JRSSEM 2023, Vol. 03, No. 01, 189 – 202
E-ISSN: 2807 - 6311, P-ISSN: 2807 - 6494

EFFECT OF SHELF LIFE ON IL6 AND CD62P THROMBOSITE CONSENTRATE LEVELS (EXPERIMENTAL STUDY AT UDD PMI SEMARANG CITY)

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Abstracts: **Background:** Thrombocyte concentrate is a blood product that is labile and easily damaged by its blood cells. Storage time is expected to cause changes in several conditions so that it will affect the quality of TC which can affect levels CD62P and levels *interleukins 6* (IL-6). **Objective:** The purpose of this research is to determine the effect of the length of storage of thrombocyte concentrate (TC) on IL-6 levels and CD62P levels in UDD PMI Semarang City. **Methods:** This research is research *experimental*, where this study analyzes how changes in levels IL-6 and CD62P levels on TC based on length of storage at PMI Semarang Blood Donor Unit. The research design was divided into groups on day 0, day 1, day 3, day 5 and day 7. Population in this study were 5 TC bags produced and stored at the PMI Blood Donor Unit in Semarang City. The research sample consisted of 5 TC bags using purposive sampling technique. IL-6 levels were analyzed using the ELISA method. Examination of CD62P Levels use flow cytometer device. IL-6 levels were tested differently using repeated ANOVA and continued with the LSD Post Hoc test to show differences between groups ($P<0.05$). For CD62P, the data were analyzed using the Friedman test and followed by the Wilcoxon test to show differences between groups ($P<0.05$). **Results:** The research results show that the lowest levels of IL-6 and CD62P in TC were found on day 0 and the highest levels of IL-6 and CD62P in TC were found on day 7. Analysis of differences in IL-6 and CD62P levels between TC storage on day 0, day 1, day 3, day 5, and day 7 showed significant results except on day 3. **Conclusion:** The effect shown was the increase in IL-6 and CD62P levels.

Keywords: CD62P, IL-6, storage time, thrombocyte concentrate

INTRODUCTION

Thrombocyte concentrate (TC) is a blood component that contains platelets, some leukocytes, and red blood cells, as well as plasma. Clinicians use TC to treat a wide range of diseases, and many clinicians want TC products with a shelf life of less than 3 days, so many TC products are wasted. Regulation of the minister of health (Permenkes) No. 91 of 2015 explains that the safe storage time of TC used is 5 days with a closed system and 4 hours with an open system. So far, there's been

no research to prove the long-standing safe storage of TC. The limited storage time of TC is due to the risk of contamination by bacteria, and during the storage process of platelets, they are susceptible to environmental changes that can affect quality and are known as platelet storage lesions. The blood component of TC remains awake and functioning properly when stored for 5 days, and after that, it will gradually lose the viability and function of the platelets during its storage (Armenia & Tambunan, 2020).

Thrombocyte concentrate (TC) ranks second in terms of blood product requirements requested by clinicians. This is due to Indonesia being a dengue-endemic country. Given the importance of platelets and their benefits in therapy, the availability of TC is very necessary. The PMI Blood Donor Unit has the capacity and authority to produce TC blood components. The PMI Blood Donor Unit in Semarang City produces around 10,000–15,000 bags per month, and 40% of them are TC products. Platelet concentrate is a blood product that is labile and easily damaged by its blood cells; therefore, TC is a blood component that needs to be watched out for due to the processing conditions of its component products through a long process, namely centrifugation twice. Storage time is expected to cause changes in several conditions that will affect the quality of TC. Platelet cells survive at a temperature of 20°C-24°C with storage on an agitator to prevent platelet clumping in the plasma (Aubron et al., 2018).

Platelet quality can be seen from the proportion of activated platelets, and platelet damage can be seen by looking at the activation of platelets in TC. The number of activated platelets can be known and measured from several parameters, one of which is measuring CD62P levels in platelet concentrate. Poor TC quality will increase post-transfusion risks such as thrombosis. In in vitro conditions, the quality of TC is strongly influenced by the length of storage; some conditions that will occur will reduce the quality of TC. In vitro, the coagulation process affects inflammatory activity, resulting in up-regulation of pro-inflammatory cytokines. To determine this, interleukin 6 (IL6) levels can be examined (Anggini et al., 2019).

