INDONESIAN JOURNAL OF
CLINICAL PATHOLOGY AND MEDICAL LABORATORY
Majalah Patologi Klinik Indonesia dan Laboratorium Medik

PAGE 144
2023 March; 29(2): 144-149
p-ISSN 0854-4263 e-ISSN 2477-4685
Available at www.indonesianjournalofclinicalpathology.org

A Comparative Study of PTS and Manual Transportation for Platelet Count and Aggregation Test

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ABSTRACT

The transportation effect of the Pneumatic Tube System (PTS) on platelet activity remains controversial. This study aimed to analyze the effect of PTS in the platelet aggregation test in Dr. Cipto Mangunkusumo Hospital, Jakarta. This cross-sectional study was carried out in the Clinical Pathology Laboratory of Dr. Cipto Mangunkusumo Hospital (RSUPNCM) from March to April 2021. There were 50 subjects involved in this study, each of whom 6 sodium citrate blood tubes were extracted. Three tubes were sent through PTS while the rest were transported manually. All tubes were then tested for platelet count and platelet aggregation using ADP agonists of 1 µM, 5 µM, and 10 µM. There was a lower platelet count (p=0.046) and platelet aggregation in ADP 1 µM (p=0.037), ADP 5 µM (p <0.001), and ADP 10 µM (p <0.001) at PTS-transported samples. Eleven samples were interpreted distinctively as low platelet aggregation in PTS transportation became normal in manual delivery. Cohen's Kappa value was 0.51 (p <0.001). A decreasing platelet count and platelet aggregation in PTS samples indicated that acceleration and deceleration during transportation could lead to platelet activation, thus resulting in a lower result after being added to an agonist. Cohen's Kappa test showed that manual transportation could not be replaced with PTS for the platelet aggregation test. Platelet count and platelet aggregation were found to be lower in PTS-transported samples. It was suggested to centralize specimen taking for platelet aggregation tests, thus manual transportation can be conducted more efficiently.

Keywords: Pneumatic tube system, platelet aggregation, manual transportation

INTRODUCTION

A pneumatic Tube System (PTS) is a transportation system using pneumatic tubes in hospitals, which provides fast interconnection among units and has been widely used to transport samples to laboratories, thereby reducing sample delivery time and turnaround time in the laboratory. During transportation, various physical factors such as rapid acceleration, deceleration, and the radial gravitational force received by the sample can cause preanalytical stage problems, such as hemolysis, cell damage, and activation, which can affect the analysis results.[1]

Problems in the preanalytic stage still occur in the hemostasis test, including during sampling, sample transportation, and sample storage. Transport through PTS in hemostasis studies has been investigated and yielded contradictory results. According to Lorenzen et al., sample acceleration and deceleration in PTS affect platelet function. A platelet function test can be carried out by analyzing its aggregation.[1] Several studies demonstrated decreased platelet aggregation in samples transported via PTS and recommended manual transport for this assay, while other studies found no effect of PTS transport on platelet aggregation assays.[1]

This study was performed to determine the influence of PTS compared to manual transportation on the platelet count and platelet aggregation at the Clinical Pathology Laboratory of RSUPNCM.

METHODS

This study used a cross-sectional design conducted at the Clinical Pathology Laboratory of RSUPNCM from March 2021 to April 2021. The target population was the general population at RSUPNCM. The research subjects were students of Specialist Medical Education and laboratory staff at the Department of Clinical Pathology, Faculty of Medicine, University of Indonesia (FKUI)/RSUPNCM who met the inclusion criteria. The inclusion criteria in this study were all research subjects aged 20-60 years, adult age according to the World Health Organization (WHO), and were willing to fill out informed consent. The exclusion criteria in this study

were patients without fasting for at least 8 hours before sampling, clotted, lysed, insufficient blood sample, patients who smoked within 30 minutes before sampling, and patients whose platelet count was less than 100,000/µL in samples transported by manual delivery.[2] Calculation of the sample size was determined based on the regulation by Clinical and Laboratory Standards Institute (CLSI) EP09-A3, which required a minimum sample size of 40 to analyze the comparison between the two methods.[3] The sample size in this study was set at 50 samples. The accuracy test carried out was a within-run test 5 times in a row from one normal subject on the same day. The basic data on the characteristics of the research subjects such as age and gender were taken from the National Identity Card (KTP). Blinding was not implemented in this study because the type of data was objective data obtained from measurements following the research flow in Figure 1.

