Calcium Supplementation in Blood Calcium Levels and Paresthesia Events in Thrombopheresis

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Abstract: The use of anticoagulants in the process of thrombopheresis aims to make the blood flow smoothly. In the use of anticoagulants citrate, it is necessary to pay attention to the occurrence of hypocalcaemia. Efforts are needed to minimise the impact of hypocalcaemia both arrhythmias and parasthesias during thrombopheresis by giving calcium tablets. The purpose of this study was to determine the effect of oral administration of Calcium tablets on blood calcium levels and the incidence of paresthesia in Thrombopheresis donors.This type of research is true experiment with pre posttest control group design. The treatment group was given calcium tablets before thrombopheresis and the control group was not given calcium tablets before thrombopheresis. All statistical analyses were performed using IBM SPSS for Windows, version 20 (IBM Corp, Armonk, NY, USA). Whereas categorical data were given as numbers and proportions, continuous variables were reported as the median and quartile. The correlation was discovered through binary logistics. It was deemed statistically significant when $P < 0.05$.Blood calcium levels between the two groups of results Analysis using independent T test showed no significant difference, namely p value 0.67. The incidence of paresthesias between the two groups, both groups that consumed calcium tablets and groups without calcium tablet consumption, from the results of the Chi-Square test showed a significant difference, namely p value 0.003.The conclusion in this study is that there is a significant difference in the average decrease in blood calcium between the group that consumes calcium tablets and the group that does not consume calcium tablets. The incidence of paresthesias There was a significant difference between the groups that consumed calcium tablets and the groups that did not consume calcium.

Keywords: Thrombopheresis, Hypocalcaemia, Paresthesia

INTRODUCTION

Blood transfusion is the transfer of blood from a donor to recipient who needs it. The blood transferred can be whole blood or part of the blood composition. Blood transfusion should be done efficiently and rationally, which means that the blood transfused to the patient only contains the components needed by the patient and other components can be donated to other patients who are more in need (Nelma & Purba, 2024).

Blood donation is the act of taking blood from someone voluntarily, stored in a blood bank and used for blood transfusion purposes. Thrombopheresis blood donation is a technique where all the blood

is removed from the body and one particular blood component is separated. Thrombopheresis technique allows the collection of certain desired blood cells in large quantities and can return the remaining unused blood cells (Schwartz et al., 2016). In thrombopheresis, the machine performs several cycles according to the desired number of platelets. During the thrombopheresis procedure, donor blood repeatedly (cycles) enters the extracorporal circulation(Connelly-Smith et al., 2023). For this reason, anti-coagulant citrate is required. The amount of citrate used depends on the number of cycles of extracorporal circulation (Cardinale et al., 2023)

Citrate anticoagulant is used to prevent clotting in the thrombopheresis device (Lokhande et al., 2021). In the use of citrate anticoagulants, it is necessary to pay attention to the amount of anticoagulant used, because in the administration of large amounts of citrate calcium can decrease significantly and symptoms such as muscle spasms, cardiac arrhythmias, nausea, vomiting and paresthesias will occur (Plasma Protein Therapeutics Association, 2012).

The impact of citrate anticoagulant use is certainly very disturbing for donors and can be a barrier for them to participate in repeated blood donation activities. Therefore, efforts to prevent or minimise the occurrence of hypocalcaemia and parasthesias in thrombopheresis donors are very important.

This study was conducted to explore the potential of calcium supplementation as an intervention to prevent the occurrence of hypocalcaemia and parasthesias in thrombopheresis donors. This study is expected to make a significant contribution in improving the safety and comfort of thrombopheresis procedures, as well as opening opportunities for the development of safer and more effective protocols in the management of thrombopheresis donors.

METHOD

This type of research is experimental research (true experiment) with pre posttest control group design.The treatment group is a group that is given calcium tablets before thrombopheresis and the control group is a thrombopheresis donor who is not given calcium tablets. This study was divided into two groups by random sampling, the sample size of each group was 16 people determined by the federer formula.

