In-vivo Assessment of a Manual Single Lumen Alternating Micro-Batch Hemodiafiltration (mSLAMB) System

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Background

The manual single lumen alternating micro-batch hemodiafiltration (mSLAMB) system is a closed-loop dialysis system designed to provide kidney support in emergency situations (e.g., fluid overload, hyperkalemia, acidemia). If done repeatedly in small batches at high flow rates, this system is reported to achieve clearance levels comparable to traditional renal replacement therapy (RRT)[1]. The purpose of this system is to help patients with acute kidney injury (AKI) in austere environments at a low cost (<$25). The manual circuit requires no electricity or batteries and uses a more modest vascular access than traditional modalities.

Methods

Nephrectomized pigs (n=3, 15±1kg) were treated with mSLAMB to assess removal of uremic toxins and an exogenous florescent tracer, fluorescein-isothiocyanate (FITC)-sinistrin, an inulin analogue[2], which had been administered as part of a separate study. Using a 16g x12cm catheter in the femoral vein, RRT with mSLAMB was performed using a REXEED25A (Asahi Kasei) hemofilter. Active or passive ultrafiltration and variations in dialysate flow were tested based on adjusting height of circuit elements. Eight to sixteen cycles were completed on each animal then 300mL of an isotonic bicarbonate solution was administered IV. Samples were taken periodically to analyze clearance of toxins from blood as well as quantify cleared molecules in dialysate using traditional formulas.

Batch volume, ultrafiltrate, and replacement fluid volumes were recorded for each cycle. Spent dialysate volume was determined at the study end. Potassium was measured bedside using an iSTAT analyzer. Creatinine and BUN were assayed using commercial kits (Stanbio Laboratory). FITC-sinistrin concentration was determined by fluorescence using a M5 Spectramax spectrophotometer.

