

Access this article online
Quick Response Code:

Website: www.ajts.org
DOI: 10.4103/ajts.AJTS_114_17

Prophylactic administration of oral calcium carbonate during plateletpheresis: A bicentric prospective study

Prashant Kumar Pandey, Aseem Tiwari¹, Nitin Agarwal, Ravi C. Dara²

Abstract:

BACKGROUND: Administration of anticoagulant citrate and dextrose (ACD-A) chelates ionized calcium in blood and causes hypocalcemia in plateletpheresis donors. The aim of the study was to observe the effects of oral calcium (Ca) supplementation during plateletpheresis on various parameters related to calcium metabolism.

MATERIALS AND METHODS: This study was performed between January 2014 and December 2014 on 200 plateletpheresis donors. They were divided into two groups. In group A donors (n=100), no prophylactic oral calcium supplementation was given. In group B (n=100) donors, 2000 mg of calcium was given one hour before the start of the procedure, 500 mg was given at the start of the procedure and 500 mg calcium was given just before the end of procedure. Biochemical parameters like serum total calcium (T Ca), serum total magnesium (T Mg) and ionized calcium level (iCa) were measured before and after the procedure. Relative risk of citrate toxicity was measured between the two groups.

RESULTS: There was a significant fall in total calcium (pre 9.02 mg/dl, post 8.23 mg/dl), ionized calcium level (pre 1.14 mmol/L, post 0.91 mmol/L) and total magnesium (pre 1.92 mg/dl, post 1.79 mg/dl) amongst the donors who did not receive prophylactic calcium supplementation. Despite calcium intake, in prophylactic calcium intake group, we did observe a significant drop in total magnesium (pre 2.04 mg/dl, post 1.94 mg/dl) and ionized calcium level (pre 1.25 mmol/L, post 1.12 mmol/L, $p < 0.01$). We did observe a drop in total calcium level, however, this observation was not statistically significant. The risk (RR=5.44) of citrate toxicity was higher among group A donors.

CONCLUSION: Prophylactic oral calcium carbonate supplementation would help in to reduce the risk of citrate toxicity. Therefore, we suggest for prophylactic oral administration of 3000 mg elemental calcium carbonate in three divided doses to make PP procedures uneventful.

Keywords:

Citrate toxicity, hypocalcemia, oral calcium carbonate, plateletpheresis

Introduction

Single donor platelet (SDP) concentrate is widely used for transfusion in patients for various indications. There could be several reasons for increasingly larger consumption of SDP such as better awareness, easier availability of cell separators, and

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

periodic dengue epidemic.^[1,2] The primary anticoagulant used in donor apheresis procedures is acid citrate dextrose (ACD). The anticoagulant effect of citrate results from its ability to chelate calcium resulting in these ions being unavailable to participate in biological reactions such as the coagulation cascade.^[3,4] This can lead to various symptoms of hypocalcemia in the donors such as nervousness, irritability, flushing,

How to cite this article: Pandey PK, Tiwari A, Agarwal N, Dara RC. Prophylactic administration of oral calcium carbonate during plateletpheresis: A bicentric prospective study. Asian J Transfus Sci 2020;14:19-22.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

Department of Transfusion
Medicine, Jaypee Hospital,
Noida, Uttar Pradesh,
¹Department of
Transfusion Medicine,
Medanta-The Medicity,
Gurgaon, Haryana,
²Department of
Transfusion Medicine,
Manipal Hospital, Jaipur,
Rajasthan, India

Address for correspondence:

Dr. Prashant Kumar Pandey,
Department of Transfusion
Medicine, Jaypee
Hospital, Sector-128,
Noida - 201 304,
Uttar Pradesh, India.
E-mail: pkpandey2007@
gmail.com

Submission: 31-08-2017
Accepted: 08-01-2018
Published: 24-07-2020

shivering, nausea, vomiting, chest discomfort, muscle cramps, tremors, and perioral or acral paraesthesia. The aim of the study was to observe the effect of oral calcium (Ca) supplementation before and during plateletpheresis (PP) on various parameters related to calcium metabolism.

Materials and Methods

This prospective observational study was performed at a tertiary health-care center in the national capital region of India, from January 2014 to December 2014 on 200 PP donors. All PP procedures were performed using a fully automated platform of PP, COM.TEC (Fresenius Kabi, Germany) using the closed system kits and the ACD-to-whole blood ratio was kept in the range of 1:9–1:10, throughout the procedure. For the study *per se*, all the PP procedures done on single arm only were taken into account. Departmental standard operating procedure (SOP) was followed with strict adherence to the manufacturer's instructions.

