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Editorial Adress:
d/a Laboratorium Patologi Klinik RSUD Dr. Soetomo, Gedung Diagnostik Center Lt. IV
Jl. Mayjend. Prof. Dr Moestopo 6–8 Surabaya, Indonesia
Telp/Fax. (031) 5042113, 085-733220600 E-mail: majalah.ijcp@yahoo.com, jurnal.ijcp@gmail.com
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RESEARCH

ANALYSIS OF ERYTHROCYTE INDICES IN STORED PACKED RED CELLS AT THE BLOOD BANK OF DR. WAHIDIN SUDIROHUSODO HOSPITAL

(Analisis Indeks Eritrosit Darah Simpan Packed Red Cells di Bank Darah RSUP Dr. Wahidin Sudirohusodo Makassar)

Fitrie Octavia, Rachmawati Muhiddin, Mansyur Arif

ABSTRAK

Komponen darah Packed Red Cells (PRC) sering ditransfusikan kepada pasien dengan petunjuk untuk memperbaiki dan mempertahankan sebaran oksigen ke jaringan. Eritrosit mengalami perubahan metabolik selama masa penyimpanan kantong darah PRC di Bank Darah yaitu deplesi 2,3-diphosphoglycerate (DPG) dan Adenosine Triphosphat (ATP) yang juga disebut dengan jejas penyimpanan dan disebabkan oleh penurunan pH darah, peningkatan kepekatan kalium dan laktat. Tujuan penelitian ini untuk mengetahui pengaruh penyimpanan terhadap indeks eritrosit pada darah simpan PRC di Bank Darah. Penelitian deskriptif potong lintang dilakukan masa waktu Februari hingga April 2015 dengan menggunakan 35 sampel darah simpan PRC yang disimpan dan batal ditransfusikan lalu diperiksa nilai indeks eritrositnya dengan menggunakan alat Hematology Analyzer Sysmex XT-2000i pada hari pertama (hari-1), keempat (hari-4) dan ketujuh (hari-7) penyimpanan di Bank Darah RSUP Dr. Wahidin Sudirohusodo Makassar. Hasil uji statistik Friedman didapatkan perbedaan bermakna di semua tolok ukur indeks eritrosit pada hari pertama, keempat dan ketujuh penyimpanan. Lanjutan dengan Uji Post Hoc Wilcoxon didapatkan perbedaan bermakna tolok ukur MCV antara hari-4 dan hari-7 (p=0,000), hari-1 dan hari-7 (p=0,001); MCH antara hari-1 dan hari-7 (p=0,018); MCHC antara hari-1 dan hari-4 (p=0,000), hari-4 dan hari-7 (p=0,002), hari-1 dan hari-7 (p=0,000); RDW antara hari-1 dan hari-4 (p=0,011), hari-4 dan hari-7 penyimpanan (p=0,004). Hasil Penelitian ini menunjukkan nilai indeks eritrosit darah simpan PRC mengalami perubahan bermakna dari hari pertama hingga ketujuh penyimpanan di Bank Darah walaupun nilai indeks eritrosit semua tolok ukur masih dalam batas normal.

***Kata kunci**: Indeks eritrosit, darah simpan, packed red cells, jejas penyimpanan*

ABSTRACT

The blood components such as, Packed Red Cells (PRC) are frequently transfused to patients with indications to improve and maintain oxygen distribution to body tissues. Erythrocytes in stored PRC blood bag subjects undergo metabolic changes during the storage time in the blood bank, including depletion of 2,3-diphosphoglycerate (DPG) and Adenosine Triphosphate (ATP), also called storage lesion caused by decreased blood pH, increased concentration of potassium and lactate. This study was aimed to find out the effect of storage time on erythrocyte indices of stored PRC in blood bank. A descriptive cross-sectional study was conducted from February until April 2015 and involved 35 samples of stored PRC that was kept and cancelled for transfusion. Erythrocyte indices of stored PRC were evaluated using Hematology Analyzer Sysmex XT-2000i at day 1, day 4 and day 7 of storage in the blood bank of the Dr. Wahidin Sudirohusodo Hospital Makassar. Friedman test results showed statistical significant differences in all erythrocyte indices parameters at day 1, day 4 and day 7 of storage. Further analysis with Post Hoc Wilcoxon test showed statistically significant differences for MCV parameter between day 4 and day 7 (p=0.000), day 1 and day 7 (p=0.001); MCH between day 1 and day 7 (p=0.018); MCHC between day 1 and day 4 (p=0.000), day 4 and day 7 (p=0.002), day 1 and day 7 (p=0.000); RDW between day 1 and day 4 (p=0.011), day 4 and day 7 of storage (p=0.004). Study results indicated that erythrocyte indices of stored PRC were altered significantly from the first day to seventh day of storage in blood bank, even though the erythrocyte indices of all parameters remained within normal range.