mSLAMB system

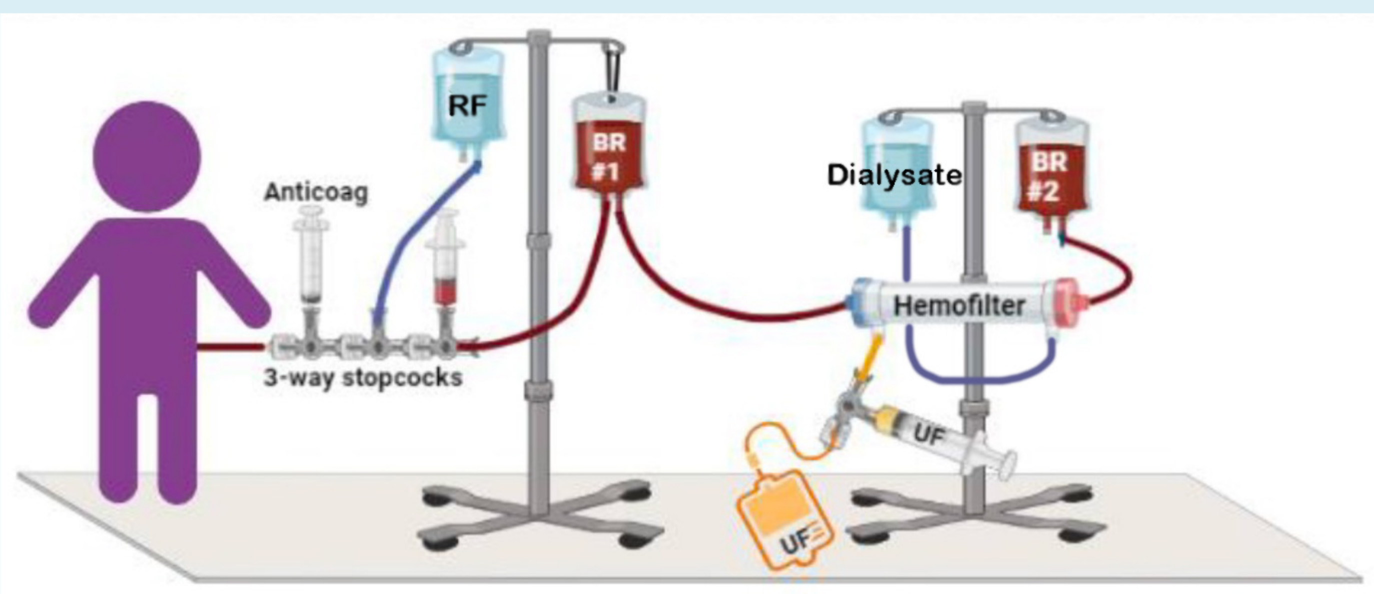


Figure 1. Illustration of the Manual Single Lumen Alternating Micro-Batch Hemodiafiltration (mSLAMB) system. A batch of blood is removed from the patient manually using a syringe then moved through the closed loop system using gravity flow by adjusting the height of the reservoir bags. Blood is returned by performing maneuvers in reverse order. Ultrafiltration can be performed manually or can be passively achieved during dialysate flow. BR=blood reservoir, RF=replacement fluid, UF=ultrafiltrate.

Results

	Pig 1	Pig 2	Pig 3
RRT type	HDF w/ predilution	HDF	HDF
Dialysate Flow	Static (changed btwn cycles)	High Flow	Mod. Flow
UF Removal	Active	Passive	Passive
Batch Vol. (mL)	100	150	100
Avg. UF Pulled Per Cycle (mL)	14	31.5	15
K+ Clearance (mL/min)	5.25 ± 1.14	8.8 ± 0.44	4.6 ± 1.1
BUN Clearance (mL/min)	4.6 ± 0.45	9.0 ± 1.7	8.6 ± 2.7
Creatinine Clearance (mL/min)	1.1 ± 2.3	5.7 ± 0.7	5.9 ± 0.4
FITC Clearance (mL/min)	9.23	11.53	9.13
Total Fluid Removed in 8 Cycles (mL)	101	250	125
Total Dialysate Used in 8 cycles (mL)	700	4600	2550

Figure 2. Summary of key treatment parameters from animal studies.

