Hemolytic Uremic Syndrome-Induced Acute Kidney Injury Treated *via* Immunomodulation with the Selective Cytopheretic Device

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Introduction

Shiga-toxin associated-hemolytic uremic syndrome (STEC-HUS) is the most common cause of thrombotic microangiopathy (TMA) in children. Although most children recover, about 5% die and 30% develop long-term renal morbidity. HUS pathophysiology includes activated neutrophils which damage vascular endothelial cells, resulting in inflammation, vasoconstriction, and thrombosis. Therapeutic immunomodulation of activated neutrophils may alter the progression of organ dysfunction in STEC-HUS. We present 3 pediatric patients treated with the selective cytopheretic device (SCD, see Fig 1-2) who had rapid improvements in stigmata of TMA.

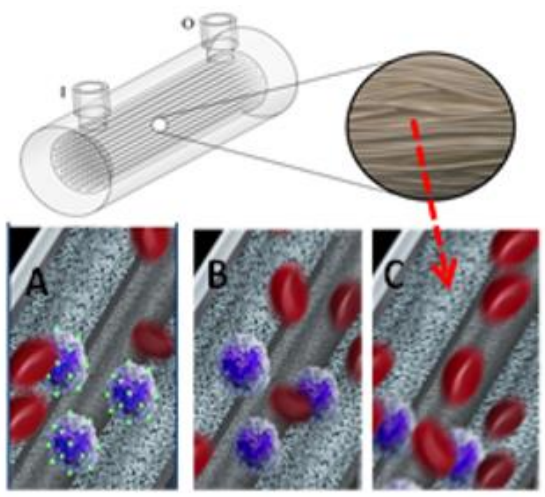

Figure 1: SCD Design and Mechanism of Action. SCD consists of a polycarbonate housing with an inlet (I) and outlet (O) for blood, and potted polysulfone-based fibers. Circular blow-up of the fibers. Activated leukocytes adhere to the outer surface of the hollow fiber membranes where they are deactivated in a low ionized calcium environment (0.25-0.40 mmol/L) achieved by RCA.

Panel A: Selective binding (catch) of activated LE with integrin binding sites, acutely mobilized to the cell membrane (green).

Panel B: Bound LE are transiently sequestered in the SCD low iCa environment.

Panel C: Immunomodulated LE are released from fibers back into systemic circulation. Erythrocytes are red and Leukocytes are purple.

Results

Patient 1 had Trisomy 21 and obesity and presented with diarrhea, microangio-pathic anemia, thrombocytopenia, acute hepatitis, and AKI due to STEC-HUS who received a total of 7 days of SCD and CKRT treatment. Once started on CKRT with SCD treatment, he stabilized and showed steady improvement, with normalizations of elevated WBC, platelets, transaminases, and hemodynamics, was able to be extubated, and had gradual return of kidney function (see Table 1). His SCD treatment was associated with recovery of multiorgan dysfunction. 60-day follow-up evaluation demonstrated normal hematologic parameters and renal function.

Patients 2 and 3 presented with STEC-HUS with AKI requiring kidney support therapy. Each twin received 24 hours of SCD therapy (see Fig 3). With CKRT and SCD treatment both patients underwent successful extubation to room air with discontinuation of CKRT and SCD treatment. Thereafter, both patients' hematologic parameters, urine output, and kidney function all gradually improved. Patient 2 required 3 PRBC and 3 platelet transfusions pre-SCD and 2 PRBC transfusions post; Patient 3 required 2 PRBC and 1 platelet transfusion pre-SCD and none post. There was normalization (patient 2) and near-normalization (patient 3) of kidney function at 60d follow-up post SCD initiation.

	WBC, K/µL	Plt, K/µL	Hgb, g/dL	ALT, U/L	AST, U/L	BUN/SCr, mg/dL	NGAL, urine, ng/mL
Patient 1							
Admission	18.2	99	11.1	10302	>20000	37/2.45	
Pre-SCD	11.0	99	10.1	7346	8563	56/4.1	
Post-SCD	8.8	78	8.8	511	97		
Discharge	8.7	556	9.1	128	48	89/6.9	
60-day f/u	5.0	328	12.5			28/1.0	
Patient 2							
Admission	8.1	309	12.9	23	40	8/0.2	
Pre-SCD	26.0	22	7.9	49	62	73/3.4	3182
Post-SCD	23.6	49	7.6	17	30		2273
Discharge	5.2	224	6.7	38	38	45/0.57	107
60-day f/u	5.6	11.1	376			23/0.36	
Patient 3							
Admission	13.7	366	12.1	33	64	11/0.3	4782
Pre-SCD	24.1	66	6.4	216	169	62/4.5	9166
Post-SCD	30.0	54	10.6*	74	36		2032
Discharge	5.5	366	7.6	55	30	68/1.92	194
60-day f/u	6.7	302	11.1			35/0.69	

Table 1: Clinical Laboratory Values. Pre-SCD refers to laboratory values just prior to SCD treatment initiation (or, in the case of BUN and creatinine, prior to any RRT for patients 2 and 3). An asterisk indicates that the patient received a transfusion within 24h of the reported laboratory value. **Post-SCD** refers to laboratory values just after last SCD treatment. **Discharge** refers to laboratory values after last SCD treatment and last value prior to or at hospital discharge. Blank spaces mean that no value sent.

