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RESEARCH ARTICLES

Differences in Haemoglobin Levels Related to The Shelf Life of Packed Red Cells (PRC) on Day 1, Day 7 And Day 15 at UTD Pirngadi Medan

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Abstract: Packed red blood cells (PRC) are blood components separated from whole blood, consisting of red blood cells with most of the plasma, leukocytes, and platelets removed. Haemoglobin is the main protein in red blood cells responsible for transporting oxygen from the lungs throughout the body and carrying carbon dioxide back to the lungs for excretion. During storage, red blood cell membranes become more fragile due to oxidative stress and metabolic changes. Membrane damage can cause hemolysis, which is the rupture of red blood cells that release free haemoglobin into the storage solution. This study aims to determine the difference in HB levels with the shelf life of packed red cells (PRC) on haemoglobin levels on day 1, day 7 and day 15 at UTD Pirngadi Medan. This type of research is a prospective study; this study was conducted at various times for comparison. The total sample in this study was 75 people. Data analysis was processed using SPSS. First, a normality test was carried out; the normality test used was Kolmogorov-Smirnov. After the normality test, a homogeneity test was carried out. If the data are homogeneously/normally distributed, a One-Way ANOVA test is performed to compare. Results: There is a significant difference between haemoglobin levels on day 1, day 7, and day 15. The storage period of PRC can affect haemoglobin levels.

Keywords: Storage period, packed red cell, haemoglobin level

INTRODUCTION

Packed red blood cells (PRBCs) are a blood component separated from whole blood, consisting of red blood cells with most of the plasma, leukocytes, and platelets removed. Storage of PRBs must be done carefully to ensure effectiveness and safety for transfusion recipients. There are several

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important aspects to PRB storage. PRBs are typically stored at 1-6°C. Packed red blood cells stored with CPDA-1 have a shelf life of up to 35 days at 1-6°C. During this period, CPDA-1 helps maintain RBC viability and function, although some storage changes do occur. During storage, RBCs undergo biochemical and physical changes known as "storage lesions." These changes can include Adenosine triphosphate (ATP), the primary energy source for RBCs. During storage, ATP levels decrease, which can affect the RBCs' ability to maintain membrane integrity and cellular function. Mechanical Changes Due to Hemolysis: Hemolysis results in the release of free haemoglobin into the storage solution, which can potentially cause transfusion reactions if used in patients.[1]

Haemoglobin is the main protein in red blood cells responsible for transporting oxygen from the lungs throughout the body and carrying carbon dioxide back to the lungs for excretion. Haemoglobin levels in red blood cells are an important indicator of the quality and effectiveness of transfused blood. Changes During Storage: Cell Membrane Damage During storage, red blood cell membranes become more fragile due to oxidative stress and metabolic changes. Membrane damage can cause hemolysis, which is the rupture of red blood cells that releases free haemoglobin into the storage solution. The State of Hemolyzed Erythrocytes and Its Effect on Haemoglobin Levels in Stored Red Blood Cells.[2]

Hemolysis is the process by which red blood cells (erythrocytes) rupture and release haemoglobin into the surrounding solution. Hemolysis can occur during storage of Packed Red Cells (PRC) and has a significant impact on haemoglobin levels. How does hemolysis affect haemoglobin levels in stored PRC? A decrease in pH occurs. Anaerobic metabolism produces lactic acid, lowering the pH in the PRC bag. A decrease in pH can affect haemoglobin stability and accelerate red blood cell destruction. Haemoglobin Level Measurement: Total Haemoglobin. Total haemoglobin levels in PRC are usually measured immediately after collection and periodically during storage to monitor changes. Free Haemoglobin resulting from hemolysis can be measured to assess red blood cell damage during storage. Effect of Hemolysis on Haemoglobin Levels: Increase in Free Haemoglobin. When erythrocytes hemolyze, haemoglobin is released from the cell into the storage solution, increasing the concentration of free haemoglobin. Free haemoglobin does not function the same as haemoglobin in erythrocytes to transport oxygen. Changes in Haemoglobin Measurement: Haemoglobin measurement in PRC usually includes total haemoglobin, but hemolysis causes changes in the distribution between haemoglobin in erythrocytes and free haemoglobin. Free haemoglobin resulting from hemolysis can cause adverse transfusion reactions, such as hyperpotasemia, haemoglobinuria, kidney damage, and vascular disorders.[3]