A platelet aggregation test was carried out to analyze the function of platelets by using ADP agonists with concentrations of 1 M, 5 M, and 10 M. The test used a whole blood sample from a vein which was collected in a 3 mL tube containing 0.109 M Na citrate anticoagulant in 6 tubes with Na citrate: blood equal to 1:9. Three tubes were sent via PTS and the remaining three tubes were sent via manual delivery and were then analyzed within 30-120 minutes.

First, Platelet Rich Plasma (PRP) was prepared by centrifuging the blood at a speed of 1000 rpm or 100 g for 15 minutes and then the plasma obtained was transferred to a cuvette of at least 1500 L, the platelet count was analyzed using a Sysmex XN-1000 hematology analyzer. The PRP platelet count should be 200,000-300,000/L; a platelet count of less than 100,000/L will lead to difficult to determine an optical baseline. Furthermore, the remaining blood in the citrate tube was centrifuged again at 2400 g for 20 minutes and was then transferred to a 500 L cuvette as Platelet Poor Plasma (PPP).[4]

Platelet aggregation test was carried out using a Chrono-Log 490 aggregator with the Turbidimetric method according to Born based on changes in light transmission as shown in Figure 2. Before the addition of agonists, PRP light transmission was low because platelets were still homogeneously suspended. After the addition of an agonist, platelets undergo primary aggregation, then the aggregate releases endogenous ADP, which causes secondary aggregation and precipitates, leading to the production of clear plasma and increased light transmission as described in Figure 3. The biological

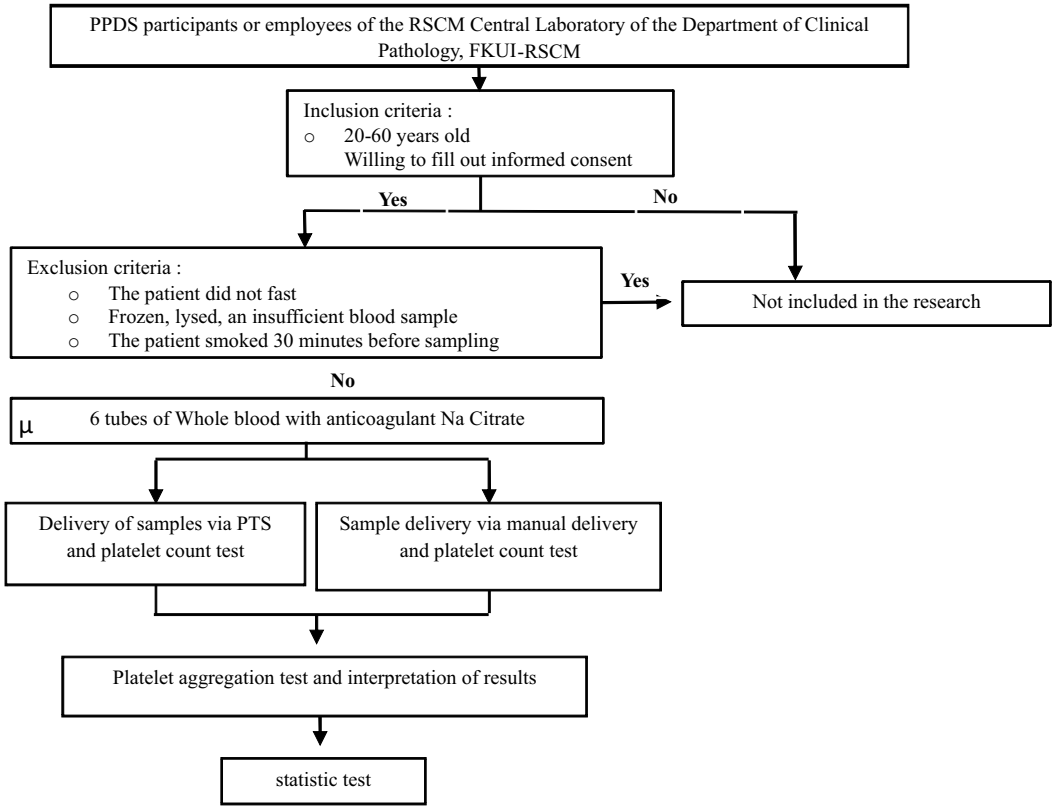

Figure 1. Research flowchart

reference value for ADP 1 M was 3-15%, ADP 5 M was 25-68%, and ADP 10 M was 49-84%.[4]