The independent variable in this study was oral administration of calcium tablets and the dependent variable was blood calcium level and paresthesia condition. The action of giving calcium tablets to the treatment group was carried out 30 minutes before thrombopheresis. The average amount of blood calcium levels examined in both groups who took calcium tablets and those who did not before and after thrombopheresis with units of mmol /L and data scale type ratio .

In the treatment group, 250 mg calcium tablets were given 1 hour before thrombopheresis. Before thrombopheresis, 3 ml venous blood was taken with a vacutainer tube. Then the venous blood sample was centrifuged for 15 minutes at 3000 rpm. After centrifugation, separate the serum into a test tube. The next step is to check calcium (ca+) with an electrolyte analyser. After thrombopheresis, 3 ml venous blood was taken again with a vacutainer tube. Then the venous blood sample was centrifuged for 15 minutes at 3000 rpm. After centrifugation, separate the serum into test tubes. and then calcium (ca+) was examined with an electrolyte analyser. The stages of data collection in the control group were the same as those in the treatment group, but the control group was not given 250 mg calcium tablets before thrombopheresis.

The results of the study were analysed using spps version 16. To determine the average difference in blood calcium reduction between the two groups used un paired t test. To analyse the difference in the incidence of tingling between the two groups, the Chi-Square test was used. It was deemed statistically significant when $P < 0.05$.

RESULTS

The results of univariate and bivariate analyses of differences in donor blood calcium levels before and after thrombopheresis in the treatment group and control group.

Characteristics of research respondents

The characteristics of respondents in the study presented data based on age, gender, body weight, haemoglobin levels, platelet levels, blood pressure. Data on the characteristics of respondents and the description of thrombopheresis actions are presented in table 4.1

Table 1:
Overview of research respondents and aphersis actions in the treatment group and in the control group
ket #: in thousands

Administratuon respondents	Characteristics of Calcium administration					Group without Calcium					*P-value*
	F	%	M	SD	min-max	F	%	M	SD	min-max	
Gender											
Male	15	93,6				16	100				0,94*
Female	1	6,2				0	0				
Age			44	8,7	32-59			41	1,1	21-56	0,58**
Blood presure:											
Systole			129,3	11,2	120-160			81,5	6,2		0.18***
Diastole			126,2	15,4	110-180			80	3,6		0.42***
Haemoglobin			14,8	0,85				14,6	1,04		0,39**
Platelets#			315	6.01	227-444			294	5.0	218-385	0.36**

* p value by Fisher's test

** p value with independent T test

*** p value by Mann-Whitney test

Table 1 shows that the majority of respondents in both group 1 and group 2 or both in the group who took Calcium tablets and in the group who did not take Calcium tablets were male. The average age of group 1 was 44 years and the age of group 2 was 41 years. The gender in group 1 and group 2 was mostly male, while blood pressure appeared in all groups within normal limits of both systole and diastole pressure. Haemoglobin levels in both groups both in the group that took Calcium tablets and in the group that did not take.

Calcium tablets were all within normal limits, while platelet levels in both groups were also within normal limits.

Table 1 also shows that the characteristics of respondents in both groups, both in the group that consumed Calcium tablets and in the group that did not consume Calcium tablets, were homogeneous or there was no significant difference as evidenced by the results of the difference test in both groups, all of which showed a P value 0.05 >.

a. Aphersesis action

The thrombopheresis action in both study groups described the thrombopheresis status including the routine of action, the duration of thrombopheresis action in hours and how many cycles of thrombopheresis in each study respondent both in the group that took calcium tablets and in the group that did not. taking Calcium tablets. Data on the description of thrombopheresis is presented in the following table.

