

Retrospective Analysis of Patient and Circuit Complications using Heparin versus Citrate Anticoagulation with Membrane Therapeutic Plasma Exchange in the Pediatric Population

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Objectives

- We sought to better understand patient and machine complications of membrane therapeutic plasma exchange (mTPE) using heparin anticoagulation versus citrate anticoagulation.
- We hypothesize that our mTPE protocol for systemic heparin anticoagulation and citrate anticoagulation is well tolerated.

Background

- Data is limited on complications with mTPE using heparin anticoagulation and even more sparse data on mTPE using citrate anticoagulation.
- Membrane TPE with citrate anticoagulation is more challenging than using heparin anticoagulation.
- Citrate anticoagulation is beneficial in circumstances in which systemic heparin is considered unsafe.

Patients and Methods

- We performed a single-center retrospective chart review of children and young adults who required TPE from 2012 through 2019 at Children's of Alabama.
- Patient and machine complication rates were compared between the subjects who received mTPE with heparin anticoagulation versus mTPE with citrate anticoagulation.
- Inclusion criteria:** All children and young adults from birth to 21 years of age who required mTPE.
- Exclusion criteria:** No use of anticoagulation
- Indications for TPE were based on the requesting service in consultation with the attending nephrologist.

Results

Table 1. Patient Demographics & Complications

	All N=48	Prisma Citrate N=6	Prisma Heparin N=42	p-value
Age (yrs)	5.3+3.6	8.2+6.8	4.8+2.8	0.0001
Weight (kg)	21.4+13.8	33.9+25.0	19.5+10.6	0.0001
Patient Complications	18 (37.5)	2 (33.3)	16 (38.1)	1
Bleeding	0 (0.0)	0 (0.0)	0 (0.0)	
Fever	1 (2.1)	0 (0.0)	1 (2.4)	
Hypertension	1 (2.1)	0 (0.0)	1 (2.4)	
Hypotension	7 (14.6)	0 (0.0)	7 (16.7)	
Allergy	2 (4.2)	1 (16.7)	1 (2.4)	
Low Ionized Calcium	8 (16.7)	1 (16.7)	7 (16.7)	
Other	0 (0.0)	0 (0.0)	2 (4.8)	
Machine Complications	28 (52.1)	3 (6.3)	25 (59.5)	0.683
Air in System	3 (6.3)	1 (16.7)	2 (4.8)	
Blood Leak	5 (10.4)	0 (0.0)	5 (11.9)	
Circuit Clotted	13 (25.0)	1 (16.7)	12 (28.6)	
Machine Malfunction	3 (6.3)	1 (16.7)	2 (4.8)	
Access Pressure/Slow	11 (22.9)	0 (0.0)	11 (26.2)	
Blood flow				
Other	1 (2.1)	0 (0.0)	1 (2.4)	

All values are N (%) except those with ± which represent mean and standard deviation
P-Values represent Fischer's Exact Test except those with a * which represents a T-Test

Table 2. Patient Diagnosis

	All N=48	Prisma Citrate N=6	Prisma Heparin N=42	p-value
Diagnosis				0.0111
Cardiology	4 (8.3)	0 (0.0)	4 (9.5)	1
Transplant Rejection	4 (8.3)	0 (0.0)	4 (9.5)	
Hematology	3 (6.3)	1 (16.7)	2 (4.8)	0.3363
Neutropenia	0 (0.0)	0 (0.0)	0 (0.0)	
TTP/HUS	3 (6.3)	1	2 (4.8)	
Kidney	9 (18.8)	1 (16.7)	8 (19.0)	0.571
Crescentic	0 (0.0)	0 (0.0)	0 (0.0)	
Glomerulonephritis				
FSGS	0 (0.0)	0 (0.0)	1 (2.4)	
Good Pasture	0 (0.0)	0 (0.0)	0 (0.0)	
Transplant	1 (2.1)	1 (16.7)	0 (0.0)	
Transplant Rejection	0 (0.0)	0 (0.0)	6 (14.3)	
Sickle Cell	0 (0.0)	0 (0.0)	0 (0.0)	
Vasculitis	1 (2.1)	0 (0.0)	1 (2.4)	
Liver	3 (6.3)	1 (16.7)	2 (4.8)	0.3363
Transplant Rejection	2 (4.2)	0 (0.0)	2 (4.8)	
Liver Failure	1 (2.1)	1 (16.7)	0 (0.0)	
Neurology	17 (35.4)	0 (0.0)	17 (40.5)	0.0766
ADEM	2 (4.2)	0 (0.0)	2 (4.8)	
Guillain-Barre	4 (8.3)	0 (0.0)	4 (9.5)	
Myasthenia Gravis	0 (0.0)	0 (0.0)	0 (0.0)	
NMDA Receptor	2 (4.2)	0 (0.0)	2 (4.8)	
Encephalitis				
Neuromyelitis Optica	0 (0.0)	0 (0.0)	0 (0.0)	
Optic Neuritis	1 (2.1)	0 (0.0)	1 (2.4)	
Pompe Disease	0 (0.0)	0 (0.0)	0 (0.0)	
Transverse Myelitis	8 (16.7)	0 (0.0)	8 (19.0)	
Neurological Decline	0 (0.0)	0 (0.0)	0 (0.0)	
Sjogren's syndrome	0 (0.0)	0 (0.0)	0 (0.0)	
Rheumatology	3 (6.3)	0 (0.0)	3 (7.1)	1
HLH	1 (2.1)	0 (0.0)	1 (2.4)	
Lupus	1 (2.1)	0 (0.0)	1 (2.4)	
MAS	1 (2.1)	0 (0.0)	1 (2.4)	
Multi-Organ Failure	8 (16.7)	3 (50.0)	5 (11.9)	0.0497
TAMOF	8 (16.7)	3 (50.0)	5 (11.9)	
Other	1 (2.1)	0 (0.0)	1 (2.4)	1
Group B Strep	1 (2.1)	0 (0.0)	1 (2.4)	