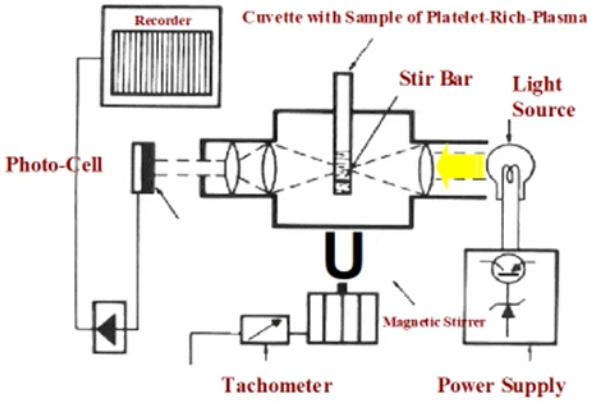

Figure 2. The working principle of the light transmission device according to Born[5]

The PTS is a transportation system for distributing goods between units using tubes, consisting of a sending station and a receiving station connected by a pressurized pipeline, as shown in Figure 4. At the sending and receiving stations there are blowers or air pumps as well as sounds or lights, which flash to signal when a tube has just been received. The blower can suck air from the tube or blow air into it according to the needs of the tube delivery direction, the tube movement speed is determined by the blower force, the stronger the suction force or the blower thrust force, the faster the tube movement. Its speed can reach 10 m/s, equivalent to 5-6 times faster than walking.[6]

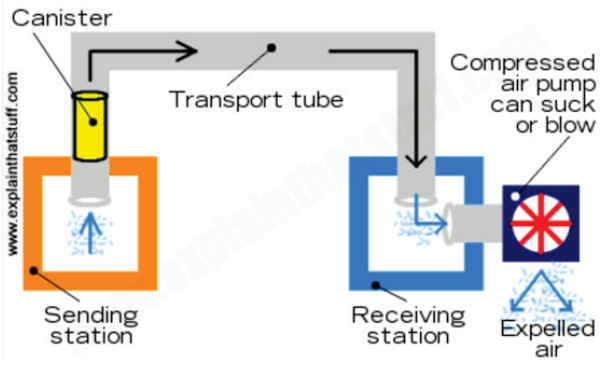

Figure 4. Pneumatic tube system[6]

The Clinical Pathology Laboratory of RSUPNCM uses the PTS Aerocom AC3000 fully automatic system in which users do not need to search for the address of the destination station but simply place a tube carrier on the sending panel, each of which connects each station. The PTS speed used is 3-4 m/s from all stations and the return speed to all stations is 6-8 m/s, the speed can be changed as needed. Speed is affected by the load of the sample being sent, a maximum of 2.5 kg. The size of the system used is Outside Diameter 110 (OD 110), i.e., the pipe diameter at the PTS is 110 mm. The sample receiving line uses rails to reduce impact when the tube carrier containing the sample arrives. The length of the PTS line at the 24-hour laboratory counter to the Clinical Pathology Laboratory RSUPNCM is 75 m.[7] Manual delivery is a method of sending samples by courier on foot from each counter to the Clinical Pathology laboratory using a sample storage box without ice cubes, the sample is in a position vertically at room temperature.