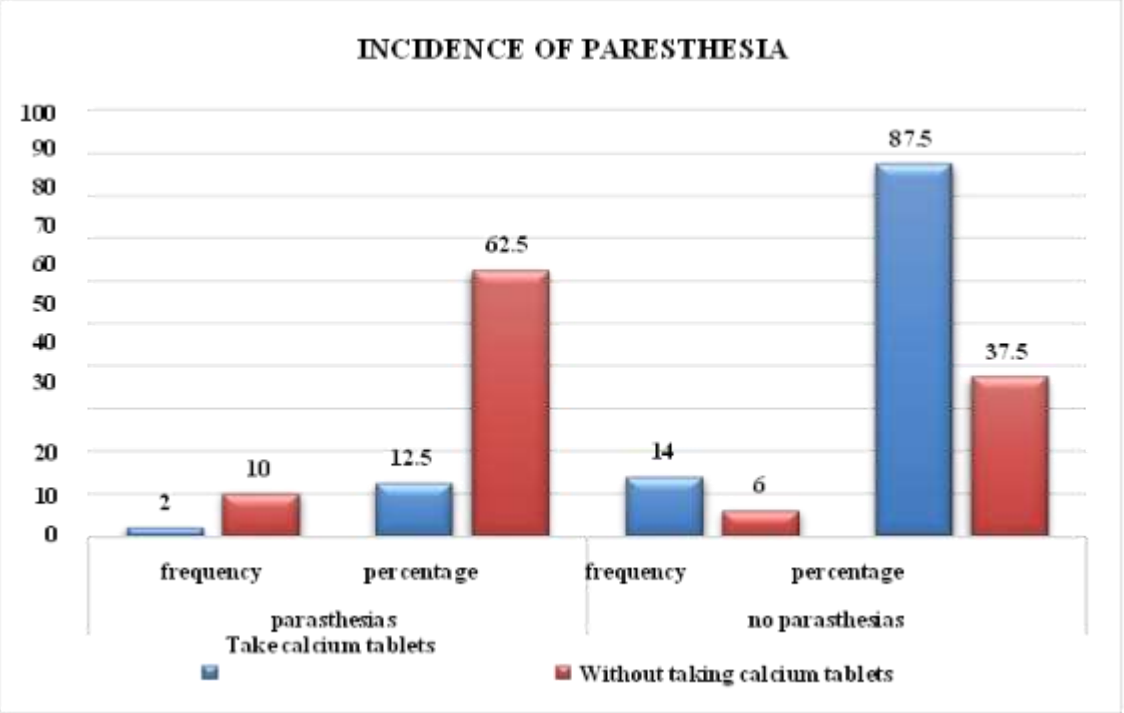
Table .2.
Overview of apheresis actions in the treatment group and in the control group at UDD PMI Semarang City (n = 32)

Trombopheresis Procedure	Calcium administration group					Without Calcium administration					P *value*
	F	%	M	SD	min-max	F	%	M	SD	min-max	
Trombopheresis Status											
Routine	13	40.6				15	46,9				0,81*
Not routine	3	9,4				1	3,1				
Thrombopheresis Cycle											
4 times	5	15,6				7	21,9				0,74*
5 times	10	3,12				8	25				
6 times	1	31,1				1	3.1				
Trombopheresis Duration											
1 hour	14	43,8				15	46,9				0.56*
1.5 hours	2	6,2				1	3,1				

ket # : in thousands
* *Fisher's* test p value

The description of thrombopheresis action shown in table 4.2 in all groups both in the group that consumed Calcium tablets and in the group that did not consume Calcium tablets the majority was carried out routinely. The thrombopheresis action cycle in both groups was mostly carried out 5 times, while for the duration of thrombopheresis action the majority in all groups was carried out for 1 hour. from table 1 it also appears that the characteristics of respondents of thrombopheresis action carried out in both groups are homogeneous as evidenced by the results of the difference test in both groups all show a P value of 0.05>.

Table .3. Overview of blood calcium levels of both groups at pre and post- treatment observation . (n: 32)



In the table 3, it can be seen that quantitatively there was an incidence of paresthesias in both groups, both the group that consumed calcium tablets and the group without calcium tablet consumption. the incidence of paresthesias in the group without calcium tablet consumption showed a greater percentage of 62.5% than the group that consumed calcium tablets, which was 12.5%.

b. Analysis of differences in mean blood calcium before and after apheresis in both groups.

Blood Calcium data is declared normally distributed with the results of the Shapiro Wilk test the p value > 0.05 was obtained, so to determine the average difference in the decrease in blood calcium levels in the two groups, an independent T test was used. The difference in blood calcium levels measured before and after thrombopheresis in both groups, both groups taking calcium tablets and groups without calcium tablet consumption, is presented in Table 4.