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Research by Pesalmen Saragih et al (2019) on the effect of Packed Red Cells (PRC) storage time on changes in haemoglobin levels at H. Adam Malik General Hospital, Medan, Indonesia showed that the results of the study showed changes in haemoglobin levels with the length of PRC storage time, which showed significant results. This was caused by factors that increased free Hb and F2α-isoprostane levels during PRC storage. Total haemoglobin levels in PRC may appear to increase due to the presence of free haemoglobin, even though the number of intact erythrocytes actually decreased.[4]

Therefore, this study aims to determine the differences in haemoglobin levels in PRC in three different groups: haemoglobin levels on day 1, day 7, and day 15 at the PirngadiMedan UTD. It is hoped that the results of this study will provide us with a better understanding of the relationship between haemoglobin levels and PRC storage duration.

METHOD

This study received ethical approval. This prospective study is a forward-looking study aimed at determining differences in haemoglobin levels and the shelf life of PRC on days 1, 7, and 15. This study was conducted in April 2024, using a sample of 75 blood bags at the PirngadiMedan Blood Transfusion Unit (UTD).

Normality and homogeneity tests were performed, followed by ANOVA testing. The Kolmogorov-Smirnov test was first performed because the sample size was greater than 50 people. Before the ANOVA test, a Bonferroni test was performed. If the data were homogeneously distributed, an ANOVA test was performed to determine whether there were significant differences between the variables.

The method is written in Times New Roman, size 12, beginning paragraph 1 cm with a space of 1.15. The method must list the methods used in the research and preparation of the article completely and clearly

The table must be written in Arial Narrow, size 10, with a space of 1 and sequential table numbers according to the order in which they are mentioned in the text. Each table is given a short title. Each column is given a title and a short subtitle. Place the explanation in the footnote, not in the title. Describe in the footnotes all non-standard abbreviations present in the table. The maximum number of tables is six. Try to make sure every 1000 words in the article can be clarified in 1 table.

Statistical methods should be described in detail in the methods chapter and supported by references. An unusual method should be written in detail along with references to the method.

RESULT

Haemoglobin levels were examined using a POCT Hameque Hb 301 device with a photometer. Measurements were taken on days 1, 7, and 15. The results of the haemoglobin levels in this study.

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Table 1. Sample Distribution Based on Average Initial Haemoglobin Level

Group	Mean (± SD)	Median	Mode
Early HB	15,2 ±1,17	15,2	16,50

Based on the results of the average initial haemoglobin in Table 1, the average was 15.2 g/dL with a median of 15.20 g/dL and a mode of 16.50 g/dL.

Table 2. Sample Distribution Based on the Average Descriptive Test of Examination on Day 1, Day 7, and Day 15

Group	Mean (± SD)	Median	Mode
Day 1	22,3 ± 9,1	22,4	21,7
Day 7	22,7 ± 8,5	22,7	23,7
Day 5	23,2 ± 7,9	23,2	24,1

Based on the haemoglobin test data in Table 2, the average, median, and mode values for PRC donor blood storage on the first, seventh, and fifteenth days showed an increase in haemoglobin levels.

The average value on the first day was 22.3 g/dL, with a median of 22.4 g/dL and a mode of 21.7 g/dL. On the seventh day, the average haemoglobin level was 22.7 g/dL, with a median of 22.7 g/dL and a mode of 23.7 g/dL. On the 15th day, the average was 23.2 g/dL, with a median of 23.2 g/dL and a mode of 24.1 g/dL. Based on the haemoglobin levels in the table above, the highest average was on day 15 with an average level of 23.2 g/dL) and the lowest was on day 1, namely (22.3 g/dL).

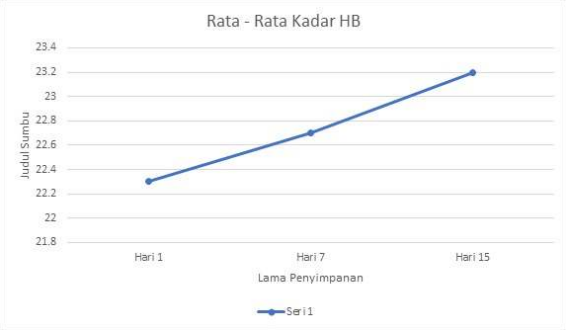

Figure 1. Graph of Haemoglobin Changes in PRC Blood on Day 1, Day 7, and Day 15

Based on the data in Table 2 to see the average difference in haemoglobin levels in the blood. The data in Table 2 is plotted into a graph as shown in Figure 1. The results show that on day 1 the haemoglobin level is around 22.2 g / dL, on day 7 the haemoglobin level rises to around 22.8 g / dL, on day 15 the haemoglobin level reaches around 23.3 g / dL, this graph shows that the average haemoglobin level increases with increasing storage time from day 1-15.

