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Estimation of serum calcium levels in apheresis platelet donors

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Abstract:

INTRODUCTION: Apheresis is practiced widely to collect single donor platelets (SDPs). This procedure utilizes an anticoagulant acid citrate dextrose to prevent clotting of blood in the extracorporeal circuit which chelates divalent ions like calcium. This alters the calcium homeostasis resulting in hypocalcemia causing acute adverse events.

AIM: The study aimed to know the calcium homeostasis in apheresis platelet donors.

MATERIALS AND METHODS: This cross-sectional study was conducted from January 2020 to December 2020 in the department of transfusion medicine. The sample size was 50. Donors who walk in for voluntary SDP donation were selected. Total and ionized calcium, pH, and serum albumin for all the donors at baseline and ionic calcium at the end of the procedure and 30 min after the procedure were measured.

RESULTS: According to statistical analysis of the ionic calcium level at pre procedure, immediate post procedure and 30 minutes post procedure, there was decrease in the value immediate post procedure and values returned to baseline within 30 minutes. The levels of pH change were analyzed. On comparing the preprocedure and immediate postprocedure values, there was a significant lowering of pH value from the baseline ($P = 0.5$), indicating acute lowering of pH immediate postprocedure. Hence, most of the citrate metabolism can be achieved within 30 min after completion of the apheresis procedure.

CONCLUSION: SDP collection is essentially a safe procedure with minimal adverse effects. Toxicity of citrate is not much pronounced. Recovery of calcium levels is within 30 min of completion of plateletpheresis.

Keywords:

Apheresis, calcium homeostasis, ionic calcium

Introduction

Apheresis is a common procedure employed in most of the blood centers. During the procedure, blood from the donor is drawn into the extracorporeal circuit and processed to obtain components of interest. In order to prevent coagulation in the extracorporeal circuit, acid citrate dextrose (ACD) is used as an anticoagulant. The citrate component in it is known to cause chelation of divalent cationic ions such as calcium and magnesium. This might cause hypocalcemia and its consequences in apheresis donors. In a healthy individual, ionized calcium is in equilibrium with protein-bound calcium. Any transient drop in the ionized calcium can be compensated by the concomitant release of calcium. The albumin calcium buffer is pH sensitive. Alkaline pH leads to fall in ionized calcium and acidic pH leads to its rise. This study was performed to know the changes in the ionic calcium levels during the course of the plateletpheresis procedure.

Aim

To study calcium homeostasis in apheresis platelet donors.

Materials and Methods

This was a descriptive study, in which donors who are selected to undergo apheresis

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platelet donation by standard selection protocol were recruited for the study after taking their consent. Donors who walked in for voluntary single donor platelet donation were selected based on the standard criteria for platelet donation. Age group of the study population was ranging from 18 to 50 Years. Donors were checked for certain parameters. First, platelet count should have been within the normal limits of 1.5 lakh to 4 lakh cells/μl and packed cell volume should be within 40%–50%. Hemoglobin level ranged from 12.5 to 16.5 g/dL. Donor weight should be above 50 kg. They should have been screened negative for routine viral markers. The procedure was done using an automated platelet collection equipment COM.TEC Fresenius Kabi. The machine was primed with 0.9% normal saline and ACD anticoagulant. The anticoagulant and blood were used in the ratio of average of 1:7.5. The donor was supplemented with 1 g of oral calcium carbonate tablet half an hour before the start of the procedure. At the start of the procedure, the first sample was drawn from the diversion pouch. There was no interference of ACD into this diversion pouch. Postcollection of the first sample, the diversion pouch was completely emptied. The second sample was collected immediately after the procedure from the diversion pouch used initially. Thirty minute postprocedure, the third sample was collected from the donor from his/her other vein other than the vein used for the procedure. The consent for this additional prick was taken from the consent before the start of the procedure. The first preprocedure sample collected was sent for central laboratory for baseline levels of serum calcium and serum albumin. Another Vacutainer of sample was sent to the emergency department or intensive care unit for venous blood gas analysis to obtain ionized calcium and pH of the blood. Following this, the second sample was sent for venous blood gas analysis for ionized calcium and pH levels immediate postprocedure. The same investigations were performed on the third sample collected 30 min postprocedure. All the donors were continuously monitored for the signs and symptoms of citrate toxicity.