Key words: Erythrocyte indices, stored blood, packed red cells, storage lesion

Department of Clinical Pathology, Faculty of Medicine, University of Hasanuddin- Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia. E-mail: fitieoctavia@gmail.com

INTRODUCTION

Blood transfusion is a process of transferring blood or blood components from donors to recipients in order to improve oxygen transport, enrich platelet count, or advance blood clotting as required. Blood transfusion can be classified into three types based on the length of storage. First, fresh blood is blood six hours after collection. Second, new blood is blood from six hours to six days after collection. The last, stored blood is blood saved at an optimum temperature for more than six days after collection. The temperature set for storing blood components, from 2°C to 6°C, should always be monitored.[1,2]

Anticoagulant usually used for blood bags is Citrate Phosphate Dextrose Adenine (CPDA-1), as much as 49 mL for 350 mL of complete blood. In 100 mL of CPDA-1, there are 0.299 g of Citric Acid (anhydrous), 2.63 g of Sodium Citrate (dehydrate), 0.222 g of Monobasic Sodium Phosphate (monohydrate), 3.19 g of Dextrose (monohydrate) and 0.0275 g of Adenine. The citrate compound contained in the blood bag is useful to prevent coagulation by binding calcium in the plasma of donors. Meanwhile, phosphate serves as a buffer for maintaining blood pH and preventing a decrease in 2.3 Diphosphoglycerate (DPG). The 2.3 DPG serves to facilitate erythrocyte function as an oxygen transporter. Furthermore dextrose, is also added to the blood bag to meet the energy demands of cells acting as substrates for producing ATP. Meanwhile, adenine works for the regeneration of Adenosine Triphosphate (ATP) so that blood stored at 2–6°C can last up to 35 days since collection.[1,3–5]

One of the most commonly supplied blood components for improving and maintaining oxygen distribution to tissues is Packed Red Cells (PRC). Packed red cells contains erythrocyte cells that have been separated from Whole Blood by apheresis process or centrifugation process. The blood bag is centrifuged with a special centrifuge to separate the solid part from the blood. Afterwards, the centrifuged plasma is passed into the satellite blood bag so that only erythrocytes and little plasma remain. A PRC unit contains 100–125 mL of complete blood. As a result, blood should be concentrated to achieve a hematocrit concentration of 70–80%, hemoglobin level of 42.5–80 g/dL and Fe level of 147–287 mg in hemoglobin. A PRC unit may increase Hb level in adults, about 1 g/dL or 3%, as well as in neonates with an administration dose of 10–15 mL/kg BW.[2,3]

In addition, erythrocyte indices are values illustrating erythrocyte characteristics in terms of size, content and concentration. Erythrocyte indices consist of four indicators. First, Mean Corpuscular Volume (MCV) describes the mean of erythrocyte volume showing the size of erythrocytes expressed in units of femtoliter (fL). Second, MCH illustrates the mean of hemoglobin per erythrocytes expressed in picogram (pg). Third, Mean Corpuscular Hemoglobin Concentration (MCHC) depicts the concentration of hemoglobin per erythrocytes expressed in hectogenous (gr/dL). Fourth, Red Cell Distribution Width (RDW) indicates results of quantitative measurements of variations in erythrocyte volume, representing microscopic examination to determine the degree of anisocytosis.[6]

