

Explosive Diarrhea as a Novel Complication of TPE in Patients Treated for Recurrent FSGS

Jason H. Kang, MD

Lauren Jefferies-Zeitler, BA, RN, HP(ASCP)

Phillip J. DeChristopher, MD, PhD



Study Methods

- Retrospective chart review
- Time span, 38 months: September 2007 to December 2010
- Patients are renal allograft transplantation recipients with recurrent focal segmental glomerulosclerosis (FSGS)
- 330 therapeutic plasma exchanges (TPEs)
- 6 patients: 4 males; 2 females
- Median age: 55 years (range 46 – 65)
- Median TPEs per patient: 50 (range 22 – 93)



Apheresis Materials and Methods

- Outpatient TPEs using the Caridian COBE Spectra Blood Cell Separator
- Vascular access: venous / AV fistula
- 1 plasma volume removed
- Anticoagulant: ACD-A (AC/WB = 1:15)
- Replacement fluid: 5% human albumin
- Fluid balance: 100%
- Calcium repletion: 2% calcium gluconate, piggybacked into replacement fluid



TPE-associated Diarrheal Syndrome (TADS)

- All renal allograft patients with recurrent FSGS
- All patients on 1 or more immunosuppressive medications, including past or current mycophenolate mofetil
- No pre-existing diarrheal illness
- All GI distress episodes (nausea, abdominal cramping, intense urge to defecate) temporally associated with TPE
- Explosive, watery diarrhea occurred during or immediately after being disconnected
- Diarrhea resolved spontaneously, but could last 24 hours after TPE ended



Clinical Correlates

- TADS not observed in any other patient cohort or any other form of therapeutic apheresis (TA)
 - 800 to 1000 TA procedures performed annually
- No *clear* association with total or ionized serum calcium
- Preventative strategies that appear *ineffective*:
 - Ramping up calcium repletion rate
 - Avoidance of heavy AM meals prior to TPE
 - Use of prophylactic loperamide (Imodium) [questionable compliance]

Historical Comparisons of Reported Acute Adverse Effects of TPE

Date	Lead Author	Evaluable Procedures (#)	GI Signs or Symptoms (%)	Diarrhea (%)
1989	Sutton	5335	N/V, abdominal pain (1.5)	0
1994	Mokrzycki	699	N (0.6)	0
1996	Weinstein	636	0	0
1999	McLeod	3421	Citrate N/V (1.2) Vasovagal N/V (0.5)	0
2000	Rizvi	884	0	0
2000	Korach	126,770	N / V (0.1 to 1.6)	0
2005	Basic-Jukic	4857	N / V (0.16)	0
2005	Yeo	568	0	0
2006	Howard	(57 patients)	0	0
2007	Shemin	1727	N (4.7) / V (4.5)	0
2011	Current Study	330	N (2.4) / V (1.2)	11.5

Legend: N, nausea; V, vomiting

Prevalence of Complications & Comparison to Recent Historical Control

Complication	Fraction of TPEs with Complication (%)	Odds Ratio vs. Ref¹	Relative Risk vs. Ref¹
Any	60 / 330 (18.2)	----	----
Explosive Diarrhea (<i>TADS</i>)	38 / 330 (11.5)	----	----
Suspension or discontinuation of TPE	19 / 330 (5.8)	----	----
Hypotension requiring treatment	12 / 330 (3.6)	0.46	0.65
Nausea	8 / 330 (2.4)	0.26	0.28
Vomiting	4 / 330 (1.2)	0.13	0.13
Lightheadedness	4 / 330 (1.2)	0.57	0.57

¹Shemin, D, *et al*, **J Clin Apheresis** 2007;22: 270-76.

Male Patients Appear More Susceptible to TADS

Complication	Male Episodes	Female Episodes
<i>TADS</i>	36	2
Other Adverse Effects	8	6

Fisher's Exact Test, $p = 0.00298$



Etiologic & Therapeutic Considerations: Hypothetical Risk Factors

- Degree of renal insufficiency
- Serum albumin level
- Electrolyte dysregulation
 - (?) Unique citrate toxicity in this patient cohort
 - Ionized serum calcium
 - Ionized serum magnesium
- Immunosuppression regimens, drug interactions (?)
- Donor allograft origin (?)



Study Limitations

- Single institution
- Retrospective / non-random
- Selection bias
- Comparison only to historical controls
- Incomplete retrospective laboratory data



Conclusions

- Reporting a high prevalence of an unexpected & previously unrecognized GI complication associated with TPE.
- TADS appears to specifically affect the cohort of renal allograft recipients with recurrent FSGS.
- The prevalence of TADS has a marked male preponderance.
- Etiologies, risk factors and prophylactic measures remain uncertain and will be the focus of future evaluation.