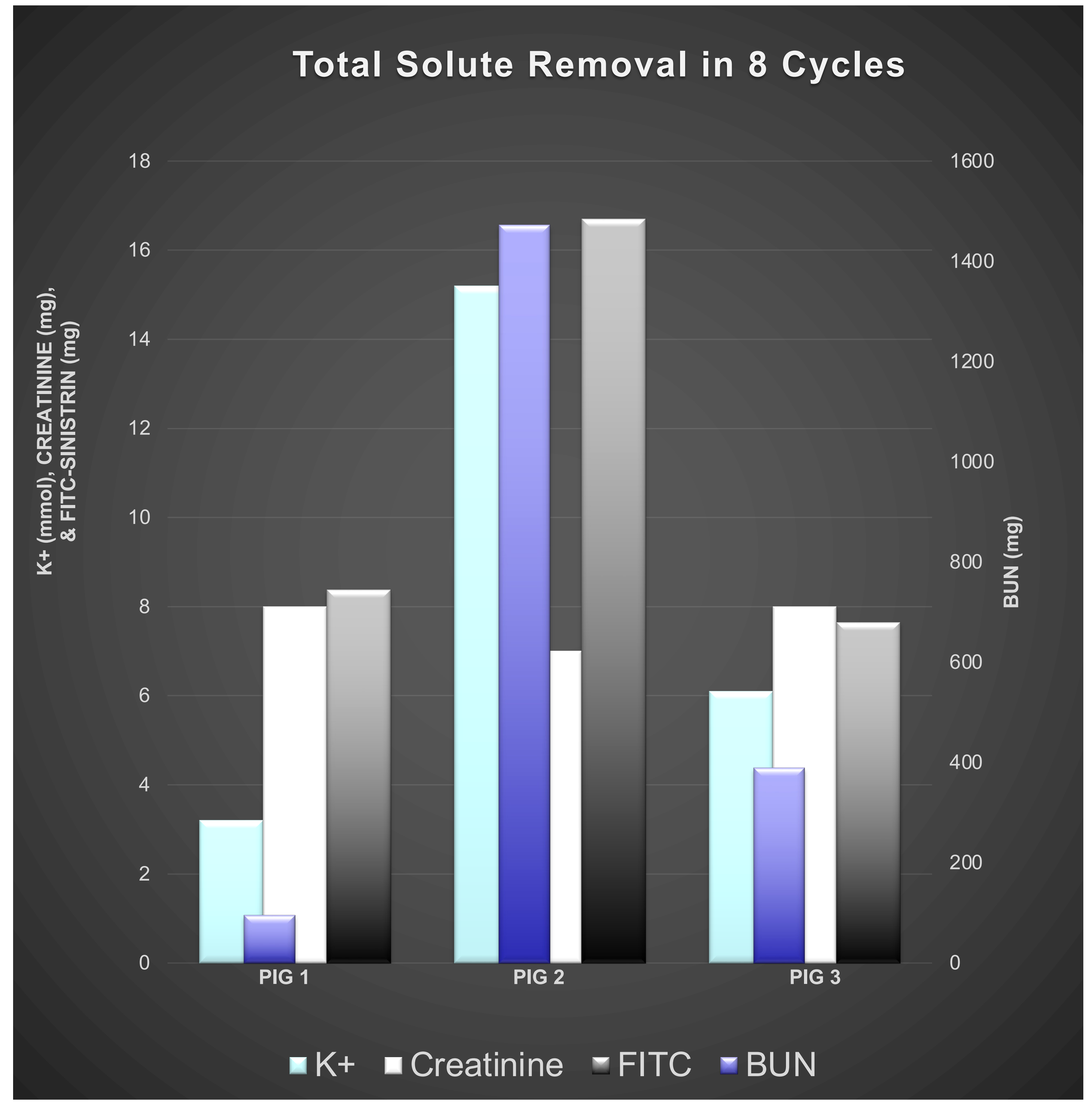
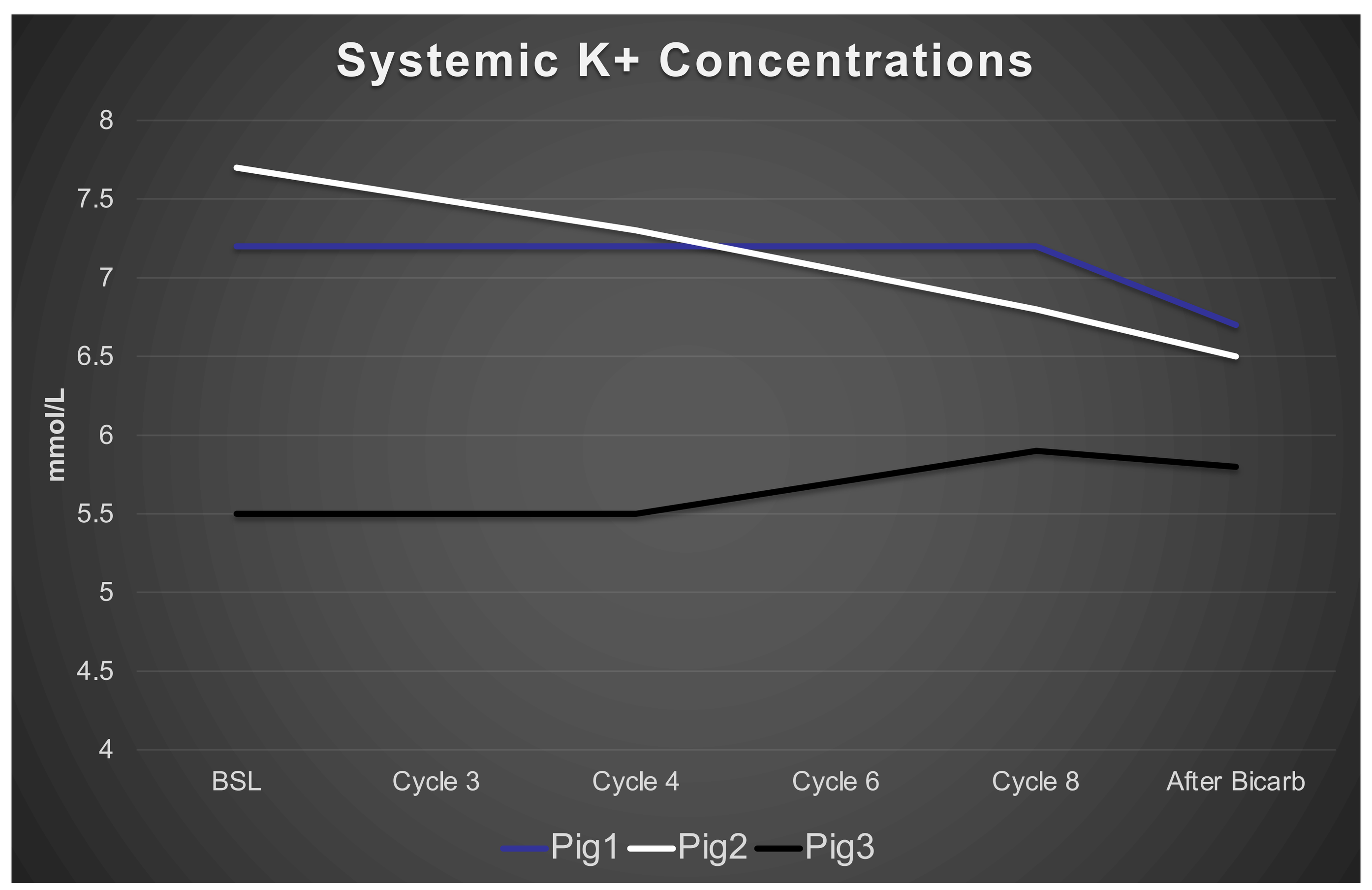
