (mg/dl) before SLED		194.54 ± 63.12
Serum Creatinine (mg/dl) before SLED		7.09 ± 2.37
Blood pH before SLED		7.31 ± 0.07
Serum K^+ before SLED (mEq/L)		4.90 ± 0.86
Serum HCO_3^- before SLED (mEq/L)		18.45 ± 4.90

All 43 patients completed at least two SLED sessions. After giving 2 SLED treatments, renal function of 1 patient improved and so, he did not require any RRT further. BP of another patient improved, and so, he was given intermittent HD assuming he would tolerate it. Remaining patients (n=41) got 3rd session of SLED (i.e. total 3 sessions each). As 8 more patients became haemodynamically stable with improvement of BP after 3 SLED sessions, they were switched to intermittent HD.

Figure 1: Flow chart showing number of study patients receiving SLED
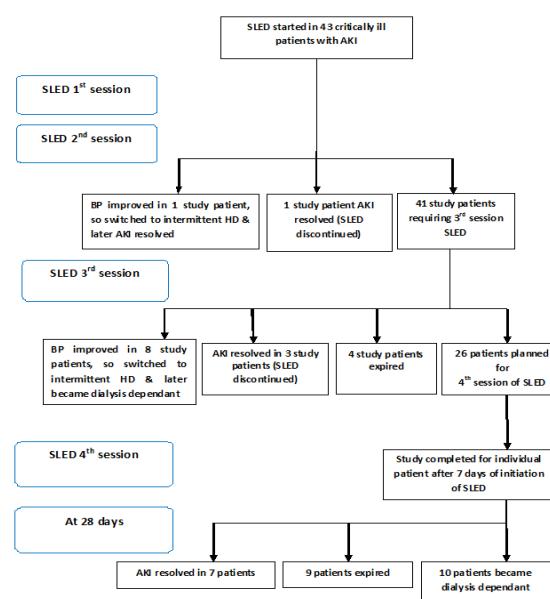
Renal function improved in 3 patients in whom RRT was discontinued and 4 patients died. Finally, 26 patients got 4th session of SLED during the data collection period (total 7 days after initiation of SLED in each of remaining 26 patients) (Figure-I).

Fourteen (32.55%) out of 43 patients had de novo AKI. Rest 29 patients (67.44%) had CKD prior to ICU admission with mean serum creatinine 2.56 ± 0.62 mg/dl (ranged from 1.5 to 3.8 mg/dl).

All study patients tolerated SLED very well. Thirty one SLED sessions (20.26%) were associated with hypotension which was overcome by increasing the dose of inotrope. As there was no complication, SLED was not discontinued in any patient.

There was significant reduction of serum creatinine, blood urea and serum K^+ level with significant improvement of pH and HCO_3 level after SLED in all patients regardless of their prior renal function (table II).

Table II: Comparison of post-SLED values with pre-SLED values of de novo AKI (Group 1, n=14) and AKI on CKD (Group II, n=29)

		Pre-SLED	Post-SLED	*p*-value
Blood Urea	Gr I	188.71 ± 62.24	117.79 ± 50.85	0.007
	Gr II	194.6 ± 62.41	114.65 ± 69.86	0.0001
Serum Creatinine	Gr I	6.02 ± 1.6	3.81 ± 1.23	0.001
	Gr II	7.39 ± 2.41	4.5 ± 1.66	0.0001
K+	Gr I	4.81 ± 0.86	3.98 ± 0.55	0.0005
	Gr II	4.99 ± 0.85	4.15 ± 0.54	0.0002
pH	Gr I	7.32 ± 0.04	7.39 ± 0.03	0.0001
	Gr II	7.3 ± 0.08	7.37 ± 0.05	0.0001
HCO_3^-	Gr I	18.8 ± 5.1	23.5 ± 1.88	0.004
	Gr II	18.5 ± 4.79	23.18 ± 3.26	0.0001

All variables are expressed in mean ± SD

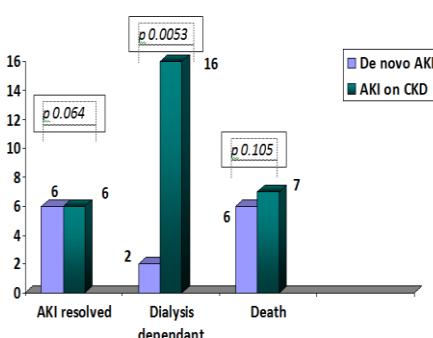Outcome of these 43 patients have been shown in Figure 2.