All values are N (%) except those with ± which represent mean and standard deviation
P-Values represent Fischer's Exact Test except those with a * which represents a T-Test

Table 3. TPE treatment characteristics based on total number of therapies performed

	Prisma Citrate N=23	Prisma Heparin N=357	p-value
Pre Ionized Calcium			
Mean (95% CI)	1.21 (1.16-1.27)	1.23 (1.22-1.25)	0.4405
Normal 1.0-1.3	21 (91.3)	339 (95.0)	0.345
Low <1.0	0 (0.0)	8 (2.2)	1
High >1.4	2 (8.7)	16 (4.5)	0.2983
First Ionized Calcium			
Mean (95% CI)	1.12 (1.05-1.18)	1.25 (1.24-1.27)	0.0001
Normal 1.0-1.3	23 (100.0)	336 (89.6)	0.6278
Low <1.0	4 (17.4)	18 (5.0)	0.036
High >1.4	0 (0.0)	19 (5.3)	0.618
Last Ionized Calcium			
Mean (95% CI)	1.16 (1.11-1.20)	1.28 (1.26-1.29)	0.0917
Normal 1.0-1.3	23 (100.0)	314 (88.0)	0.0917
Low <1.0	0 (0.0)	8 (2.2)	1
High >1.4	0 (0.0)	36 (10.1)	0.1489
Replacement			0.0001
Albumin	2 (8.7)	237 (66.4)	
FFP	20 (87.0)	56 (15.7)	
Both	1 (4.4)	64 (17.9)	
Tandem	5 (21.7)	6 (1.7)	0.0002
Prime			0.1836
Albumin	0 (0.0)	24 (6.7)	
Saline	22 (95.7)	278 (78.7)	
Blood	1 (4.4)	52 (14.6)	

All values are N (%) except those with ± which represent mean and standard deviation
Fischer's Exact Test for categorical variables and T-Test for continuous variables

Table 4. TPE patient and machine complications based on total number of therapies performed

	Prisma Citrate N=23	Prisma Heparin N=357	p-value
Patient Complications	2 (8.7)	21 (5.9)	0.2728
Bleeding	0 (0.0)	0 (0.0)	
Fever	0 (0.0)	1 (0.3)	
Hypertension	0 (0.0)	1 (0.3)	
Hypotension	0 (0.0)	8 (2.2)	
Low Ionized Calcium	1 (4.4)	7 (2.0)	
Allergic Reaction	1 (4.4)	1 (0.3)	
Other	0 (0.0)	3 (0.8)	
No Problems	21 (91.3)	336 (94.1)	
Machine Complications	3 (13.0)	61 (17.4)	0.1058
Air in System	1 (4.4)	2 (0.6)	
Blood Leak	0 (0.0)	5 (1.4)	
Circuit Clotted	1 (4.4)	24 (6.7)	
Machine Malfunction	1 (4.4)	1 (0.3)	
Access			
Pressure/Slow	0 (0.0)	27 (7.6)	
Blood flow			
Other	0 (0.0)	3 (0.8)	
No Problems	20 (97.0)	295 (82.6)	

All values are N (%) except those with ± which represent mean and standard deviation
Fischer's Exact Test for categorical variables and T-Test for continuous variables

Results Summary

- A total of **48 subjects** met inclusion/exclusion criteria with a total of **380 therapies** performed.
- Those treated with heparin anticoagulation were younger and weighed less (Table 1).
- There were no significant differences in indications for TPE between the two groups (Table 2).
- Those treated with citrate anticoagulation had more hypocalcemia with the first measured ionized calcium (Table 3).
- There were no other significant differences in patient-related or machine-related complications during treatments (Table 4).
- Albumin replacement was used more often in the heparin therapies while more FFP replacement was used in the citrate therapies (Table 3).

Conclusion

- Our mTPE protocol with citrate anticoagulation is not associated with higher rates of machine-related complications.
- Although the overall rate of hypocalcemia at the first measured ionized calcium occurred more commonly with citrate anticoagulation, with adjustment of calcium infusion, sustained hypocalcemia was rare.
- The finding of higher rates of hypocalcemia may be due to other factors such as more treatments in the citrate group used FFP.

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