Table 4.
Mean difference of blood calcium level before and after thrombopheresis in both groups (n:32)

Group	Blood calcium levels before treatment (X ± SD)	Blood calcium levels after treatment (X ± SD)	P value
Take calcium tablets	1.04 ± 0.32	0.40 ± 0.43	0.00*
Without taking calcium tablets	1.16 ± 0.25	0.44 ± 0.35	0.00*

Description: (X ± SD) in mmol/L

* *Paired T test* results

,Table .4 shows that the significance value of the difference in blood calcium levels between before and after thrombopheresis in both groups, both groups that consume calcium tablets and groups without consumption of calcium tablets, presented all groups of the results of the dependent T test test showed a significant difference, namely p value 0.00.

c. Mean difference in blood Calcium reduction between groups

The data on the average decrease in blood calcium is normally distributed with the results of the Shapiro Wilk test obtained p value 0.67, so to determine the difference in the average decrease in blood calcium levels in the two groups using the independent T test. The results of the analysis of the average difference in the decrease in blood calcium levels in both groups both

groups that consume calcium tablets and groups without consumption of calcium tablets are presented in table 5.

Table 5.
Difference in mean reduction in blood calcium levels between the two groups (n:32)

Group	Calcium tablet consumption group	Group without Calcium tablet consumption	P value
	(X ± SD)	(X ± SD)	
Average decrease in blood calcium	0.60 ± 0.38	0.72 ± 0.39	0.67*

Description: (X ± SD) in mmol/L

* *un paired T test* results

Table 5 shows that the significance value of blood calcium levels between the two groups, both the group taking calcium tablets and the group without calcium tablet consumption, presented all groups from the independent T test results showed no significant difference, namely p value 0.67.

d. Difference in incidence of paresthesia

Data on the incidence of paresthesia in both groups, both groups taking calcium tablets and groups without calcium tablet consumption, are nominal data and there is no expectation value of less than 5 more than 20%, so to determine whether there is a difference in the incidence of paresthesias using the Chi-Square test. The results of the difference analysis are presented in table .6.

Table 6. Differences in the paresthesia between the two groups

parameter	Paresthesia incidence				P value
	Yes		no		
	F	%	F	%	
Take calcium tablet	2	12,5	14	87.5	
No calcium tablet consumption	10	62.5	6	37.5	0.003*

(n:32)

Description : * *Chi-Square test result*

Table .6 shows that the significance value of the incidence of paresthesias between the two groups, both the group taking calcium tablets and the group without calcium tablet consumption, from the results of the *Chi-Square* test shows a significant difference, namely *p value* 0.003.

DISCUSSION

As listed in table .1. from the results of the t-test showed that statistically the characteristics between the two groups, namely the group both the group that consumed calcium tablets and the group without calcium tablet consumption about data on age, gender, weight, haemoglobin levels, platelet levels and blood pressure values, there were no significant differences, so it can be said that the data characteristics of respondents were homogeneous.

Data on thrombopheresis measures contained in table 2 from the results of the t- test showed that statistically between the two groups, namely the group both groups that consume calcium tablets and the group without calcium tablet consumption about thrombopheresis status data, duration of thrombopheresis measures and thrombopheresis measures cycle there is no difference, so it can be said that the data characteristics of respondents are homogeneous.

In order to minimise bias in research, it is necessary to control variables that may interfere so that if there is a change in the dependent variable, the change can be ascertained as the effect of the independent variable. In this study, if there is a change in the parameters of blood calcium levels or the incidence of paresthesias, it can be controlled by the independent variable. was confirmed as a result of the Calcium tablet consumption treatment on the respondents.