Statistical analysis

Data were presented as mean, standard deviation, percentages, and number of cases. The difference between continuous variables was analyzed using Student's *t*-test and one-way ANOVA. Categorical data were compared with Pearson's Chi-square tests. Significance was defined by $P < 0.05$ using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Science Inc., Chicago, IL, USA).

Results

Fifty platelet donors were included in the study and all were male donors. The age group distribution of the study population was between 18 and 50 years. The average weight of the donors was 75 kg and the average height was 172 cm. Majority of the donors in the study population was first time platelet donors (n=32 or 64%), second time donors constituted 16%(n=8), while third time donors were 8 in number (16%) and there were 2 donors who donated for four times (8%). The distribution of study variables used in the study is shown in Table 1.

The bar diagram represented in Figure 1 shows the variations in the ionic calcium levels measured during the procedure. The blue-colored bars represent dynamics of ionized calcium values which were lower than the normal values (normal = 4.61–5.33 mg/dL) preprocedure, immediate postprocedure, and 30 min postprocedure. On comparing it with the number of donors on the Y-axis against the ionized calcium values on the X-axis, it clearly indicated that the increase in ionized calcium value immediate postprocedure from the baseline in 40 donors and 30 min postprocedure in

Table 1: Distribution of study variables

Variables	Minimum	Maximum	Mean±SD
Age (18-55)	19	46	28.78±6.76
Hemoglobin (g/dL) (12.5-17.5)	12.5	17.5	14.69±1.15
PCV (%) (40%-50%)	38.2	50.8	44.19±2.66
Platelet count (normal range=1.5-4 lakh cells/cubic mm)			
Preprocedure	1.57	3.95	2.82±0.48
Total calcium	7.9	10.6	9.65±0.44
Ionic calcium (normal range=4.61-5.33 mg/dL)			
Preprocedure	0.4	5.09	2.18±1.12
Immediate postprocedure	0.03	3.94	0.97±0.98
30 min postprocedure	0.26	4.33	2.24±1.03
pH (normal range=7.350-7.450)			
Preprocedure	7.28	7.49	7.34±0.03
Immediate postprocedure	6.8	7.44	7.13±0.2
30 min postprocedure	7.26	7.54	7.34±0.04
Serum albumin (normal range=3.5-5.2 g/dL)	3.3	5.3	4.63±0.37

SD=Standard deviation, PCV=Packed cell volume

11 donors returned to the nearest baseline value. Thirty-five donors had highest calcium level pre procedure, while immediate post procedure only seven donors had highest calcium value. Almost 37 donors had recovery to the values more than their baseline post 30 minutes the procedure.

The comparative values of ionized calcium preprocedure and immediate postprocedure are tabulated in Table 2. Table 3 gives the cross-tabulation of ionic calcium values pre- and 30 min postprocedure.

Figure 2 represents the bar diagram showing the pH changes preprocedure, immediate postprocedure, and 30 min postprocedure in donors.

The comparison of pH values preprocedure and immediate postprocedure is tabulated in Table 4. It shows that 33 donors had initial pH in the lower limit of normal range, while 16 of them had within the normal range and only 1 donor had higher pH. Immediate postprocedure, 43 (43%) donors recorded lower pH and 7 had within normal range and none of the donor had higher pH.

The cross-tabulation results of pH values preprocedure and 30 min postprocedure are shown in Table 5. Thirty minutes postprocedure, it was recorded that 31 (62%) donors had lower pH, 18 of them had within the normal range, and 1 recorded higher pH.