Figure 2: Outcome of the study patients

The following table (table III) demonstrates the relationship of outcome of the study patients with their age.

Table III: Relation of 28-day mortality with age

	Up to 40 yrs (n=3)	41-60 yrs (n=19)	>60 yrs (n=21)	p-value
Alive (n=30)	1	13	16	0.314
Dead (n=13)	2	6	5	

Thirty out of 43 patients required inotrope support and 25 out of 43 study patients were on mechanical ventilator (MV) support. Relation of inotrope and MV support with 28-day mortality have been shown in table IV and V respectively.

Table IV: Relation of 28-day mortality with Inotrope requirement

	Patients requiring Inotrope (n=30)	Patients not on Inotrope (n=13)	p-value
Alive (n=30)	18	12	0.017
Dead (n=13)	12	1	

Table V: Relation of 28-day mortality with MV support

	Patients requiring MV (n=25)	Patients not on MV (n=18)	p-value
Alive (n=30)	15	15	0.0505
Dead (n=13)	10	03	

The cost of per session of SLED in BIRDEM Hospital was 8000 BDT (100 USD) during the study time. This cost was exclusive of daily ICU cost and medications. In this study, each patient had to pay same amount for each SLED session irrespective of duration of the session.

Discussion

Renal replacement therapy for the AKI patients in ICU can be offered in several different formats. Among them, CRRT has been advocated in haemodynamically unstable patients as a means of mitigating the blood pressure that may occur with conventional intermittent HD. However, randomized controlled trials have not demonstrated superior survival in patients treated with CRRT.[7,8] Moreover, implementation of a CRRT programme 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 intermittent HD have been introduced into 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.[9] Though solute and fluid removal are slower than conventional intermittent HD, but faster than CRRT; several prospective controlled studies have shown that SLED clears small solutes with an efficacy comparable to that of intermittent HD and CRRT. At the same time it is less expensive than CRRT.[10,11] So, SLED combines the therapeutic advantages of CRRT with the logistic and cost advantages of intermittent HD.

Epidemiologic studies have shown an increased incidence of AKI in men as compared with women; men constitute 59% to 64% of cases of severe AKI among critically ill patients.[12] This study also had male preponderance (67.4%). Similar gender distribution was observed in the SLED study by Schwenger[13] (62.6% male), Carvalho[1] (60% male) and Kilhara[14] (male 54.5%).

The mean APACHE II score of these critically ill patients were 26.88 ± 6.257 with 52.14% expected mortality. 30 (69.8%) of these critically ill patients required inotrope support and 25 (58.1%) mechanical ventilator support. Prospective controlled studies[13,15] have shown that SLED clears small solutes with an efficacy comparable to that of intermittent HD and CRRT, even when the latter employs high rates of fluid substitution. Metabolic changes were measured in terms of reduction in the levels of blood urea and serum creatinine, as well as normalization of serum potassium, pH and bicarbonate. Although it is beyond the scope of this study to provide a full measurement of solute clearance; good control of urea, creatinine, potassium, pH and bicarbonate was achieved with SLED as depicted in table II. Nirmal Kumar[16] in 2007 demonstrated normalization of blood urea, serum creatinine, potassium, pH and bicarbonate with SLED which resulted in earlier amelioration of uremic symptoms.

Carvalho demonstrated that 25.5% of their AKI patients recovered renal function after receiving SLED whereas 18.6% developed ESRD and

46.5% died.[1] Almost similar result was found in this study; AKI was resolved completely in 27.9%, and 32.6% patients expired. Mortality in ICU patients with AKI does not solely depend on renal function. Ninety five percent of patients were suffering from cardiogenic, or septic shock, or both. There is a wide range of mortality rates of AKI patients in ICU reported from 36% to 90%.[17] The factors associated with mortality in AKI patients included the number of underlying diseases and on admission GCS and APACHE II score.[18] As mentioned in table I, 69.8% of the study patients were on inotrope support, 58.1% needed positive pressure ventilation, and mean APACHE II score of all study patients was 26.88 ± 6.257 with expected mortality of 52.14% indicating that all the patients were truly very sick.