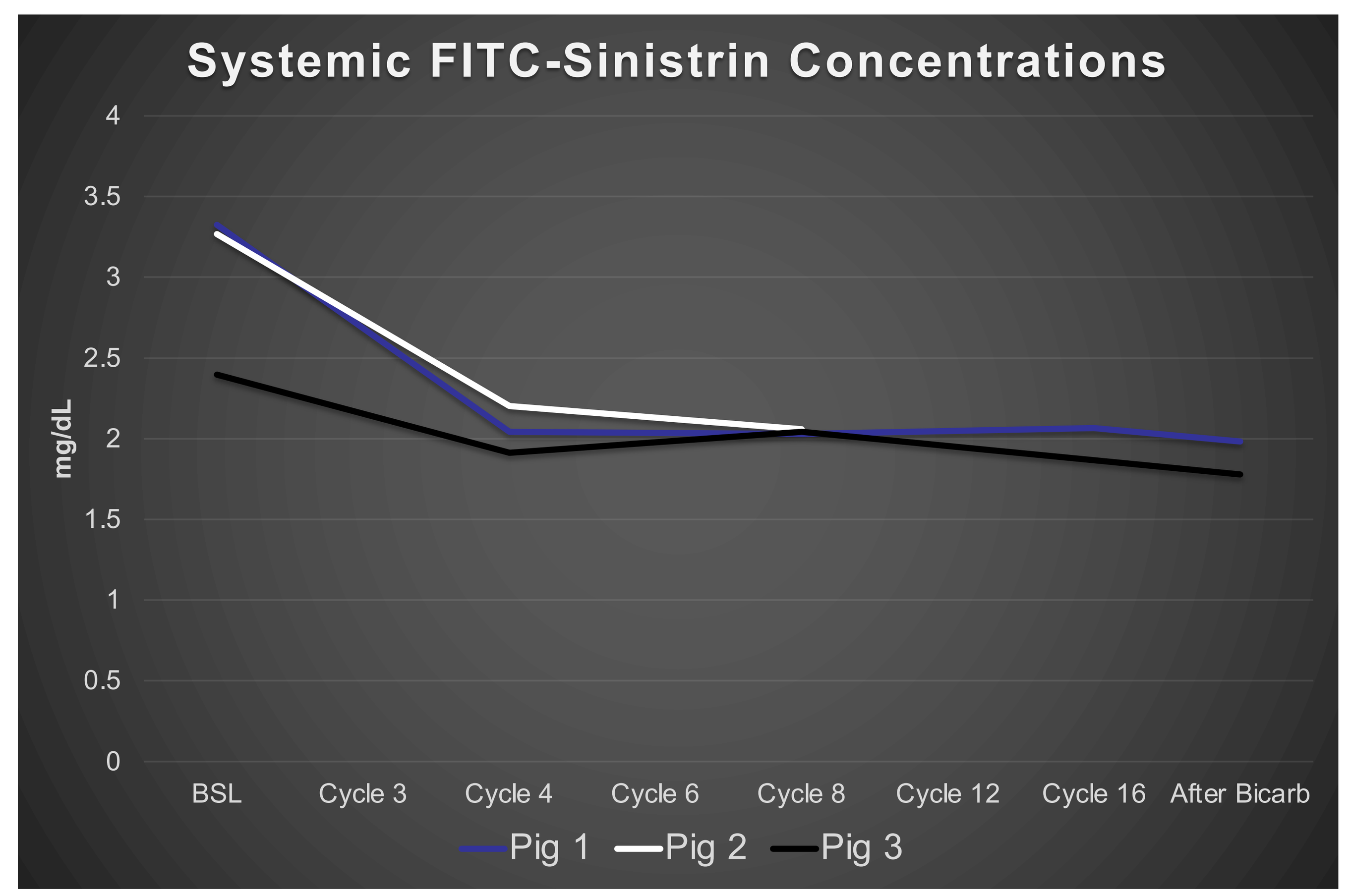