Previous studies examined the effect of TC storage duration on pH, glucose, LDH, and calcium levels, but no one has studied IL6 and CD62P levels in TC. The results of these studies prove a decrease in TC quality characterized by a decrease in platelet count and an increase in the value of mean platelet volume (MVP). In addition, the longer the storage time, the lower the pH levels, glucose levels, LDH levels, and calcium levels (Samad et al., 2014). Testing the effect of platelet shelf life is needed in order to estimate the best product quality and shelf life needed to be transfused to patients. Research and testing were conducted to determine the effect of TC storage time on the

number of IL6 levels and CD62P levels so as to determine the maximum storage time limit.

Interleukin-6 (IL6) is one of a group of pro-inflammatory cytokines that may be used as an indicator to assess the level of inflammation experienced by vascular endothelial cells. IL-6 circulates in multiple glycosylated forms with sizes varying between 22 and 27 kDa. Elevated serum IL-6 levels can lead to downregulation of NO production by inhibiting endothelial nitric oxide synthase (eNOS), thereby facilitating thrombus formation and consequently increasing the risk of cardiovascular disease events. Elevated levels of inflammatory markers are associated with endothelial dysfunction and are used to identify patients with more severe conditions (Arif, 2017).

IL-6 levels are elevated in patients with obesity and insulin resistance and correlate well with BMI. IL-6 is mainly secreted by adipocytes, especially from visceral adipose tissue, which produces two to three times more IL-6 compared to subcutaneous adipose tissue. IL-6 production is increased by adipose tissue during obesity. The increase in fatty acids and IL-6 through the hepatic circulation results in increased hepatic lipid accumulation, contributing to the development of atherosclerotic lesions through paracrine, autocrine, and endocrine effects. IL-6, a potent proinflammatory cytokine produced by several cell types, including activated macrophages, T cells, endothelial cells, and smooth muscle cells, to stimulate the immune response during infection (Squires, 2015), has been recognized as a potential marker associated with cardiovascular disease events.

Interleukin-6 (IL-6) plays a role in increasing the titer of anti-platelet and anti-endothelial antibodies. This increase in anti-platelet antibody titer is related to platelet damage. Changes in platelet quality can have an impact on platelet viability and decrease hemostasis function. The mechanism leading to a platelet storage lesion is multifactorial and not clearly understood. Several factors, including the method of blood tapping, component manufacturing process, storage, and manipulation after blood tapping, can lead to a platelet storage lesion.

Serum IL-6 levels may increase with age. At the age of 65 to 74, the average IL-6 level is 1.4pg/ml in men and 1.1pg/ml in women. At the age of over 85, the average IL-6 level in men was 3.5pg/ml and 2.1pg/ml in women. The age-related increase in IL-6 levels is due to stimulation of IL-6 production related to an increase in the number of oxygen free radicals. Another cause is the disruption of normal regulation of gene expression that regulates IL-6 production (Fauzan et al., 2020). The link between gender and IL-6 levels stems from several studies showing that decreased production and levels of

steroid hormones in the circulation cause mild pro-inflammatory conditions in the elderly. For example, dehydroepiandrosterone hormone (DHEA) and GHEA sulfate have a negative correlation with serum IL-6 levels and inhibit IL-6 secretion from mononuclear cells. Thus, the relationship between gender and IL-6 levels is related to the sex hormones produced by the body. Menopausal women will experience an increase in IL-6 levels. Estrogen therapy in menopausal women will reduce IL-6 levels in the circulation (Qu et al., 2014). Smoking can trigger IL-6 production by leukocytes. IL-6 has an important role in the synthesis of CRP and other acute-phase proteins by the liver. IL-6 also has different characteristics from other cytokines because most of them are in the circulation (Fatiah, 2017). IL-6 has an important role in the pathogenesis of hypertension through the angiotensin II (ANG II) pathway (Fernanda & Sa'adi, 2019). Elevated IL-6 is a risk factor for type 2 DM in healthy people. IL-6 also affects glucose metabolism in the body by causing increased basal glucose uptake and altering insulin sensitivity (Amalia, 2022). IL-6 has a role in the pathogenesis of coronary heart disease and is closely associated with atherosclerosis. High IL-6 levels are associated with mortality in patients with acute coronary syndrome (Slichter et al., 2019).

ELISA (enzyme-linked immunosorbent assay) is a biochemical technique widely used in the field of immunology to detect the presence of antibodies or antigens in a sample. ELISA was introduced in 1971 by Peter Perlmann and Eva Engvall to analyze the interaction of antigens with antibodies in a sample using enzymes as label reporters. There are several types of ELISA techniques, namely: (1) indirect ELISA; (2) direct ELISA; (3) sandwich ELISA; (4) multiplex ELISA; and (5) biotin streptavidin ELISA.