These 200 donors were further divided into two groups. In Group A donors ($n = 100$), no prophylactic oral calcium supplementation was given ("no prophylactic oral calcium supplementation group"). In Group B ($n = 100$) donors, ("prophylactic oral calcium supplementation group"), 2000 mg of calcium was given 1 h before the start of the procedure, 500 mg was given at the start of the procedure, and 500 mg calcium was given just before the end of procedure (total 3000 mg).^[5]

Samples for the postprocedure changes in these parameters were collected after 2 h of the completion of procedure by venepuncture of antecubital vein with proper aseptic technique. Biochemical parameters such as serum total calcium (T Ca) and serum total magnesium (T Mg) were analyzed on Vitros 5600 (Ortho-Clinical Diagnostics, Johnson and Johnson, USA) and ionized calcium (iCa) level on ABL800 Basic (Denmark). All the analyses were done using the manufacturer's instructions and the SOP of the department. We could not measure ionized magnesium as this parameter was not available on this machine.

Statistical analysis

Pre- and postprocedure demographic data and biochemical parameters were maintained on an Excel sheet. Data were further analyzed using the Statistical Package for the Social Sciences version 21 (SPSS, Chicago, IL, USA). All the results were calculated as mean \pm standard deviation, range. Within the group for all biochemical parameters, difference of mean before and after the procedure was compared using paired *t*-test. $P < 0.05$ was considered statistically significant. Between the two groups, postprocedure drop in T Ca, T Mg, and

iCa was compared using independent two-sample *t*-test. The $P < 0.05$ was considered statistically significant. To study the strength of association of calcium intake and its role in prevention of adverse effects due to hypocalcemia, relative risk (RR) was calculated.

Results

Demographic details

Donors in both the groups were comparable with respect to gender, age, weight, and blood counts. No significant difference was shown in any parameter between the two groups [Table 1].

Effect of plateletpheresis on calcium levels

Amongst the 100 PP donors, who did not receive prophylactic calcium before and during the procedures, there was a statistically significant fall in T Ca (pre 9.02 mg/dl, post 8.23 mg/dl, $P < 0.01$), iCa level (pre 1.14 mmol/L, post 0.91 mmol/L, $P < 0.01$), and T Mg (pre 1.92 mg/dl, post 1.79 mg/dl, $P < 0.01$) [Table 2]. Likewise, despite calcium intake, in prophylactic calcium intake group, we did observe a significant drop in T Mg (pre 2.04 mg/dl, post 1.94 mg/dl, $P < 0.05$ and iCa level (pre 1.25 mmol/L, post 1.12 mmol/L, $P < 0.01$). In this category of PP donors, we did observe a drop in T Ca level; however, this observation was not statistically significant (pre 8.49 mg/dl, post 8.27 mg/dl, $P = 0.197$) [Table 3]. The difference of postprocedure mean ionized calcium level between Group A and Group B was found to be statistically significant (0.91 mmol/l vs. 1.12 mmol/l, $P < 0.05$) [Tables 2 and 3].

Adverse reactions related to calcium loss

There were 10 PP donors in "no prophylactic oral calcium supplementation category" and 2 donors in "prophylactic oral calcium supplementation category" who presented with symptoms of hypocalcemia. All these donors, however, had mild symptoms and could be managed conservatively and the procedures were completed successfully. In PP donors who did not receive prophylactic oral calcium carbonate supplementation as per the study protocol, we did

Table 1: Demographic and common hematological profiles of donors in each group

Parameters	Group A	Group B
Number of donors	100	100
Male:female ratio	97:3	98:2
Mean age (years)	38.8	35.9
Mean weight (kg)	70.5	69.2
Preprocedure Hb, g% (range)	14.1 (12.5-16.9)	13.7 (12.5-15.8)
Mean platelet count, $\times 10^9/L$ (range)	225 (150-379)	232 (150-420)

*No significant difference was noted in any parameter between the two groups ($P > 0.05$). Hb = Hemoglobin

Table 2: The effect of plateletpheresis on biochemical parameters of donors without prophylactic oral calcium carbonate supplementation (n=100)