Figure 3. Uremic toxins and FITC-sinistrin were quantified in spent dialysate to assess total removal with 8 cycles of treatment.





Figures 4 & 5. Systemic concentrations of Potassium and the exogenous florescent tracer agent, FITC-Sinistrin, over the course of treatment.

Discussion

- These experiments demonstrate proof of concept for the manual single lumen alternating micro-batch hemodiafiltration (mSLAMB) system with efficacy for removal of fluid and uremic toxins in-vivo.
- Hemodiafiltration was easily performed by 2 or 3 individuals by assigning roles to control different aspects of flow through the system (e.g. blood withdrawal followed by adjusting height of blood bags or clamping/unclamping of lines for dialysate flow and UF removal).
- Efficient clearance of small and middle molecules was observed with each modality.
- Not surprisingly, High flow HDF had the greatest solute and fluid removal.
- Fluid removal by ultrafiltration was achievable with active or passive systems. Passive fluid removal during dialysate flow was relative to the height of the dialysate collection bag.
- With a treatment batch of 1-1.5% of body weight and cycle length of 5-6 minutes, treatment of the entire blood volume is achieved in about 1 hour.
- Based on these results, in patients 15kg$_{BW}$ we could expect to achieve a decrease in systemic Potassium concentration of up to 1 mmol/L per hour of treatment with a high flow dialysis regimen.
- Serum potassium levels were readily stabilized or decreased with mSLAMB RRT in this peracute AKI model.
- The reduction of serum FITC-sinistrin levels suggests systemic impact on other molecules is likely, although levels of BUN and Creatine were not altered with only 8 treatment cycles in this study (data not shown).

Conclusions

Electrolyte derangements and volume overload remain life threating emergencies in low resource settings. With the mSLAMB hemodiafiltration system, micro-batch processing was successful at removing a significant fluid volume and also effective at clearing uremic toxins as well as the exogenous florescent tracer. These studies demonstrate proof of concept for efficacy of mSLAMB dialysis in treatment of AKI by providing removal of potassium as well as excess fluid, such that additional stabilizing therapies, such as isotonic bicarbonate solutions, can safely be administered.

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References:
1. Chawla, L.S. Single Lumen Alternating Micro-Batch Hemodiafiltration (SLAMB-HDF): A Device for Minimally Invasive Renal Replacement Therapy. Kidney360 September 2020, 1 (9) 969-973.
2. Pill J et al. Fluorescein-labeled sinistrin as marker of glomerular filtration rate. Eur J Med Chem. 2005 Oct;40(10):1056-61.