The values of erythrocyte indices are obtained from a direct calculation using an automatic tool, whereas the values of MCV, MCH, MCHC and RDW are obtained from an equation using a semi-automatic tool. There are four equations used. First, MCV is obtained by dividing hematocrit (%) with the number of erythrocytes (million/μL), multiplied by 10 and then expressed in femtoliter (fl) with a reference value of 82–92 fl. Second, MCH is obtained by dividing hemoglobin (gr/dL) with the number of erythrocytes (million/μL), multiplied by 10 and then expressed in picogram (pg) with a reference value of 27–31 pg. Third, MCHC is obtained by dividing hemoglobin (gr/dL) with hematocrit (%), multiplied by 100 and then expressed in gr/dL with a reference value of 32-37 g/dL. Fourth, RDW can be calculated in the form of RDW Standard Deviation (SD) and Coefficient of Variation (CV). Red cell distribution width SD is obtained by calculating the histogram of erythrocyte size distribution, while RDW CV is obtained by dividing 1 SD with MCV, multiplied by 100 and then expressed in percent (%).[6,7]

During the storage time, PRC in the Blood Bank can experience structural and functional changes. Erythrocytes experience metabolic changes due to different atmospheres with in vivo, namely decreased density of Adenosine 5'-triphosphate (ATP) and 2,3 Diphosphoglycerate (DPG), decreased blood pH, increased potassium and lactate concentration, erythrocyte cell changes, erythrocyte vitality lost and hemolysis.[8,9]

Blood care time at the Blood Bank of the Dr. Wahidin Sudirohusodo Hospital is for 3 (three) days and can be extended once for 3×24 hours. Blood is usually deposited at the Blood Bank of the Dr. Wahidin Sudirohusodo Hospital for the preparation of surgeries. Unfortunately, there are still many cancelations in blood transfusion, leading to increased number of wasted blood bags. As a result, many researches are interested in examining the erythrocyte indices of stored PRC to reveal whether the quality of transfused

venous blood stored is still feasible to be administered to other patients by re-performing a cross-match test procedure for finding new recipients. A previous research performed by Sugiarta and Soemarsono found that the Complete Blood Count (CBC) parameter of blood stored in a refrigerator for 24 hours did not change significantly. Meanwhile, other previous researches conducted by Berenzina, Zaets, Morgan, Spillert, Kamiyama, Spolarics, *et al.*[10] showed that there were significant changes in erythrocyte form, starting in the second week of the storage.[10,11] Therefore, this research aimed to reveal changes in erythrocyte indices of stored blood during storage timee in refrigerator at the Blood Bank of the Dr. Wahidin Sudirohusodo Hospital in Makassar.

METHODS

This research was an observational research with a cross-sectional approach conducted from February to April 2015. The population of this research was all PRC taken from blood stored at the Blood Bank of the Dr. Wahidin Sudirohusodo Hospital in Makassar. Samples of this research were all PRC taken from blood, both stored and canceled for transfusion. The number of samples obtained was thirty-five samples taken from one of the PRC blood bag lobes and then inserted into tubes to examine their erythrocyte indices on the first day (day-1), the fourth day (day-4) and the seventh day (day-7). Next, the erythrocyte indices were examined using a Sysmex XT-2000i Hematology Analyzer. Afterwards, data obatined were analyzed using a SPSS statistic program with Friedman test, continued with Post-Hoc Test. Results of the analysis then were displayed in tables and graphes, as well as interpretated.

RESULTS AND DISCUSSION

This research was conducted at the Blood Bank of the Dr. Wahidin Sudirohusodo Hospital in Makassar from February to April 2015. This research collected thirty-five samples of PRC taken from blood, both stored and canceled for transfusion. Table 1 showed the characteristics of stored blood based on blood type.

The data in Table 1 showed that the blood samples consisted of 11 samples classified into A blood type (31.4%), 8 samples classified into B blood type (22.8%), 13 samples classified into O blood type (37.1%) and 3 samples classified into AB blood type (8.57%).