Methods and Materials

We describe a 12 yo (Patient 1) and two 2 yo twins (Patients 2 and 3) with STEC-HUS requiring continuous kidney replacement therapy (CKRT) who were enrolled in two separate studies of the SCD; Patient 1 in an ongoing multicenter single-arm study (NCT02820350) and Patients 2 and 3 as part of a subsequent study (NCT04869787).

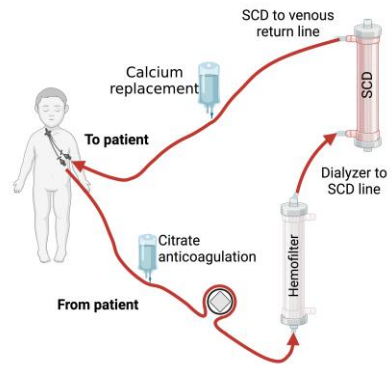

Figure 2: Schematic of integration of SCD in the CKRT blood circuit with regional citrate anticoagulation. The SCD is placed in-line with the hemodiafilter and uses standard calcium/citrate anticoagulation for CRRT.

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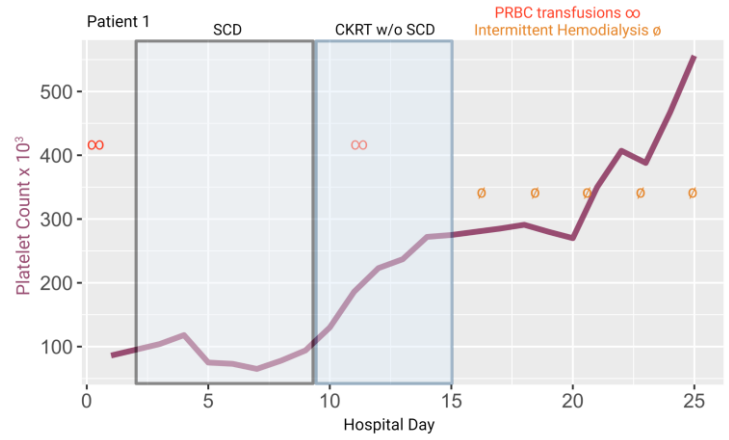

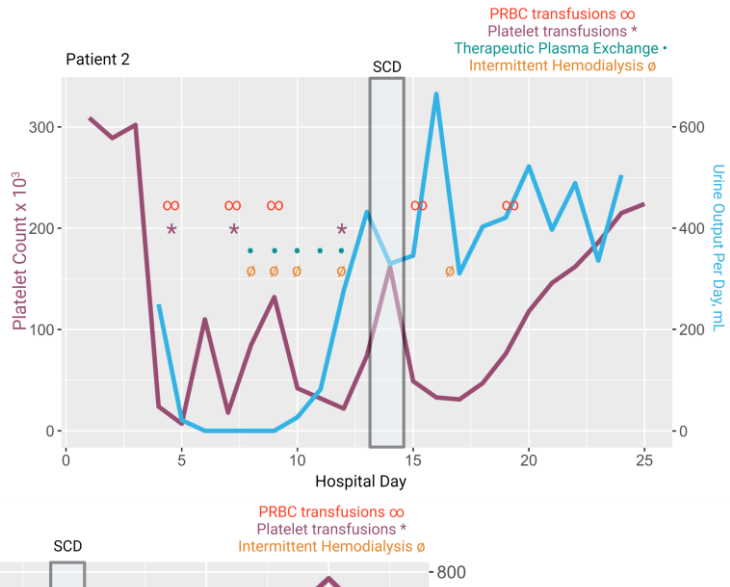

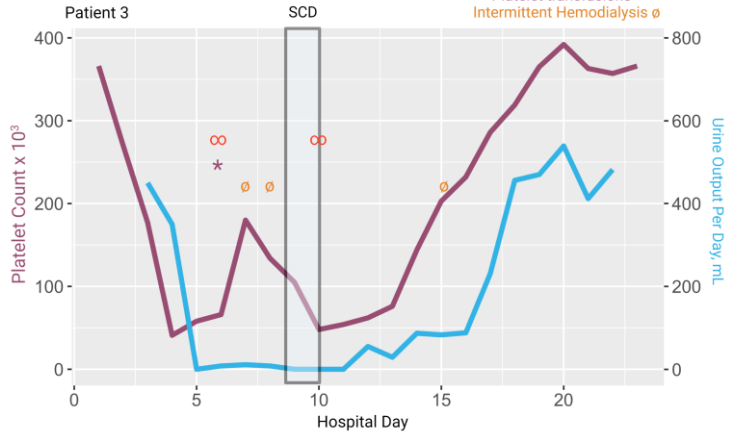

Figure 3: Clinical course of Patients 1-3. Continuous kidney replacement therapy (CKRT), packed red blood cells (PRBC), selective cytopheretic device (SCD). No patient required platelet transfusions post-SCD treatment. All patients received fewer or no PRBC transfusions post-SCD. Urine output was not charted consistently for Patient 1, so only platelet trend is presented.

Discussion and Conclusions

Immunomodulatory treatment with the SCD resulted in improvements across multiple disease parameters in STEC-HUS induced AKI and was well-tolerated without any device-related adverse-events. This report expands on previously reported cases of successful SCD use across multiple underlying etiologies in AKI.