



Routine Prophylactic Intravenous Calcium Supplementation To Prevent Citrate Reactions During Plasma Exchange Is Not Indicated

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Background

- **Transient hypocalcemia develops during therapeutic plasma exchange (TPE) when ACD-A is used as an anticoagulant via the chelation of calcium by sodium citrate**
- **Severe symptomatic hypocalcemia, however, is much less common**

Clinical Manifestations of Citrate-Induced Hypocalcemia

- **MILD**
 - Paresthesias, mild nausea, abdominal discomfort
- **MODERATE**
 - Hypotension, vomiting, diarrhea, vibrating sensation in chest, muscle tightness
- **SEVERE**
 - Confusion, tetany, seizures, and life-threatening dysrhythmias and laryngeal spasm

Literature Review

- **Mokrzycki et al. - 1994**
 - 12 hypocalcemic reactions in 699 TPE procedures
 - 6/66 (9.1%) procedures in which calcium supplementation was not given
 - 6/633 (1%) procedures in which IV calcium supplementation was given

- **Shemin et al. – 2007**
 - All patients had received intravenous calcium supplementation
 - Prospective analysis of 1,727 TPE procedures; 126 had hypocalcemic reactions (or 7.3%)

Literature Review

- **R. Weinstein (1996) analyzed incidence of citrate reactions in 3 treatment arms:**
 - **Group A (n=360) no IV Ca supplementation**
 - **reactions in 35.6%**
 - **Group B (n=102) periodic small bolus of 10% Ca gluconate**
 - **reactions in 29.4%**
 - **Group C (n=174) 10% Ca gluconate added to return (replacement) fluid**
 - **reactions in 8.6% of treatments**

Literature Review

- **Kankirawatana, S. et al. (2007) studied prophylactic calcium supplementation**
 - **Retrospective review of complications of 581 TPE on 84 patients, with 5% albumin supplemented with calcium gluconate and potassium chloride**
 - **Hypocalcemic reactions reported in 2.7% of patients**
 - **Advocate using prophylactic continuous calcium administration**
 - **enhanced patient comfort**
 - **lack of adverse events**

Current Practice

- **The above mentioned studies recommend supplementing replacement fluid with IV calcium gluconate to prevent citrate reactions**
- **However, there are no current guidelines or randomized controlled studies to support these recommendations**
- **In addition, recently there has been a national shortage of calcium gluconate**

Study Background

- **At our institution we do not routinely supplement IV calcium during our TPE procedures**
 - **Akin to not pre-medicating for blood transfusions in patients with no prior history of reactions**

Methods

- **We examined records of consecutive TPE procedures performed for neurological disorders between 3/1/10 and 12/31/10 at newly opened Apheresis Center to assess incidence of citrate reactions and the need for calcium supplementation**
- **362 TPE procedures were performed on 50 patients for various neurologic disorders**
 - **32 females and 18 males**
 - **Mean age: 46.2 years (range: 16-75 years)**

Indications for TPE

Diagnosis	Number of Patients (% of Total)	Number of Procedures (% of Total)
Multiple Sclerosis	19 (38%)	96 (26%)
Neuromyelitis Optica	10 (20%)	79 (22%)
Myasthenia Gravis	6 (12%)	87 (24%)
Transverse Myelitis	7(14%)	33 (9%)
Chronic Inflammatory Demyelinating Polyneuropathy	2 (4%)	29 (8%)
Demyelinating Disease NOS	2 (4%)	10 (3%)
Paraneoplastic Syndrome	1(2%)	6 (2%)
Guillain Barré Syndrome	1 (2%)	7 (2%)
Stiff Person Syndrome	1(2%)	10 (3%)
Polyneuropathy	1 (2%)	5 (1%)
Total	50 (100%)	362 (100%)

Methods

- **Most procedures were performed using Spectra Optia cell separator**
- **Replacement fluid**
 - 5% albumin
- **Anticoagulant: ACD-A**
 - **Our starting default parameters**
 - Whole blood to anticoagulant (WB: AC) ratio was 12:1
 - Citrate infusion rate: 0.8mL/L-TBV/min