The data in Table 2 showed the results of the erythrocyte indices examined on PRC of blood stored

Table 1. Characteristics of the research samples

Variables		n (35)	%
Blood type	A	11	31.4
	B	8	22.8
	O	13	37.1
	AB	3	8.57

Table 2. The mean erythrocyte indices on the first, fourth and seventh days of the storage time at the blood bank

Erythrocyte indices (n=35)		Mean (SD)	p Value
MCV (fl)	Day-1	85.64 (6.54)	0.000
	Day-4	86.22(6.71)	
	Day-7	86.97 (6.68)	
MCH (pg)	Day-1	28.11(2.66)	0.035
	Day-4	27.76 (2.14)	
	Day-7	27.70 (2.08)	
MCHC (gr/dL)	Day-1	32.95 (1.65)	0.0000
	Day-4	32.19 (1.11)	
	Day-7	31.84 (1.09)	
RDW (%)	Day-1	15.39 (2.64)	0.010
	Day-4	15.71 (2.63)	
	Day-7	15.47 (2.56)	

* Friedman Test

at the blood bank on the first, fourth and seventh days. The mean erythrocyte indices of MCV parameters were 85.64±6.54 on the first day, 86.22±6.71 on the fourth day and 86.97±6.68 on the seventh day. The results of the Friedman test then indicated a statistically significant difference (p=0.000). On the other hand, the mean erythrocyte indices of MCH parameters were 28.11±2.66 on the first day, 27.76±2.14 on the fourth day and 27.70±2.08 on the seventh day. The results of the Friedman test also indicated a statistically significant difference (p=0.035).

Moreoever, the mean erythrocyte indices of MCHC parameters were 32.95±1.65 on the first day, 32.19±1.11 on the fourth day and 31.84±1.09 on the seventh day. The results of the Friedman test showed a statistically significant difference (p=0.000). Meanwhile, the mean erythrocyte indices of RDW parameters were 15.39±2.64 on the first day, 15.71±2.63 on the fourth day and 15.47±2.56 on the seventh day. The results of the Friedman test also showed a statistically significant difference (p=0.010).

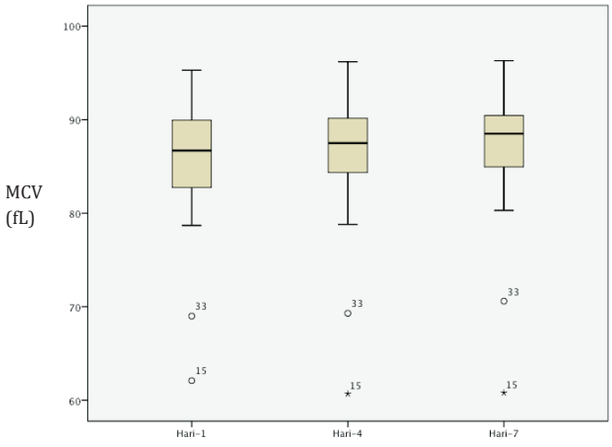

Figure 1. Comparison of MCV and PRC values of the stored blood between day-1 and day-4 (p=0.062); between day-4 and day-7 (p=0.000); as well as between day-1 and day-7 (p=0.001)

The comparison of MCV and PRC values of the stored blood on the first day, fourth day and seventh day of the storage timee was presented in Figure 1. Results of the Post-hoc test showed that there was no statistically significant difference in MCV values between day one and day four (p=0.062). Nevertheless, there were statistically significant differences in MCV values between day four and day seven (p=0.000), as well as between day one and day seven (p=0.001).

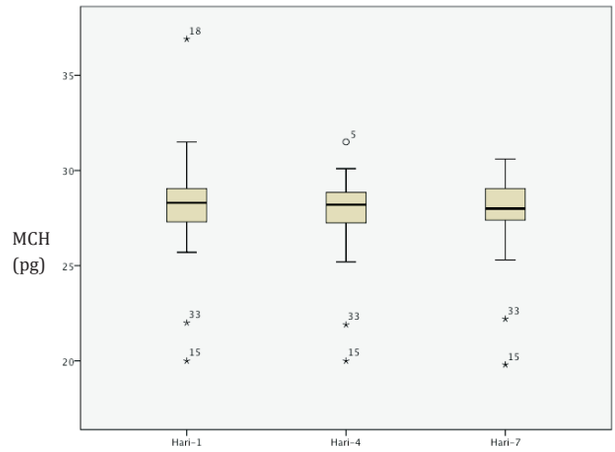

Figure 2. Comparison of MCH and PRC values of the stored blood between day-1 and day-4 (p=0.157); between day-4 and day-7 (p=0.483); as well as between day-1 and day-7 (p=0.018)