The function of an ELISA examination is not only to determine the presence of an antigen with an antibody but also to measure the level of the antigen or antibody using a spectrophotometer. A spectrophotometer is a device that can measure the amount of light that penetrates the well of the microplate. The antigen-antibody complex that occurs in the microplate well and, after the administration of the substrate, the enzyme bound to the second antibody in the antigen-antibody complex formed will give a color change in the liquid, so that it will have a different optical density. Optical density can be expressed as an increase or decrease based on the dilution of standard material, so that it will produce a dose-response curve that will be used to estimate the levels in the sample (Ghartimagar, 2017). Measurement of IL-6 levels or concentrations can be done with the ELISA test.

P-selectin (CD62P), which is a 140 kD protein found inside platelet alpha granules and Weibel-Palade bodies of endothelial cells, is a member of the

selectin family of adhesion molecules, which plays an important role in reproduction and hemostasis. CD62P is released from the cell surface and circulates as a soluble molecule in plasma. Both membrane and soluble forms of p-selectin are agonists of thrombosis and inflammatory processes. Furthermore, P-selectin (CD62P) can support platelets and platelet interactions and plays an important role in the early stages of inflammation, thrombosis, and atherosclerosis by mediating plaque formation and progression.

Thrombocyte concentrate (TC) is a blood component that contains platelets, some leukocytes, and red blood cells, as well as plasma. Optimal storage of TC should be maintained at a temperature range of 20°C to 24°C with agitation. TC components are obtained in two ways: platelets obtained from whole blood (single whole blood) and platelets obtained from the apheresis system (Ariani et al., 2021).

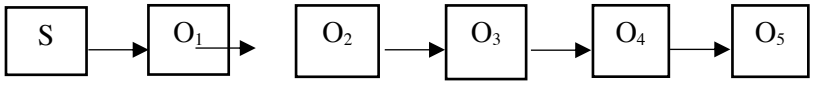
TC factors are pH, storage temperature, plasma volume in TC, length of storage, agitation during storage, lactic acid accumulation in TC, anticoagulants used in WB collection, blood bags used, and TC preparation methods to be studied. While factors for the recipient include the age of the recipient, gender, splenectomy, the presence of bleeding, fever, infection, disseminated intravascular coagulation (DIC), the presence of lymphocytotoxin antibodies, recipients receiving heparin or amphotericin therapy, and an increased frequency of platelet transfusions (Tong et al., 2015).

Therefore, in accordance with the description above, the general objective of this study was to determine the effect of storage time of thrombocyte concentrate (TC) on IL6 levels and CD62P levels at UDD PMI Semarang City. While the specific objectives are: (1) To determine IL6 levels and CD62P levels on TC days 0, 1, 3, 5, and 7, (2) To analyze the differences in IL6 and CD62P levels between the immediate TC storage on days 1, 3, 5, and 7.

METHODS

This type of research is experimental, and this research will analyze changes in IL6 and CD62P levels in TC based on the length of storage in the Semarang City PMI Blood Donor Unit. The research design was divided into groups of days 0, 1, 3, 5, and 7 from five TC bags.

This research was conducted in several places, namely: (1) UDD PMI Semarang City. (2) Faculty of Medicine, Public Health, and Nursing, Gadjah Mada University (FK-KMK UGM), Yogyakarta, and (3) Faculty of Medicine, UNISSULA Semarang. This research was conducted from June 8, 2023, to June 15, 2023.



S = Sample
O_1 = Observation Day -0
O_2 = Observation Day-1
O_3 = Observation Day-3
O_4 = Observation Day-5
O_5 = Observation Day-7

Figure 1. Schematic of Research Design

Figure caption:

S = Samples in the form of TCs totaled five bags and were taken by purposive sampling.

O1 = Observation of IL6 and CD62P levels on day 0

O2 = Observation of IL6 and CD62P levels on day 1

O3 = Observation of IL6 and CD62P levels on day 3

O4 = Observation of IL6 and CD62P levels on day 5

O5 = Observation of IL6 and CD62P levels on day 7

The population in this study was 5 bags of TC produced and stored at the Semarang City PMI Blood Donor Unit. The samples in this study were TCs produced at the Semarang City PMI Blood Donor Unit on June 8, 2023.