Our stepwise approach to management of Citrate reactions

- **First line therapy**
 - Decrease inlet infusion rate (by 25-30%) or
 - Pause the procedure until symptoms subside (up to 20 minutes)
 - Administer calcium carbonate (Tums) orally
 - Resume procedure at slower rate than previously run

Our stepwise approach to management of Citrate reactions

- **Second line therapy: Intravenous calcium gluconate supplementation**
 - Symptoms non-responsive to the first-line measures, resulting in patient discomfort
 - Patients with autonomic instability (e.g. patients with Guillain Barré Syndrome)
 - Patients requiring IV calcium gluconate in the past
 - One gram of calcium gluconate (10ml of 10% solution) added to each liter of 5% albumin by pharmacy
 - Requires 45-60 minutes of pharmacist's time

Calcium Supplementation by Diagnosis

Neurologic Disorder		No supplementation	Oral calcium carbonate (Tums)	Intravenous calcium gluconate
Multiple Sclerosis	(n=19)	7 (37%)	7 (37%)	5 (26%)
Neuromyelitis Optica	(n=10)	4 (40%)	3 (30%)	3 (30%)
Myasthenia Gravis	(n=6)	3 (50%)	1 (17%)	2 (33%)
Transverse Myelitis	(n=7)	4 (57%)	1 (14%)	2 (29%)
Paraneoplastic Syndrome	(n=1)	0 (0%)	0 (0%)	1 (100%)
Guillain Barré Syndrome	(n=1)	0 (0%)	0 (0%)	1 (100%)
CIDP	(n=2)	0 (0%)	0 (0%)	2 (100%)
Stiff Person Syndrome	(n=1)	0 (0%)	0 (0%)	1 (100%)
Demyelinating Disease-NOS	(n=2)	0 (0%)	2 (100%)	0 (0%)
Polyneuropathy	(n=1)	1 (100%)	0 (0%)	0 (0%)
Total	(n=50)	19 (38%)	14 (28%)	17 (34%)

Calcium Supplementation by Gender

	No calcium (n=19)	Oral calcium carbonate (n=14)	Intravenous calcium gluconate (n=17)
Men	8 (42%)	5 (36%)	5 (29%)
Women	11 (58%)	9 (64%)	12 (71%)

Summary Table

Calcium Supplementation	Patients (% total)	TPE procedures (% total)
No replacement	19 (38%)	209 (58%)
Calcium carbonate (Oral)	14 (28%)	57 (15%)
Calcium gluconate (Intravenous)	17 (34%)	96 (27%)
Totals	50 (100%)	362 (100%)

Summary

- **We do not routinely use intravenous calcium supplementation prophylactically**
- **Treat hypocalcemic symptoms clinically**
 - **Pause the procedure and/or**
 - **Decrease inlet flow rate to give less ACD**
 - **Administer oral calcium carbonate (Tums)**
 - **If necessary, administer IV calcium gluconate**
- **73% of all TPE procedures did not require IV calcium gluconate**

CITRATE REACTIONS CHECKLIST

DATE: _____ PROCEDURE: _____ Previous IV Calcium Required? YES ___ NO ___

SYMPTOMS	CHECK IF NONE	CHECK IF PRESENT	TIME	INTERVENTION				RESPONSE TO INTERVENTION
				SLOW INLET RATE	Check Ionized Ca	TUMS	IV CALCIUM	
Numbness/Tingling								
Nausea								
Hypotension								
Abdominal cramps								
Diarrhea								
Vomiting								
Chest Vibration/Pressure								
Anxiety/Hyperventilation								
Muscle Tightness								
Positive Chvostek's sign								
Involuntary Carpo-pedal Spasm								
Grand Mal Seizures								
Frank Tetany								
Laryngeal Spasm								
Q-T interval prolongation								
Severe Cardiac Arrhythmia								

COMMENTS: _____

Operator / RN _____

Conclusions

- **Routine prophylactic intravenous calcium supplementation may not be warranted**
- **Recent national shortage in Ca gluconate**
- **Combination of reduced concentrations of ACD-A and Heparin is another option**
- **Randomized clinical trials needed to study the necessity of IV Ca supplementation**