Parameters	Mean±SD (range)			P
	Preplateletpheresis	Postplateletpheresis	Difference	
Total calcium (mg/dl)	9.02±0.60 (7.8-11.1)	8.23±1.28 (5.1-12.2)	0.79±1.01	<0.01
Total magnesium (mg/dl)	1.92±0.27 (0.99-2.3)	1.79±0.26 (1.09-2.2)	0.13±0.17	<0.01
Ionized calcium (mmol/l)	1.14±0.13 (0.9-1.5)	0.91±0.13 (0.47-1.12)	0.23±0.09	<0.01

SD = Standard deviation

Table 3: The effect of plateletpheresis on biochemical parameters of donors with prophylactic oral calcium carbonate supplementation (n=100)

Parameters	Mean±SD (range)			P
	Preplateletpheresis	Postplateletpheresis	Difference	
Total calcium (mg/dl)	8.49±1.33 (4.9-10.3)	8.27±1.27 (5.1-9.8)	0.22±1.17	0.1970
Total magnesium (mg/dl)	2.04±0.49 (1.1-4.2)	1.94±0.43 (1.5-4.4)	0.10±0.32	0.0384
Ionized calcium (mmol/L)	1.25±0.12 (1.09-1.5)	1.12±0.10 (0.85-1.5)	0.13±0.09	<0.01

SD = Standard deviation

observe ten donors (10/100, 10%) who presented with signs and symptoms suggestive of hypocalcemia in the form of perioral tingling, feeling of vibrations in extremities, and mild shivering, and finally, they required calcium supplementation. Among the PP donors who were administered prophylactic calcium before and during the procedure, only two of them presented with above symptoms (2/100, 2%) and required oral calcium supplementation above the dosage protocol of the study. Those donors who were not administered prophylactic calcium before and during the procedure showed a relatively higher risk (RR = 5.44) of citrate toxicity [not shown in table].

Discussion

In India, there is staggeringly high demand for SDP during dengue epidemics, and in most of the tertiary health-care centers, SDP is the preferred choice for platelet transfusion. Citrate is used as a primary anticoagulant in PP procedures to prevent clotting of extracorporeal blood in apheresis circuit. In general, apheresis performed with citrate anticoagulation is considered safe, and metabolism, redistribution, and short procedure duration prevent accumulation to toxic levels.^[6,7] However, repeated platelet donations or during prolonged PP, citrate accumulation may outpace its metabolism, resulting in hypocalcemia or hypomagnesemia, which may cause significant donor discomfort.^[3]

Decrease in both calcium and magnesium increases nerve membrane excitability and causes perioral and acral paraesthesia. Donors may also experience shivering, nausea, vomiting, chills and fever, lightheadedness, tremors, and muscle cramps.^[8] According to the literature, about 16%–50% PP donors develop citrate-related reactions.^[9] If hypocalcemia becomes more severe, symptoms can progress to frank tetany with spasm

in other muscle groups including life-threatening laryngospasm, Q-T prolongation, and fatal arrhythmias can also occur.^[10,11] Factors that have been found to influence the rate of citrate reactions in donor and therapeutic apheresis include alkalosis due to hyperventilation, the rate of infusion of the anticoagulant solution, the amount of citrate infused, and the donor's serum albumin level before the start of the collection procedure.^[12]

In the present study, ionized Ca was measured in addition to the total serum calcium levels because total serum level includes a protein-bound fraction, which is not available for biochemical processes, whereas ionized fraction is the physiologic active form, which is responsible for many cellular processes, including hemostasis, regulation of muscle contraction, and the stabilization of cellular membranes.^[13] In the present study, we observed that 10% of the donors in “no prophylactic calcium intake group” presented with signs and symptoms of citrate toxicity, while in “prophylactic calcium intake” group, just 2% donors showed symptoms and signs of citrate toxicity. Thus, the RR of citrate toxicity in “no prophylactic calcium intake group” was 5 times higher. The drop in iCa level was statistically significant in both groups, and the difference of postprocedure mean iCa level between the two groups was noticed to be significantly lower in prophylactic calcium intake group. This could be the most plausible explanation for the relatively lower rate of citrate toxicity in this group. In a randomized placebo-controlled study, it has been demonstrated that oral calcium supplementation of 2000 mg exerted a significant but modest improvement in total and iCa level of the donors.^[14] Das *et al.*^[15] also noticed in their study that in donors not given any supplement, mean tCa^{++} fell from 2.62 ± 0.12 to 2.36 ± 0.12 mmol/L and mean tMg^{++} from 0.89 ± 0.01 to 0.79 ± 0.01 mmol/L; however, the difference was not significant. Moreover, drop in mean

