Donor Adverse Reactions due to Citrate Infusion during Automated Collections

The 16th International Haemovigilance Seminar

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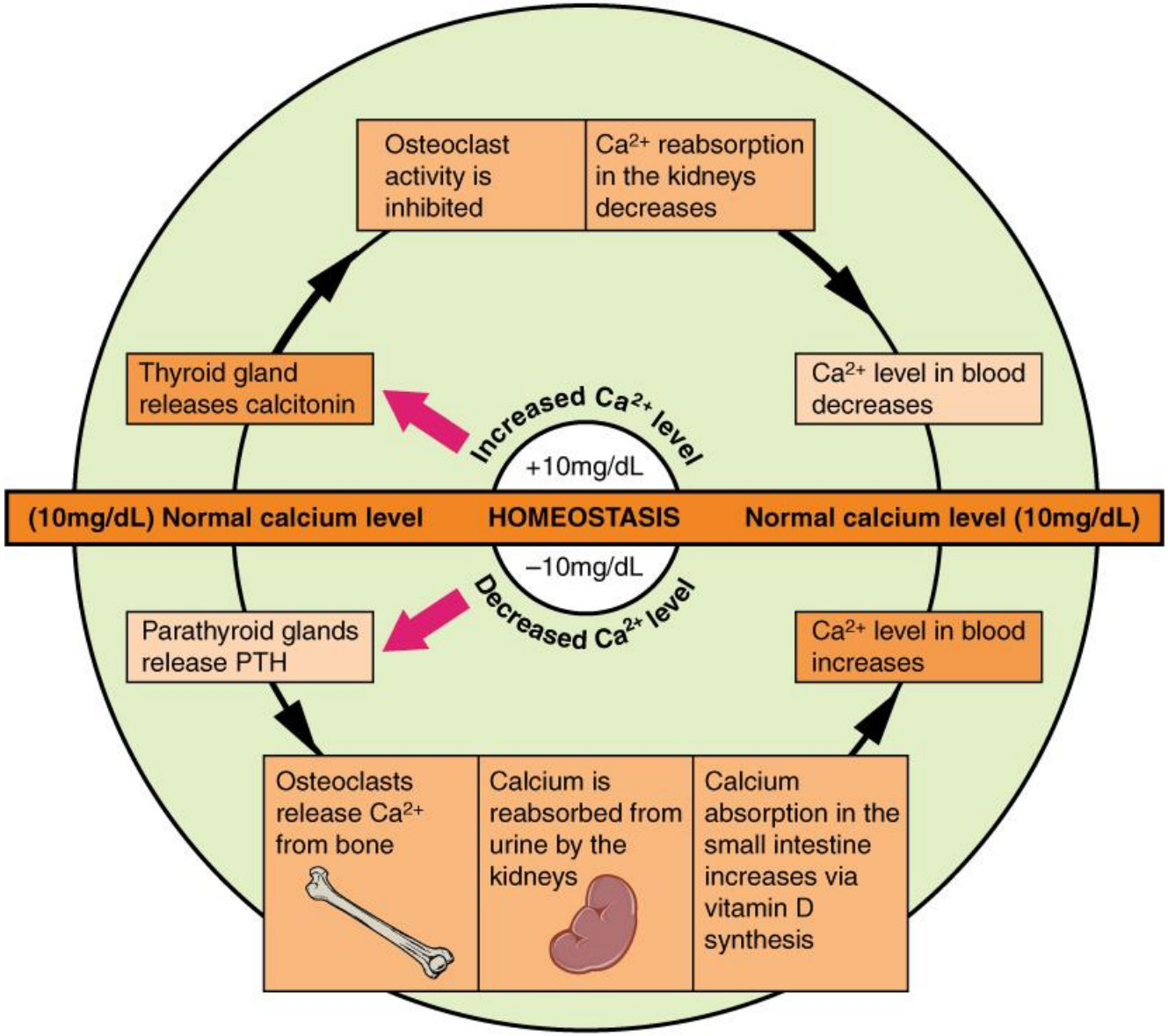
Background

- **Mild:** perioral paresthesias, twitching, shivering, light headedness, and headaches.
- **Persistent:**
  - Continuous muscle contractions, initially as carpopedal spasms which can progress to spasms in other muscle groups, tetany, and even seizures if hypocalcemia is not corrected
  - Hypotension,
  - Prolonged QTc interval
- **Long term effect on Bone Metabolism**

Pathways in Calcium Homeostasis



- **Aim.** To quantify and characterize citrate reactions (CR) in a multicenter blood collection operation.

METHODS

- Donors, donations and CR data for automated collections (AC) made between Jan 18, 2010 and Jan 17, 2013 were analyzed.

- We calculated CR rates and performed multivariable analysis (MVA) to identify variables associated with increased or decreased likelihood of CR.

- The final statistical model included donor age, gender, blood volume (BV), hemoglobin (Hb), residence altitude, experience, donation's site, collection type, device used and blood center.