The comparison of MCH and PRC values of the stored blood on the first day, fourth day and seventh day of the storage timee was illustrated in Figure 2. Results of the Post-hoc test indicated that there was no statistically significant difference in MCH values between day one and day four (p=0.157). However, there were statistically significant differences in MCH values between day four and day seven (p=0.483), as well as between day one and day seven (p=0.018).

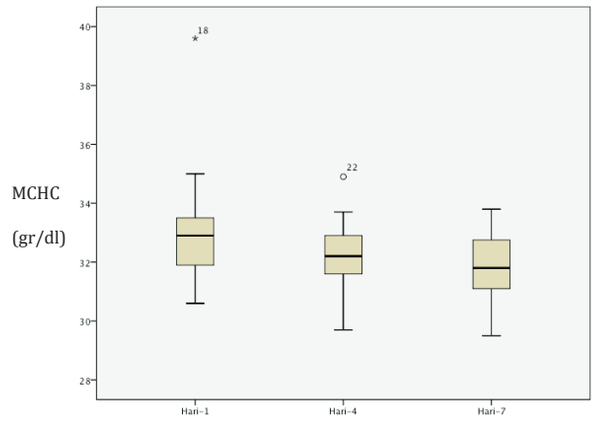

Figure 3. Comparison of MCHC and PRC values of the stored blood between day-1 and day-4 (p=0.000); between day-4 and day-7 (p=0.002); as well as between day-1 and day-7 (p=0.000)

The comparison of MCHC and PRC values of the stored blood on the first day, fourth day and seventh day of the storage timee was depicted in Figure 3. Results of the Post-hoc test revealed that there was no statistically significant difference in MCHC values

between day one and day four (p=0.000). Nevertheless, there were statistically significant differences in MCHC values between day four and day seven (p=0.002), as well as between day one and day seven (p=0.000).

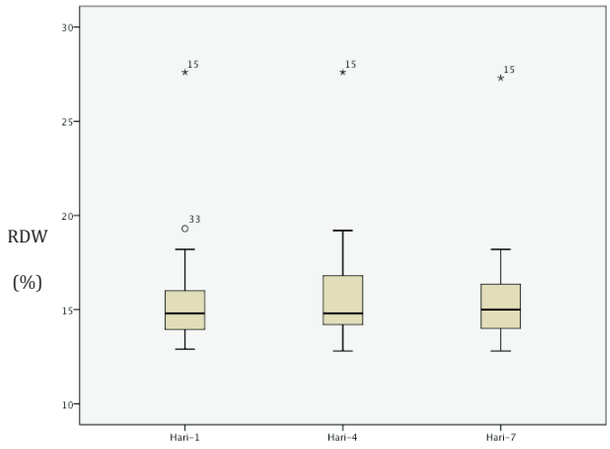

Figure 4. Comparison of RDW and PRC values of the stored blood between day-1 and day-4 (p=0.011); between day-4 and day-7 (p=0.004); as well as between day-1 and day-7 (p=0.851)

The comparison of RDW and PRC values of the stored blood on the first day, fourth day and seventh day of the storage timee was demonstrated in Figure 4. Results of the Post-hoc test showed that there was no statistically significant difference in RDW values between day one and day four (p=0.011). However, there were statistically significant differences in RDW values between day four and day seven (p=0.004), as well as between day one and day seven (p=0. 851).

In addition, this research evaluated PRC of thirty-five blood bags, both stored and canceled for blood transfusion in the Blood Bank of the Dr. Wahidin Sudirohusodo Hospital. The values of the erythrocyte indices were evaluated on the first, fourth and seventh day of the storage time at the blood bank. Changes in the erythrocyte indices then were compared between the first day and the fourth day, between the fourth day and the seventh day, as well as between the first day and the seventh day. The results showed that there were statistically significant differences in all parameters of erythrocyte indices, namely MCV (p=0.000), MCH (p=0.035), MCHC (p=0.000) and RDW (p=0.010).