The determination of sample size in this study was done using the purposive sampling technique, where sampling is based on certain considerations made by the researcher himself. Permenkes No. 91 of 2015 states that quality control of blood products is carried out on 1% of total blood products. UDD PMI Semarang City produces approximately 500 blood products per day. So that the sample taken in this study was 5 TC bags. The TC criteria used were as follows: (1) TC with negative HIV, Hepatitis B, Hepatitis C, and Syphilis test results using the CLIA method. (2) TC without hemolysis. (3) TC that was prepared on June 8, 2023.

The research tools used for this study are: (1) a platelet incubator. (2) Platelet agitator (3) 1000uL pet. (4) Microtube. (5) ELISA tool (6) Flowcytometry tool. Also, the flowcytometry used was optimized for platelet acquisition with logarithmic signal amplification in forward and side scatter of 200. For analysis, gates were made on predetermined platelet areas with the addition of anti-CD41. The data was presented as the percentage of platelets that positively expressed CD62P. The materials used are: (1) TC. (2) IL6 ELISA KIT (3) CD62P flowcytometry KIT.

TC was taken in as many as five bags on the day when it was produced and testing was completed. The TC that

has been obtained is stored in a platelet incubator at a temperature of 22^0C–24°C with agitation 60 times per minute, which aims to make the TC mixture homogeneous and ensure no platelet aggregation occurs. The platelet agitator is placed in a platelet incubator and is in an air-cooled room equipped with a thermometer as a temperature monitor. The temperature in the platelet incubator is set to remain at 22^0C–24^0C, and samples are taken by: (1) TC bag sample. (2) The hose on the TC bag is sealed to separate the sample in the hose from the entire suspension in the TC bag, then cut at the sealed hose connection to get the TC sample in the hose. (3) Transfer the TC sample from the hose to the microtube for examination. (4) The TC sample in the microtube is used for examination of IL6 and CD62P levels.

The procedure for determining IL6 levels is as follows: (1) Samples are taken from the TC bag and then placed in a microtube. (2) TC samples in the microtube are taken using a micropipette. (3) Place the sample on the microwell as much as 75 ul using a micropipette. (4) analysis was performed using the ELISA method. The procedure for determining CD62P levels is as follows: (1) Samples that have been taken from the TC bag hose are collected into a microtube. (2) Take 18 ul samples from the microtube, 5 ul anti-CD62P PE, or anti-IgG PE control, and incubate for 20 minutes at room temperature in a dark room. (3) The labeled TC samples were immediately fixed using 1 mL of 1% (w/v) paraformaldehyde at room temperature for 30 min. (4) For flow cytometry analysis, 5,000 platelet cells were analyzed using CellQuest software.

Data obtained in the examination of IL-6 levels were analyzed using descriptive tests, normality, and homogeneity. Data were normal and homogeneous ($P > 0.05$), different tests used repeated anova, and the post hoc LSD test continued to show differences between groups ($P<0.05$). In CD62P, data were analyzed using descriptive, normality, and homogeneity tests. The results of the normality analysis of the data distribution are not normal, and the homogeneity test results obtained $P > 0.05$, which means homogeneous, then a different test using the Friedman test, and continued with the Wilcoxon test to show the difference between groups ($P<0.05$).

RESULTS

This study was conducted for 7 days on June 8–15, 2023, using a sample of 5 TC bags. The study was conducted at the Clinical Pathology Laboratory of the Faculty of Medicine, Public Health, and Nursing, Gadjah Mada University, Yogyakarta. Each TC bag came from a male donor with an age range of 24–30 years. Each patient had no history of comorbidities such as diabetes mellitus, hypertension, heart disease, or smoking.

Each TC sample was examined for IL6 and CD62P levels on days 0, 1, 3, 5, and 7. During the study, all TC bags were given the same treatment, namely storage in a platelet incubator with a temperature of 22°C–24°C and agitation 60 times per minute. The results of this study were obtained by reading the results of IL-6 and CD62P levels and obtaining the following results:

Content IL-6

Analysis of IL-6 levels carried out includes descriptive analysis by presenting the mean value and standard deviation (SD), analysis of the normality of data distribution with the Shapiro-Wilk test, analysis of homogeneity of variance with Mauchly's test of sphericity, and analysis of the results of the average IL-6 levels using the repeated anova test.

Table 1. Mean IL-6 levels based on shelf-life along with the results of normality, homogeneity and independent samples tests.