Report of adverse events in donors is shown in [Table 6]. One donor reported the adverse event which was in the form of perioral parathesis, nausea, fatigue, and upper limb numbness. On supplementing with 1 g of calcium, the donor recovered within 30 min.

Discussion

Citric acid is an organic compound with three ionizable carboxyl groups. Majority of citrate present in body has all three carboxyl groups ionized. These ionized carboxyl groups are responsible for major pharmacological actions of citrate that is the binding of divalent metal ions.

Table 2: Cross-tabulation of ionic calcium level preprocedure and immediate postprocedure

Ionic calcium (mg/dL) Preprocedure	Immediate postprocedure			Total	*P*
	Low	Normal	High		
Low (<4.61 mg/dL)					
Count	10	0	0	10	0.253
Percentage within prprocedure	100.0	0.0	0.0	100.0	
Normal (4.66-5.33 mg/dL)					
Count	5	0	0	5	
Percentage within preprocedure	100.0	0.0	0.0	100.0	
High (>5.33 mg/dL)					
Count	25	3	7	35	
Percentage within preprocedure	71.4	8.6	20.0	100.0	
Total					
Count	40	3	7	50	
Percentage within preprocedure	80.0	6.0	14.0	100.0	

Table 3: Cross-tabulation of ionic calcium level preprocedure and 30 min postprocedure

Ionic calcium (mg/dL) Preprocedure	30 min postprocedure			Total	*P*
	Low	Normal	High		
Low (<4.61 mg/dL)					
Count	5	0	5	10	0.175
Percentage within preprocedure	50.0	0.0	50.0	100.0	
Normal (4.66-5.33 mg/dL)					
Count	1	0	4	5	
Percentage within preprocedure	20.0	0.0	80.0	100.0	
High (>5.33 mg/dL)					
Count	5	2	28	35	
Percentage within preprocedure	14.3	5.7	80.0	100.0	
Total					
Count	11	2	37	50	
Percentage within preprocedure	22.0	4.0	74.0	100.0	

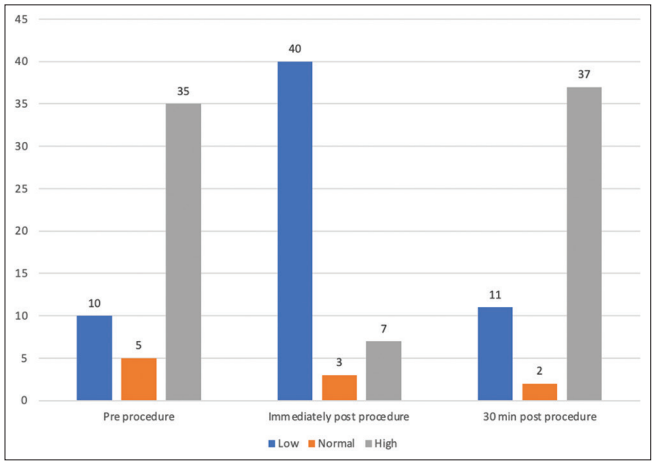

Figure 1: Distribution of ionic calcium level among platelet donors

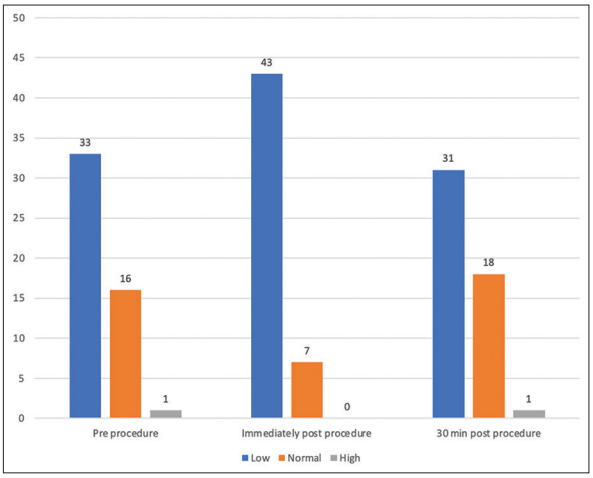

Figure 2: Distribution of pH level among plateletpheresis donors

Table 4: Cross-tabulation of pH level in preprocedure and immediate postprocedure