Moreover, the results of this research also indicated an increase in the MCV values of the stored blood PRC as the length of the storage time. From day one to day four of the storage time, there was no significant difference in the MCV values (p=0.062). But, from day four to day seven, the MCV values increased. Thus, there was a significant difference in MCV values between the fourth day and the seventh day (p=0.000) as well as between day one and day seven (p=0.001). On the other hand, MCH and MCHC values in this research declined as the length of the storage time. There was a significant difference in MCH values between the first day and the seventh day (p=0.018). Similarly, there was a significant difference in MCHC values between the first day and the seventh day (p=0.000). Unlike MCH and MCHC values, RDW values increased from the first day to the fourth day of the storage time (p=0.011), but then significantly decreased from the fourth day to the seventh day (p=0.004).

These biochemical changes during the storage time are related to changes in energy metabolism, namely depletion of 2,3-diphosphoglycerate (DPG) and Adenosine Triphosphate (ATP), also called as storage lesion. Erythrocytes rely heavily on the process of glycolysis to meet energy needs, whereas erythrocytes stored at 4°C will slow down metabolism, decline ATP production and then decrease the function of erythrocytes. A research conducted by D'Alessandro *et al.*[12] even showed that on the first seven day, there was an increase in the process of glycolysis characterized by increased levels of fructose 1.6 diphosphate metabolite, glyceraldehyde-3-phosphate, total diphosphoglycerate, Nicotinamide Adenine Dinucleotide (NAD +) and ATP. However, after seven days, the levels decreased due to a decrease in pH and lactic acid formation which was, very influential in declining erythrocyte function by activating phosphatase. As a result, diphosphoglycerate mutation occurs, namely enzyme dephosphorylating 2,3-DPG, resulting in decreased 2,3-DPG levels serving to help the transport of oxygen and the release of oxygen into the tissue.[12]

In maintaining vitality of erythrocytes as well as potassium sodium pump, ATP is required. However, during storage time in refrigerator, ATP level will decrease, thus, stimulating the potassium sodium pump of erythrocytes to balance the levels of intracellular and extracellular ions, which will gradually release potassium out of the cell and move sodium into the cells. Consequently, changes occur in cell volume and morphology. Thus, the values of MCV in PRC of the stored blood will increase during storage due to erythrocyte swelling and cytoskeleton weakening, also caused by decreased ATP and oxidation processes. The decreased cell integrity during storage can also cause

hemolysis so that the hemoglobin in the erythrocytes will come out and the concentration will decrease, indicated by decreased MCH and MCHC values in stored blood as the length of storage time. Next, the erythrocyte membrane becomes unstable, resulting in changes in the erythrocyte morphology, namely formations of ecchinocytes and spherocytes which can cause the RDW value increase. The results of this research also found that RDW values increased significantly from the first day to the fourth day of the storage time, indicating an increase in erythrocyte morphology diversity, consisted of normal erythrocyte morphology and abnormal erythrocyte morphology changing on the fourth day of storage time, but on the seventh day the values decreased significantly, therefore, the erythrocyte morphological changes that have occurred have become homogeneous.[12–14]

Similarly, a research conducted by Esper, *et al.*[15] also showed that erythrocytes stored for more than 14 days can trigger lesions in microcirculation and cannot increase cell oxygenation, which may lead to multi-organ dysfunction. Changes in the values of the erythrocyte indices are due to changes in biochemical and erythrocyte metabolites during storage, which can lead to a decrease in quality and effectiveness of oxygenation to tissues, reducing efficacy and increasing side effects in blood transfusion.[15]

CONCLUSION AND SUGGESTION

In conclusion, all parameters of the erythrocyte indices of PRC in blood stored at the Blood Bank, MCV, MCH, MCHC and RDW, changed significantly from day one to day seven during storage time even though the values of those erythrocyte indices were still within normal limits. As a result, it is recommended that the storage time of blood at Blood Bank can not be extended over 7 (seven) days.

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