Content IL-6 (pg/mL)	Shelf life (days)					*p-value*
	0	1	3	5	7	
Average±SD	4,34±0,81	5,78±0,47	5,36±0,65	7,59±0,77	10,71±1,62	
Shapiro Wilk*	0,964	0,485	0,258	0,251	0,365	
Mauchly's test of sphericity						0,302
Repeated anova						<0,001

The results showed that the highest IL-6 level at 7 days of shelf life was 10.71 ± 1.62 pg/mL and the lowest IL-6 level at day 0 TC was 4.34 ± 0.81 pg/mL. The Shapiro-Wilk test of IL-6 levels at the fifth examination time obtained a value of $p > 0.05$, which means that the data on IL-6 levels are normal. IL-6 levels in the five measurements were also homogeneous, as shown by Mauchly's test of sphericity getting a value of $p > 0.05$. The requirements for normal data distribution and homogeneity of variance were met so that the comparison of mean IL-6 levels between the five measurements was analyzed by repeated anova tests and obtained a value of $p < 0.001$ so that it was stated that there was a significant difference in mean IL-6 levels between the length of TC storage on days 0, 1, 3, 5, and 7. Significant differences in mean IL-6 levels in five replicate measurements were further analyzed by the LSD post hoc test, and the results were obtained as shown in Table 2.

Table 2. Comparative analysis of mean IL-6 levels between two shelf-life periods

Shelf life	H0	H1	H3	H5	H7
H0	-	0,001*	0,089	0,002*	0,002*
H1	0,001*	-	0,277	0,012*	0,004*
H3	0,089	0,277	-	0,021*	0,002*
H5	0,002*	0,012*	0,021*	-	0,008*
H7	0,002*	0,004*	0,002*	0,008*	-

The comparison of mean IL-6 levels between the two shelf-life periods was almost all significant, as indicated by the p value of the LSD post hoc test, each $p<0.05$; except for the comparison between the shelf-life of day 0 and day 1 with the shelf-life of day 3, which is indicated by the p values of 0.089 and 0.277, respectively ($p > 0.05$). The results of this LSD post-hoc test showed that the length of storage had a significant effect on IL-6 levels. The effect shown is to increase IL-6 levels. The length of storage that affects the increase in IL-6 levels is the length of storage for 1, 5, and 7 days. A shelf life of 7 days resulted in the highest increase in IL-6 levels compared to shelf lives of 1 and 5 days. Meanwhile, the shelf life of 3 days had no effect on IL-6 levels.

Content CD62P

Analysis of CD62P levels carried out includes descriptive analysis by presenting the mean value and standard deviation (SD), analysis of the normality of data distribution with the Shapiro-Wilk test, analysis of homogeneity of variance with Mauchly's test of spericity, and analysis of the results of the average CD62P levels using the Friedman test.

Table 3. Mean CD62P levels based on shelf-life along with the results of normality, homogeneity and independent sample t-tests

Content CD62P (%)	Shelf life (days)					*p-value*
	0	1	3	5	7	
Average±SD	13,54±9,48	10,06±6,50	20,92±8,50	40,02±9,09	70,84±4,76	
*Shapiro Wilk**	0,408	0,811	0,041	0,385	0,279	
Mauchly's test of spericity						0,842
Friedman test						0,001

The results showed that the highest CD62P level was at the 7-day shelf life of 70.84 ± 4.76%, while the lowest was at the 1-day shelf life of 10.06 ± 6.50%. In the Shapiro-Wilk test of CD62P levels at the fifth time of examination, a value of $p > 0.05$ means that the IL-6 level data is normal, except for the measurement on day 3, which got a p value of 0.041 ($p <0.05$) which means that the CD62P level on day 3 is not normal. CD62P levels in the five measurement replicates were found to

be homogeneous, as indicated by the p value of Mauchly's test of spericity of 0.842 or p > 0.05.

Efforts to transform the data of CD62P levels on day 3 measurements have been made, but the distribution of the data obtained remains abnormal because it gets a p value of 0.034 (p <0.05). The requirements for normal data distribution in each group were not all met, so the comparison of the mean CD62P levels between the five measurement replicates was analyzed by the Friedman test and obtained a value of p = 0.001, which stated that there was a significant difference in the mean CD62P levels between the TC storage times of day 0, day 1, day 3, day 5, and day 7. Significant differences in mean CD62P levels in five replicate measurements were further analyzed with the Wilcoxon test, and the results are presented in Table 4.