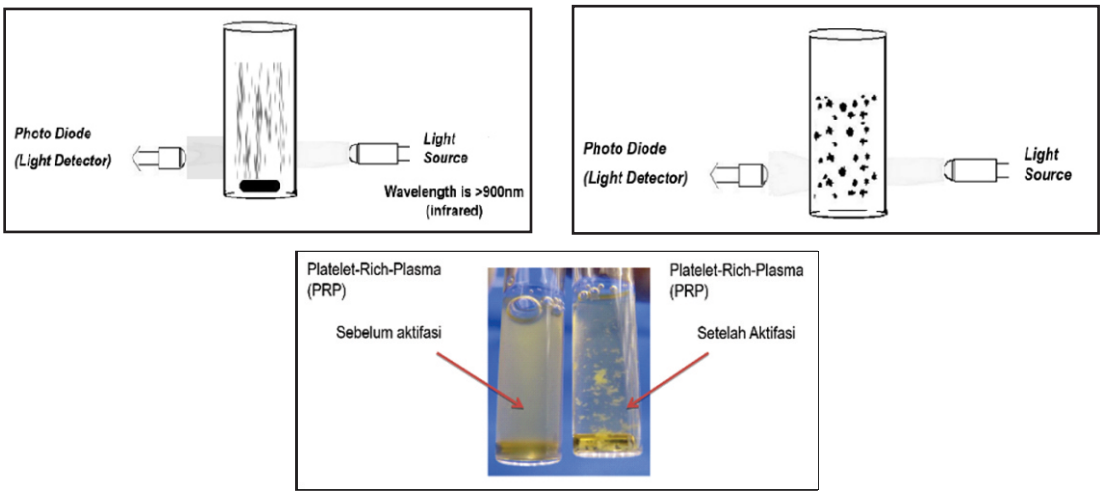

Figure 3. (A) Illustration of PRP sample before the addition of agonist, low light transmittance. (B) Illustration of PRP sample after addition of agonist, light transmittance increases. (C) PRP samples before and after the addition of agonist

Data processing was carried out using the SPSS version 25 program. The accuracy test was used to determine the average value, standard deviation, and Coefficient of Variation (CV). Numerical variables were tested for normality to determine the distribution of data using the Saphiro-Wilk test because the number of samples was < 50. Numerical data were presented in mean and standard deviation if the data distribution was normal or median and the minimum maximum value if the data distribution was not normal. If the data distribution is normal, then the mean difference between the examination results of the samples sent by PTS and manual submissions can be assessed by paired T-test. If the data distribution is not normal, then the difference between the two means can be analyzed by the Wilcoxon test. The Kappa test was conducted to assess the suitability of the interpretation of platelet aggregation results between samples sent via PTS and manual delivery.

This research has been approved by the Research Ethics Committee of the Faculty of Medicine, University of Indonesia/Cipto Mangunkusumo Hospital with the number KET-113/UN2.F1/ETIK/ PPM.00.02/2021.

RESULTS AND DISCUSSIONS

The results of the within-run platelet aggregation accuracy test using ADP 1, 5, and 10 M agonists can be seen in Table 1.

A total of 50 subjects who met the inclusion criteria were included in this study consisting of 12 (24%) males and 38 (76%) females with a median age of 34 years. The description of the characteristics of the subject can be seen in Table 2.

Table 2. Characteristics of research subjects

Characteristics	n=50
Age	34 (26-57)
Gender	
Male	12 (24%)
Female	38 (76%)

The mean platelet count and platelet aggregation with ADP agonists 1, 5, and 10 M in samples transported via PTS and manual delivery can be seen in Table 3.

The results of the Saphiro-Wilk test results showed that data of platelet count and platelet aggregation with ADP 1, 5, and 10 M in samples transported by PTS and manual delivery were not normal (p>0.05). The mean platelet count and platelet aggregation with ADP 1, 5, and 10 M were presented in the median form (min–max) and followed by the Wilcoxon test. Wilcoxon test results showed p < 0.05, which indicated that there was a significant difference between the mean platelet count and platelet aggregation results with ADP 1, 5, and 10 M in samples transported by PTS and manual delivery.

Table 1. In-run accuracy test of platelet aggregation against ADP 1, 5, and 10 M in the clinical pathology laboratory of RSUPNCM

Test	ADP 1 µM (%)	ADP 5 µM (%)	ADP 10 µM (%)
1	0	32	70
2	0	22	61
3	0	28	78
4	0	45	71
5	0	29	71
Mean	0	31.2	70.2
SD	0	8.5	6.1
CV (%)	0	27.3	8.6

Table 3. Mean platelet count, and platelet aggregation results with ADP 1, 5, and 10 M in samples transported by PTS and manual delivery

Parameter	Transportation		Difference in Results	p-value
	PTS	Manual		
Platelet count (x 10^3/µL)	230.5 (54–329)	242.5 (105–323)	7.5 (-87–159)	0.046
ADP 1 µM (%)	0 (0–11)	1 (0–12)	0 (-5–9)	0.037
ADP 5 µM (%)	15.5 (0–88)	25 (0–72)	6 (-24–43)	<0.001
ADP 10 µM (%)	35 (0–84)	60 (1–88)	9.5 (-24–50)	<0.001

Table 4. Interpretation of platelet aggregation results with ADP 1, 5, and 10 M in samples transported by PTS and manual delivery

Interpretation of Platelet Aggregation Results with ADP 1, 5, and 10 µM	Transportation	
	PTS	Manual
Low platelet aggregation	31 (62%)	20 (40%)
Normal platelet aggregation	19 (38%)	30 (60%)
High platelet aggregation	0	0