Some 40.0% patients in the study became dialysis dependant. This may be explained by the fact that 67.44% of our patients had pre-existing CKD. Significantly more patients having CKD prior to ICU admission became dialysis dependent than the patients who had normal renal function prior to admission (p <0.01) (figure II). This finding indicates that AKI places CKD patients at high risk for developing end stage renal disease (ESRD). Ishani also had similar finding when he did a study to see the development of ESRD after AKI.[19] He found that episodes of AKI accelerated progression of renal disease in patients with previously diagnosed CKD.

The actual mortality in this study was 30.23% and the expected mortality was 52.14% calculated from APACHE II severity scoring system. Mortality rate was significantly higher in patients who had cardiogenic and/or septic shock and so were on inotrope support (p 0.017) compared to those who did not require inotrope (table IV). Otherwise, there was no relation of 28-day mortality with age, prior renal function and mechanical ventilator requirement (p >0.05 in all) (table III and V).

An important aspect of use of SLED, especially in the developing countries, is the cost of care as well as availability. The conventional HD machines are used for SLED with routine dialysate concentrate and inexpensive dialyzers. So, there is significantly lower cost of the circuit tubing, membranes and the machines used in SLED compared with those used in CRRT. In fact, all centeres across the world offering SLED use various conventional HD machines without adding or altering any software or hardware.[20] In one study done in two major Philadelphia teaching hospitals, cost of CRRT and SLED were compared.[9] The daily total cost of CRRT was 1061 USD and that of SLED was 426 USD if given for 12 hours and 797 USD if given for 24 hours. These included materials cost, pharmacy cost for solution and nursing cost. Another observational pilot study was done in a university hospital of Toronto, Canada.[2] Daily cost of SLED was 238.5 USD when given for 8 hours. On the other hand, cost of 24 hours' CRRT was 372.45 USD if heparin was used, and 372.45 USD if citrate was used as anticoagulant. In our ICU, we used the same dialysis machine used for routine HD to give SLED. This resulted in substantial cost reduction. The cost of intermittent HD in BIRDEM was USD 43.75 per session, and that of SLED was USD 100 per session. The cost of CRRT in the study centre was about USD 1000 if given for 5 days. These expenditures included the cost of materials and pharmacy. Unfractionated or low molecular weight heparin was used as anticoagulant here in intermittent HD, CRT and SLED. In Bangladesh, only 4 tertiary care hospitals in the capital city have CRRT facility. But HD facility is available in many districts of the country. As SLED can be given with HD machine, so any hospital with HD facility can offer SLED to their haemodynamically unstable patients. As a result, use of expensive CRRT can be substituted by use of SLED. This has a great economic and logistic impact for patients who cannot afford CRRT or where CRRT is not available.

Overall, SLED was tolerated well by the critically ill patients, and widely accepted by our ICU staff. Studies showed, 24% of respondents used SLED for AKI in ICU.[21,22] Recent data demonstrate that neither the technique of RRT[8,23], nor the dose of RRT[24,25] 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.[21,26,27]

To increase the credibility of the study, comparison with CRRT could be made. But CRRT is

very expensive and the study patients could not afford it. Most of our patients refused CRRT due to financial constraints. As such comparison between CRRT and SLED could not be made. Secondly, as the sample size was small, the findings derived from study cannot be generalized to our reference population and the data should be interpreted with utmost caution. Thirdly, this study was carried out on adult population. So, outcome could not be applied on pediatric AKI patients.

Conclusion

This study concludes that SLED reduces blood urea, serum creatinine, and K^+, and improves arterial pH and HCO_3^- significantly. In the light of limited health care resources, SLED offers an attractive form of RRT for the AKI patients who are not able to tolerate intermittent hemodialysis. In a developing country like Bangladesh, the judicious use of SLED is practical and cost-effective in the haemodynamically unstable patients of ICU with AKI.

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