RESULTS

- Rates
- Multivariable analysis

Donor and Donation Characteristics

Donor and Donation Characteristics		All Needle In Donations	Citrate Reactions Rate/1000 donations			Persistent % of all CR
			All CR	Mild	Persistent	
Donations		634634	**0.9**	**0.8**	**0.1**	**11%**
Donors		264376	**1.9**	**1.6**	**0.2**	**12%**
Sex	**Male**	494533	**0.4**	**0.4**	**0.0**	**9%**
	Female	140101	**2.5**	**2.2**	**0.3**	**12%**
Age	**16-18**	77290	**0.3**	**0.3**	**0.1**	**16%**
	19-22	54576	**1.0**	**0.9**	**0.1**	**6%**
	23-49	259276	**0.8**	**0.7**	**0.1**	**10%**
	50-64	187043	**1.0**	**0.9**	**0.1**	**11%**
	=>65	56436	**1.2**	**1.0**	**0.2**	**15%**
FT	**First time**	73546	**0.3**	**0.2**	**0.0**	**10%**
	Repeat	561088	**0.9**	**0.8**	**0.1**	**11%**

Donor and Donation Characteristics

Donor and Donation Characteristics		All Needle In Donations	Citrate Reactions Rate/1000 donations			Persistent % of all CR
			All CR	Mild	Persistent	
Apheresis donations in the past 2 years	**0**	115,337	0.3	0.3	0.03	10.5
	1-3	164,604	1.04	0.87	0.17	16.3
	4-5	87,965	1.01	0.88	0.14	13.5
	6-9	130,059	1.01	0.95	0.07	6.8
	10-13	60,616	1.01	0.89	0.12	11.5
	=>14	76,006	0.6	0.6	0.00	0.00
	Missing data	47	0.0	0.0	0.0	

Donor and Donation Characteristics

Donor and Donation Characteristics		All Needle In Donations	Citrate Reactions Rate/1000 donations			Persistent % of all CR
			All CR	Mild	Persistent	
EBV (mL)	<3500	2534	8.3	5.9	0.0	0%
	3500-3999	19969	4.5	3.9	0.5	10%
	4000-4499	56624	2.5	2.1	0.3	13%
	4500-4999	104500	1.0	0.9	0.1	10%
	=>5000	450862	0.4	0.4	0.1	11%
BMI	<18.5 underweight	1516	2.8	1.3	0.7	23%
	18.5-22.49 low normal	53980	1.1	1.0	0.1	8%
	22.50-24.99 high normal	88562	1.0	0.8	0.2	17%
	25.00-29.99 overweight	260991	0.9	0.8	0.1	8%
	30-39 obese	202460	0.7	0.7	0.1	11%
	=>40 extreme obesity	26980	0.6	0.4	0.1	24%
Hb (g/dL)	12.5/12.99	20679	2.3	2.0	0.2	10%
	13/13.40	36515	1.7	1.4	0.2	13%
	13.5/13.99	59470	1.2	1.0	0.2	13%
	14/27	517898	0.7	0.6	0.1	10%

Donor and Donation Characteristics

Donor and Donation Characteristics		All Needle In Donations	Citrate Reactions Rate/1000 donations			Persistent % of all CR
			All CR	Mild	Persistent	
Intended Collection	Platelets	118992	2.4	2.1	0.3	11%
	Platelets + RBC	32494	2.5	2.2	0.2	7%
	Platelets + Plasma	38264	2.8	2.5	0.2	8%
	Platelets + Plasma + RBC	6388	2.9	2.5	0.0	0%
	Plasma	9943	0.3	0.3	0.0	0%
	RBC + Plasma	31078	0.3	0.2	0.0	12%
	2RBC	397475	0.1	0.1	0.0	29%
Device Group	Alyx	158917	0.2	0.1	0.1	46%
	Amicus	35423	5.5	4.7	0.7	12%
	Cymbal	4203	0.0	0.0	0.0	
	Fenwal-Auto-C	196	0.0	0.0	0.0	
	Haemonetics	192694	0.1	0.1	0.0	7%
	TRIMA	243157	1.3	1.2	0.1	7%

Donor and Donation Characteristics

Donor and Donation Characteristics		All Needle In Donations	Citrate Reactions Rate/1000 donations			Persistent % of all CR
			All CR	Mild	Persistent	
Draw time (Minutes)	0-19	24981	0.4	0.3	0.1	29%
	20-29	133158	0.2	0.1	0.0	26%
	30-44	257025	0.1	0.1	0.0	25%
	45-59	40319	1.2	1.1	0.1	8%
	60-74	41085	2.8	2.6	0.2	7%
	75-89	44842	3.2	2.8	0.3	11%
	90-104	42607	1.8	1.6	0.1	5%
	105-119	29401	2.2	2.0	0.1	6%
	=>120	21208	1.9	1.5	0.4	20%
Elevation (feet) Donor Residence - County Average	0	137540	0.1	0.1	0.0	18%
	1000	179780	1.0	0.8	0.2	18%
	2000	91251	0.3	0.2	0.0	4%
	3000	104901	0.7	0.7	0.1	8%
	4000	70877	1.1	0.9	0.2	18%
	5000	24652	0.5	0.4	0.1	18%
	6000	24975	6.7	6.3	0.1	2%