iCa from 1.33 ± 0.1 to 0.84 ± 0.1 mmol/L and mean iMg from 0.53 ± 0.01 to 0.35 ± 0.1 mmol/L was statistically significant ($P < 0.001$). The safety and feasibility aspects of PP on animal model have been studied, and it has been observed that Ca supplementation limited the clinical signs of hypocalcemia during the procedure.^[16] Thus, prophylactic administration of prophylactic elemental calcium in three divided doses did not prevent the loss of iCa during the apheresis procedure but effectively reduced the risk of the adverse events related to hypocalcemia.

Conclusion

Prophylactic oral calcium carbonate supplementation would help in to reduce the risk of citrate toxicity and will also help in future retention of these donors. Therefore, we suggest for prophylactic oral administration of 3000 mg elemental calcium carbonate in three divided doses to make PP procedures safe and uneventful.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Chaudhary R, Khetan D, Sinha S, Sinha P, Sonker A, Pandey P, *et al.* Transfusion support to dengue patients in a hospital based blood transfusion service in North India. *Transfus Apher Sci* 2006;35:239-44.
2. Makroo RN, Raina V, Kumar P, Kanth RK. Role of platelet transfusion in the management of dengue patients in a tertiary care hospital. *Asian J Transfus Sci* 2007;1:4-7.
3. Mercan D, Bastin G, Lambermont M, Dupont E. Importance of ionized magnesium measurement for monitoring of citrate-anticoagulated plateletpheresis. *Transfusion* 1997;37:418-22.
4. Bennett MW, Webster NR, Sadek SA. Alterations in plasma magnesium concentrations during liver transplantation. *Transplantation* 1993;56:859-61.
5. Hanzlik RP, Fowler SC, Fisher DH. Relative bioavailability of calcium from calcium formate, calcium citrate, and calcium carbonate. *J Pharmacol Exp Ther* 2005;313:1217-22.
6. Hester JP, McCullough J, Mishler JM, Szymanski IO. Dosage regimens for citrate anticoagulants. *J Clin Apher* 1983;1:149-57.
7. Simon TL, McLeod BC. Physiology of apheresis. In: McLeod BC, Price TH, Drew MJ, editors. *Apheresis: Principles and Practice*. Bethesda, MD: AABB; 1997. p. 67-84.
8. Strauss RG. Mechanisms of adverse effects during hemapheresis. *J Clin Apher* 1996;11:160-4.
9. Szymanski IO. Ionized calcium during plateletpheresis. *Transfusion* 1978;18:701-8.
10. Olson PR, Cox C, McCullough J. Laboratory and clinical effects of the infusion of ACD solution during plateletpheresis. *Vox Sang* 1977;33:79-87.
11. Bunker JP, Bendixen HH, Murphy AJ. Hemodynamic effects of intravenously administered sodium citrate. *N Engl J Med* 1962;266:372-7.
12. Bell AM, Nolen JD, Knudson CM, Raife TJ. Severe citrate toxicity complicating volunteer apheresis platelet donation. *J Clin Apher* 2007;22:15-6.
13. Carlon GC, Howland WS, Goldiner PL, Kahn RC, Bertoni G, Turnbull AD, *et al.* Adverse effects of calcium administration. Report of two cases. *Arch Surg* 1978;113:882-5.
14. Bolan CD, Cecco SA, Yau YY, Wesley RA, Oblitas JM, Rehak NN, *et al.* Randomized placebo-controlled study of oral calcium carbonate supplementation in plateletpheresis: II. Metabolic effects. *Transfusion* 2003;43:1414-22.
15. Das SS, Chaudhary R, Khetan D, Shukla JS, Agarwal P, Mishra RB, *et al.* Calcium and magnesium levels during automated plateletpheresis in normal donors. *Transfus Med* 2005;15:233-6.
16. Callan MB, Appleman EH, Shofer FS, Mason NJ, Brainard BM, Groman RP, *et al.* Clinical and clinicopathologic effects of plateletpheresis on healthy donor dogs. *Transfusion* 2008;48:2214-21.