pH Preprocedure	Immediate postprocedure		Total	*P*
	Low	Normal		
Low (<7.35)				
Count	31	2	33	0.054
Percentage within preprocedure	93.9	6.1	100.0	
Normal (7.35-7.45)				
Count	11	5	16	
Percentage within preprocedure	68.8	31.3	100.0	
High (>7.45)				
Count	1	0	1	
Percentage within preprocedure	100.0	0.0	100.0	
Total				
Count	43	7	50	
Percentage within preprocedure	86.0	14.0	100.0	

Table 5: Cross-tabulation of pH level in preprocedure and 30 minutes postprocedure

pH Preprocedure	30 min postprocedure			Total	*P*
	Low	Normal	High		
Low (<7.35)					
Count	26	7	0	33	<0.0001
Percentage within preprocedure	78.8	21.2	0.0	100.0	
Normal (7.35-7.45)					
Count	5	11	0	16	
Percentage within preprocedure	31.3	68.8	0.0	100.0	
High (>7.45)					
Count	0	0	1	1	
Percentage within preprocedure	0.0	0.0	100.0	100.0	
Total					
Count	31	18	1	50	
Percentage within preprocedure	62.0	36.0	2.0	100.0	

Table 6: Reported adverse events in platelet donors

Adverse events	Number of donors
No	49
Yes	1
Total	50

Anisha Appa Navkudkar in her paper, "Effect of citrate on ionized calcium levels during plateletpheresis procedures," explained about the effect of citrate in donor plateletpheresis. Plateletpheresis are well tolerated procedures. Adverse reactions are generally mild. Citrate, which enters the donor's blood circulation forms calcium citrate complexes reducing the ionized calcium levels. This complex is metabolized by liver, kidney and skeletal muscles releasing three molecules of bicarbonate leading to metabolic alkalosis causing hypocalcemia. When ionized calcium reduces, as a feedback mechanism PTH is released. Within 5–15 min of citrate infusion, PTH increases and it stabilizes during rest of the procedure. In healthy individuals, this exogenous citrate is rapidly metabolized and thus the calcium ions get released, whereas 18%–20% remains unmetabolized. In the presence of normal citrate metabolism, the half-life of citrate induced is 36 ± 18 min. Citrate levels return to normal within 4 h after halting the infusion. Donors were able to completely metabolize citrate within 24 h. Common citrate-related symptoms are mild symptoms, perioral paresthesia, flushing, shivering, light headedness, and headache. Moderate symptoms are nausea, vomiting, abdominal cramps, carpopedal spasms, tetany, tremors, and hypotension. Severe symptoms included cardiac arrhythmias and seizures. Hypocalcemia reactions are transient and self-limiting. Simple procedural modifications such as pausing the procedure and adjustments of the return flow and adjusting the citrate infusion rates can help combat the citrate toxicity.[1]

A prospective observational study was conducted by Lokhande *et al*. on 50 normal plateletpheresis donors in their institute. They analyzed the changes of ionic calcium and total serum calcium levels during and after plateletpheresis. In their study, they found a significant fall (P = 0.05) in the mean serum calcium from baseline levels (9.84 ± 0.47 mg/dl) till midprocedure (9.22 ± 0.55 mg/dl), but recovery occurred by 30 min postprocedure and their levels were near respective baseline values (9.44 ± 0.81 mg/dl). Similarly, they found a significant decrease in iCa from baseline (1.23 ± 0.07 mmol/L) to the midprocedure (1.19 ± 0.006 mmol/L), which also recovered by 30 min postprocedure (1.2 ± 0.01 mmol/L).[2]