Citrate reactions:
Phlebotomy Type and Device
Platelets Components

Phlebotomy Type	Device	Total Donations	Citrate Reactions	CR/1000 donations	Mild Citrate	Mild CR/1000 donations	Persistent	Persistent CR/1000 donations
Platelets	Amicus Single Needle	22,392	137	**6.12**	114	**5.09**	18	**0.80**
	Amicus Dual Needle	9,524	57	**5.98**	48	**5.04**	4	**0.42**
	Trima 5.1.3/6.0	87,019	98	**1.13**	89	**1.02**	8	**0.09**
Platelets + Pasma	Amicus Single Needle	2,779	6	**2.16**	3	**1.08**	2	**0.72**
	Amicus Dual Needle	728	0	**0.00**	0	**0.00**	0	**0.00**
	Trima 5.1.3/6.0	34,798	103	**2.96**	93	**2.67**	7	**0.20**
RBC + Platelets	Trima 5.1.3/6.0	32,532	82	**2.52**	73	**2.24**	6	**0.18**
RBC + Plasma + Platelets	Trima 5.1.3/6.0	6,373	19	**2.98**	16	**2.51**	0	**0.00**

Citrate reactions:
Phlebotomy Type and Device
Non-Platelets Components

Phlebotomy Type	Device	Total Donations	Citrate Reactions	CR/1000 donations	Mild Citrate	Mild CR/1000 donations	Persistent	Persistent CR/1000 donations
Plasma	Auto-C	196	0	0.00	0	0.00	0	0.00
	Trima 5.1.3/6.0	9,648	3	0.31	3	0.31	0	0.00
RBC + Plasma	Haemonetics MCS+ 8150*	16,500	2	0.12	2	0.01	0	0.00
	Trima 5.1.3/6.0	8,934	4	0.45	3	0.34	1	0.11
2RBC	Haemonetics MCS+ 8150*	176,194	13	0.07	12	0.07	1	0.01
	Cymbal	4,203	0	0.00	0	0.00	0	0.00
	Trima 5.1.3/6.0	63,853	12	0.19	11	0.17	1	0.02
	Alyx	153,238	24	0.16	12	0.08	12	0.08

Factors Associated with Citrate Reactions

Reference	Variable	OR (95% CI)
Sex: Male	**Female**	**2.6(2-3.5)**
Age: 23-49 (years)	**16-18**	1.1 (0.7-1.7)
	19-22	1.2 (.9-1.6)
	50-64	1 (0.8-1.2)
	=>65	1.1 (0.8-1.4)
EBV: =>5000 (mL)	**<3500**	1.7 (.96-3)
	3500-3999	**1.5 (1.1-2.1)**
	4000-4499	**1.7 (1.3-2.3)**
	4500-4999	**1.4 (1.1-1.8)**
Hb: >=16 (g/dL)	**12.5-13.49**	**0.7 (0.5-0.9)**
	13.5-15.49	**0.8 (0.6-0.99)**

Model with AC donations in the prior 2 year

Factors Associated with Citrate Reactions

Reference	Variable	OR (95% CI)
# of Prior Apheresis Donation in the past 2 years: =>14	0	7.5 (4.7-11.8)
	1-3	6.6 (4.7-9.2)
	4-5	4.5 (3.2-6.5)
	6-9	3.7 (2.6-5.2)
	10-13	2.6 (1.7-3.7)

Model with AC donations in the prior 2 year

Factors Associated with Citrate Reactions

Reference	Variable	OR (95% CI)
Intended Collection: R (2RBC)	**A (platelets)**	**5.8 (3.3-10.3)**
	B (RBC & platelets)	**6.4 (3.6-11.4)**
	C (plasma & platelets)	**10.8 (6.1-19.2)**
	E (platelets, plasma and red cells)	**14 (6.7-29)**
	P (plasma)	0.8 (0.2-3)
	Q (red cells & plasma)	1.3 (0.6-2.9)
Device: TRIMA	**Alyx**	1.2 (0.5-2.4)
	Amicus	**4.3 (3-6.3)**
	Cymbal	Omitted
	Fenwal-Auto-C	Omitted
	Haemonetics	**0.5 (0.2-0.97)**
Elevation: 0-2000 (feet) Donor Residence County Ave.	**2001-4000**	**2.2 (1.3-3.8)**
	4001-6000	**2.6 (1.5-4.6)**
	>6000	**12 (7.1-20.2)**

Conclusions

- CRs are strongly associated with automated collections of platelets and with female gender.
- The association of CR with donors living in high altitude warrants further investigation to understand the physiologic basis.

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