Table 5. The results of the Kappa suitability analysis of platelet aggregation in samples transported by PTS and manual delivery

		Platelet aggregation test results with PTS			Total	Kappa	p-value
		Low	Normal	High			
Platelet aggregation test results with manual delivery transport	Low	20	0	0	20	0.51	<0.001
	Normal	11	19	0	30		
	High	0	0	0	0		
	Total	**31**	**19**	**0**	**50**		

The interpretation of platelet aggregation results was divided into 3, such as low, normal, and high platelet aggregation. In samples transported by PTS, 31 subjects had low platelet aggregation and 19 subjects had normal platelet aggregation. These results were different from the samples transported by manual delivery, which showed 20 subjects with low platelet aggregation and 30 subjects with normal platelet aggregation as shown in Table 4. There were 11 samples with different interpretations: from low platelet aggregation in PTS transport to normal platelet aggregation on manual transport. Kappa analysis was carried out on the interpretation of platelet aggregation results and showed a sufficient level of Kappa suitability (Kappa=0.510; p < 0.01), as shown in Table 5.

The within-run accuracy test on the Chrono-Log 490 aggregator obtained a CV of 0% at 1 M ADP, 27.3% at 5 M ADP, and 8.6% at 10 M ADP. Overall, the CV obtained was better when compared to the research conducted by Wirawan.[4] The results of 0% CV at 1 M ADP showed that the instrument consistently gave 0% results on the same sample for 5 measurements. At 5 M ADP obtained a CV of 27.3%, this CV variation was greater when compared to research conducted by Wirawan, which reported a CV variation of 13.2%. At 10 M ADP obtained a CV of 8.6%, this result was relatively better compared to research conducted by Wirawan, which was 12.1%.[4] Platelet aggregation test with the principle of changes in light transmission is the gold standard; however, there is no commercial control available to check the validity of the test results, which results in a variable CV in some studies.[5]

This study did not analyze the characteristics of the research subjects. There was a significant decrease in the platelet count in the samples sent via PTS with a p-value of 0.046. This was similar to a study by Subbarayan *et al.* in India with a total of 75 research subjects, which reported a significant decrease in the platelet count in samples sent via PTS with a p-value of <0.001.[8]

Thalen *et al.* found a decrease of up to 20% in platelet aggregation results in all samples transported by PTS compared to manual transport with p < 0.001.[1] This was similar to several results, which found that there was a significant decrease in platelet aggregation in all concentrations of ADP and the most significant decrease in ADP 5 M and 10 M with p-values of both <0.01. The lower platelet aggregation results in PTS indicate that the acceleration and deceleration that occurs during sample delivery can trigger platelet activation, which results in lower platelet aggregation in samples sent via manual delivery when an agonist is added.

The results of the Kappa suitability analysis for platelet aggregation showed sufficient suitability of 0.51. The Kappa value, which is considered good and can replace each other is > 0.8. These results prove that the manual transportation method is not good when it is replaced with PTS in the platelet aggregation test. There were 11 samples (22%) that had contradictory results of the platelet aggregation test, namely from low platelet aggregation in samples through PTS to normal platelet aggregation in samples sent via manual delivery.

This difference in the platelet aggregation test result has a large enough impact to influence clinical decision-making, especially in patients being monitored for anti-platelet therapy, as revealed by Lorenzen *et al.*, and Magnette *et al.* also mentioned that the use of PTS significantly affects platelet function testing, rapid acceleration, and deceleration can cause excessive vibration, protein denaturation and result in hemolysis, platelet activation, and other effects.[1,9] The study stated that clinical decisions regarding platelet function and aspirin response should not be based on samples sent by PTS.

The PTS system used by other hospitals has different specifications; it cannot be assumed that the effect on platelet function will be the same. Some literature states that reducing PTS speed can reduce the risk of platelet activation due to the force that PTS exerts on the sample.

CONCLUSIONS AND SUGGESTIONS

There was a significant reduction in platelet count and platelet aggregation with ADP agonists 1, 5, and 10 M in PTS-delivered samples compared to manual delivery. The Kappa suitability test for platelet aggregation results showed sufficient suitability between samples sent via PTS and manual delivery, indicating that the PTS delivery method could not replace manual delivery for platelet aggregation testing. It was suggested that the sampling process for the platelet aggregation test was centered at only 1 counter to make efficient human resources to carry out manual deliveries.

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