Bolan *et al*. studied the comprehensive analysis of citrate effects during plateletpheresis in normal donors. Standard plateletpheresis procedure may cause donor to receive up to 10 g of citrate over 90–120 min. The author has studied the citrate metabolism inside donors' body by infusing citrate at three different infusion rates. Every donor underwent three procedures each, during which constant citrate infusion rates of 1.1, 1.4, and 1.6 mg/kg/min were used with at least 4 weeks of gap between the two successive donations. Blood samples were obtained at baseline, 30 min, 60 min, and 90 min into the procedure. All the samples were sent for iCa, iMg, and pH values. They also measured serum and urine citrate levels. The laboratory values of iCa and iMg also fell progressively during the course of the procedure and the fall was more significant with the higher citrate infusion rates. Whereas, serum citrate levels increased continuously during plateletpheresis without reaching the plateau with peak citrate level at 90 min. It was observed that PTH levels were highest at 30 min and it gradually declined. Also mean pH increased from

7.40 to 7.42. No significant changes in magnesium were noted. Hence, the author concludes that in spite of these metabolic changes, plateletpheresis is considered safe because procedures are modified in case donor develops symptoms.[3]

Mercan *et al*. studied the kinetics of ionic calcium and magnesium in 15 healthy plateletpheresis donors. They observed that ionized calcium dropped sharply and then more progressively, from an initial mean of 1.25 ± 0.04 mmol/L to a low of 1.03 ± 0.03 mmol/L at 120 min ($P < 0.001$). More than half the drop occurred within the first 30 min of the apheresis. Ionized calcium dropped to initial values recovering almost 73% of loses within 30 min of the procedure ($p<0.001$). No significant changes in pH levels were observed.[4]

Toffaletti *et al*. conducted a study to know the changes in concentrations of different forms of calcium and the responses of PTH during citrate-induced hypocalcemia. They studied 12 healthy donors. There was decrease in ionized calcium in every donor, most rapidly in first 15 minutes, and by 90 minutes it was 25% lower than pre-Apheresis values. Total calcium also decreased during first 15 minutes of the procedure and by 90 minutes it was reduced only by 6%. Whereas, protein bound calcium decreased by 35% at 90 minutes which dominated the calcium component which decreased the most.[5]

In comparison of the above studies to our study, the ionic calcium value at the start of the procedure was compared with the levels of ionic calcium immediate postprocedure and 30 min postprocedure. Figure 1 depicts the changes in the ionic calcium among the donors. Ten donors had preprocedure ionic calcium levels in the lower limit of the normal range, five donors had normal ionic calcium level, and thirty-five donors had higher limit of the normal range of ionic calcium. Immediate postprocedure, 40 donors had ionic calcium levels in the lower limit of the normal range, 3 donors maintained in the normal range of ionic calcium, and 7 donors had higher levels. Post-30 min of the procedure, 11 donors had ionic calcium value in the lower level, 2 donors had normal values, and 37 donors had higher ionic calcium values.

We demonstrated the pH changes in our study during the course of the procedure. Figure 2 depicts the distribution of the pH values among the donors. During preprocedure, 33 donors had lower range of pH value, while 43 donors had lower pH immediate postprocedure and 31 donors had lower value 30 min postprocedure. Whereas, 16 donors had normal pH preprocedure, 7 maintained normal value immediate postprocedure, and 18 donors had normal pH 30 min postprocedure. Only 1 donor had higher pH preprocedure and 1 donor had higher pH 30 min postprocedure. None of the donors had higher pH immediate postprocedure.

Conclusion

Recovery of calcium levels is within 30 min of completion of plateletpheresis procedures. The toxicity of citrate is not much pronounced in most of the donors as already reviewed and hence plateletpheresis can be considered a very safe procedure to perform on healthy donors.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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