Table 4. Comparative analysis of mean CD62P levels between two shelf-life periods

Shelf life	H0	H1	H3	H5	H7
H0	-	0,080	0,225	0,043*	0,043*
H1	0,080	-	0,043*	0,043*	0,043*
H3	0,225	0,043*	-	0,043*	0,043*
H5	0,043*	0,043*	0,043*	-	0,043*
H7	0,043*	0,043*	0,043*	0,043*	-

The comparison of the mean CD62P levels between the two shelf-life periods was almost all significant, as indicated by the p value of the Wilcoxon test with a value of p <0.05, except for the comparison between the shelf-life of day 0 with day 1 and day 3, which was shown with a value of p > 0.05. The Wilcoxon test results show that shelf life has a significant effect on CD62P levels. The effect shown is to increase CD62P levels. The length of storage that affects the increase in CD62P levels is the length of storage on days 5 and 7. The 7th-day shelf life resulted in higher CD62P levels than the 5th-day shelf life. Meanwhile, the shelf lives of days 1 and 3 had no effect on CD62P levels.

DISCUSSION

The results of the examination of IL-6 levels on the shelf life of day 0 with day 1, day 0 with day 5, and day 0 with day 7 show significant differences, while on day 0 with day 3 and day 1 with day 3 there are no significant differences. The results of the examination of CD62P levels on the shelf life of day 0 with day 5, and day 0 with day 7 show a significant difference, while on day 0 with day 1 and day 0 with day 3 there is no significant difference.

CD62P levels increased until day 5 of storage but decreased on day 3. This is related to the reversible platelet activation process on the first day due to

the platelet concentrate preparation process; then, during storage, platelet activation occurs, so that CD62P levels on the platelet surface are high. During storage until the third day, there is continuous platelet activation, and after the third day, CD62P levels relatively decrease, possibly because most platelets have been activated on the third day of storage. Activated platelets will then lose CD62P on their surface but will go to the soluble form of CD62P in the plasma. Some studies suggest measuring soluble P-selectin levels as a marker of platelet activation to detect degranulated platelets, although the increased concentration in plasma may also be due to the release of CD62P from damaged endothelial cells (Herawati, 2020).

Platelets contained in TCs undergo various changes during TC collection, processing, and storage, which lead to changes in platelet structure and function and can reduce the effectiveness of TC transfusion. These changes are known as platelet storage lesions. This damage to platelets during storage causes loss of platelet function integrity, changes in the aggregation process and platelet granule release reaction, changes in the cytoskeleton of platelets, exposure of phosphatidyl serine on the outer surface of the platelet membrane, and microvesiculation (Sperling et al., 2019a). In addition, prolonged TC storage causes increased platelet activation due to conditions different from the in vivo activation environment, also influenced by platelet apoptosis in vitro, or due to other cell death processes and aging. Old platelets are usually cleared from the circulation by the spleen and liver, but old platelets in stored concentrates remain and can alter the activation state of residual platelets through the release of soluble mediators and cell-to-cell interactions (Masfufatun et al., 2018).

Shelf life also affects CD62P levels. Similar research was also shown by Tong et al. who stated that the concentration of CD62P in TC afferents increased during storage time (Tong et al., 2015). Similar results were also shown by Sperling et al. that CD62P increased during storage of buffy coat-derived platelet concentrates (BCP) and platelet afferents. The increase in CD62P occurs due to the degranulation of platelet α-granules (Sperling et al., 2019b).

Platelet quality can be seen from the proportion of activated platelets, and platelet damage can be seen by looking at the activation of platelets in TC. The number of activated platelets can be known and measured from several parameters, one of which is measuring CD62P levels in TC. CD62P levels are inversely correlated with an increase in platelet count and function. Exposure to CD62P on the platelet surface during TC storage triggers platelet clearance through CD62P, so it is said that CD62P can act as a marker of platelet activation (Qu et al., 2014). This

study is in line with the research of Samad et al., which states that TC storage for seven days cannot maintain platelet count stability and is recommended for further research.

CONCLUSSION

Based on the results of the research that has been done, it can be concluded that: (1) The lowest levels of IL-6 and CD62P in TC were found on day 0. (2) The highest levels of IL-6 and CD62P in TC were found on day 7. (3) Analysis of differences in IL-6 and CD62P levels between TC storage on days 0, 1, 3, 5, and 7 obtained significant results except on day 3. The effect shown was an increase in IL-6 and CD62P levels. The authors declared that there is no potential conflicts of interest to the research, authorship, and/or publication of this article. The author would like to impress of gratitude for all the all parties who have contribute in completion this research.

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