The average picture of calcium levels before and after thrombopheresis action contained in table 4.3 shows that there is a significant decrease in calcium levels both quantitatively and from the statistical test results contained in table 4. with a p value of 0.00. Normal blood calcium levels in humans are 2.1 to 2.6 mmol/L(Kanagal, 2014). The decrease in blood calcium levels occurs due to the effect of using citrate to prevent blood clotting during thrombopheresis (Han et al., 2018) . In the process of preventing blood clotting, citrate works by binding calcium, precipitating calcium, or by inhibiting the formation of thrombin which is needed to convert fibrinogen into fibrin. Without fibrin forming, the blood clotting process does not occur. Prevention of blood clots during thrombopheresis is done so that the circulation of extracorporal blood through the tube on the thrombopheresis device remains smooth so that the process of separating blood components is not hampered.

The average decrease in blood calcium levelsin between thegroup taking calcium tablets and the group without calcium tablet consumption as stated in table 5 quantitatively showed greater in the group without Calcium consumption, but statistically there was no significant difference. This shows the administration of calcium tablets 30 minutes before thrombopheresis is not effective in minimising the decrease of blood calcium. This condition occurs because calcium absorption has not yet occurred from the gastrointestinal tract to the blood circulation. the absorption process requires from digestion to the blood circulation requires the activity of vitamin D and hormones so that it takes a long time. The process of calcium absorption takes a long time, possibly because the absorption process involves active vitamin D and the work of parathyroid hormone. In order for calcium to be reabsorbed from the intestine to the bloodstream, it requires the role of hormones.

Parathyroid and vit D in active form. The kidneys also play a role in the process of reabsorbing calcium10. Calcium is filtered by the glomerulus and then reabsorbed along the nephron. The majority of calcium is reabsorbed from the proximal tubules (>60%) via a paracellular pathway consisting of the tight junction proteins claudins-2 and -12, a process that is driven by sodium and consequent water reabsorption10 . The thick ascending ansa henle tubule reabsorbs the next largest amount of calcium (20-25%), also via a paracellular pathway consisting of claudins-16 and -191. This pathway is regulated by the calcium-sensing receptor (CaSR), whose activity increases the expression of claudin-14, a protein that blocks paracellular calcium reabsorption. Epithelial calcium channels (ECaCs) present in the apical membrane of nephron segments are responsive to 1,25-dihydroxyvitamin D3 and are calcium channels (Gallafassi et al., 2023).

The occurrence of a decrease in blood calcium in respondents after thrombopheresis certainly has an impact on the onset of paresthesias in the mouth and extremities. In table .6, the group that consumed calcium tablets and the group without calcium tablet consumption quantitatively showed that all of them had paresthesias and from the results of the Chi-Square test obtained a p value of 0.003, so it can be said that the group that did not consume calcium tablets experienced more tingling or paresthesias than the group that consumed calcium tablets. Paresthesia is a condition where a tingling sensation occurs.

Numbness in the area around the mouth and extremities indicating spontaneous nerve activation along sensory pathways from skin receptors (Carlsson et al., 2018). The onset of tingling in thrombopheresis donors is due to a decrease in blood calcium levels. Thrombopheresis performed on donors can cause paresthesias or tingling due to mild hypocalcaemia. Mild hypocalcaemia can cause complaints of tingling in the extremities and around the mouth

(Kaeley et al., 2021). The onset of paresthesias or tingling is due to hypocalcaemia so that the blocking effect of calcium ions on sodium ion channels also decreases. As a result, depolarisation of stimulable cells occurs faster and occurs in excess due to the amount of sodium that diffuses into the nerve cell intra. This increases the excitability of the nervous system and leads to muscle spasm and the onset of paresthesias or tingling (Burgoyne et al., 2019).

CONCLUSION

Based on the results of the study, it can be concluded that there is no significant difference in the average decrease in blood calcium between the group taking calcium tablets and the group not taking calcium tablets with a p value of 0.67. The incidence of paresthesias There was a significant difference between the groups that consumed calcium tablets and the groups that did not consume calcium with a p value of 0.003.

Conflict of Interest

I declare that there is no conflict of interest in this study. I have no financial or non-financial affiliations with pharmaceutical companies, medical device manufacturers, or other institutions that have an interest in the results of this study.

Acknowledgment

The author would like to thank all those who have provided support and assistance during this research process.

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