Table 2. Parametric ANOVA Test

Group	Mean (± SD)	P Value
Day 1	22,3 ± 9,1	0,00
Day 7	22,7 ± 8,5	
Day 5	23,2 ± 7,9	

The data were analysed using the ANOVA test to see the significance of the 3 examination times, namely day 1, day 7, and day 15. If the data has a Sig <0.05, it can be concluded that there is a significant difference. Based on the data in the table that has been tested with ANOVA above, there is a Sig 0.00 where there is a significant difference in storage on day 1, day 7, and day

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15. So it can be concluded that there is a real difference between Haemoglobin levels on days 1, 7, and 15.

DISCUSSION

In this study involving 75 samples in 15 days of PRC storage, this study shows that there is a significant increase in haemoglobin in the study; Sig shows (<0.05) during fifteen days of storage. The increase in haemoglobin is likely in my study caused by an increase in free haemoglobin and F2α-isoprostane in the blood, because in this study, in line with the research of Pasalmen Saragih in 2019, there is an increase in haemoglobin during the storage process caused by factors increasing free haemoglobin and F2α-isoprostane that occurred during storage. Research by Pasalmen Saragih in 2019 found that Hb levels on day 1 were 14.9±1.9, on day 3 were 15.5±1.9, on day 5 were 15.2±1.7, and on day 7 were 15.7±1.9. 4 The same results as research conducted by Karon et al in 2012 in the United States proved that an increase in free haemoglobin and free F2α-isoprostane levels occurred during PRC storage. F2α-isoprostane is a biomarker of lipid peroxidation that indicates oxidative stress in erythrocytes during storage. This increase is expected to be a factor that causes poor outcomes in PRC transfusion recipients.[5]

Free haemoglobin (also known as "free haemoglobin") refers to haemoglobin released from red blood cells (erythrocytes). When free haemoglobin increases in plasma, it can affect the measurement of total haemoglobin levels in the blood. During storage of packed red blood cells (PRC), there is an increase in free haemoglobin in the plasma. Free haemoglobin is released from red blood cells that undergo hemolysis during storage. Hemolysis is the process in which red blood cells experience membrane damage and free haemoglobin is released into the plasma. If hemolysis occurs, the released free haemoglobin can increase the haemoglobin level in stored blood samples or packed red blood cells (PRC).[4]

Increased free haemoglobin can potentially impair vascular function and contribute to inflammation. My research suggests that during PRC storage, there is an increased risk of haemoglobin oxidation. Haemoglobin released from erythrocytes becomes more susceptible to oxidation because it is not protected by the erythrocyte membrane structure. Haemoglobin oxidation can produce products such as methaemoglobin , which has a lower oxygen-binding capacity than normal haemoglobin. This can affect the ability of PRCs to provide effective oxygen after transfusion.[6]

Elevated F2α-isoprostane: This is a type of isoprostane formed in response to oxidative stress. High levels of F2α-isoprostane can reflect high levels of oxidative stress in the body or in biological components such as stored blood. Elevated haemoglobin can be a sign of oxidative stress, a process of lipid peroxidation. The release of F2α-isoprostane, whose levels increase with the length of storage of PRC

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(Packed Red Cells), is the result of the lipid peroxidation process that occurs in erythrocytes. This process is influenced by several factors that occur during storage, namely hemolysis and damage to the erythrocyte membrane. In hemolysis, significant lipid peroxidation can cause the breakdown of red blood cells. Red blood cells undergoing hemolysis release free haemoglobin into the blood suspension. This released haemoglobin can be detected in PRC products and causes an increase in dissolved haemoglobin levels. Damage to the erythrocyte membrane: The process of lipid peroxidation can cause damage to the erythrocyte membrane. The damaged membrane becomes more permeable, allowing haemoglobin bound to the erythrocytes to leak into the packed red blood cell (RBC) suspension. This results in increased haemoglobin levels in the storage suspension. Therefore, the increased release of F2α-isoprostanes with prolonged storage of packed red blood cells is an indicator of the level of lipid peroxidation occurring in the erythrocytes. Therefore, in practice, strict control of packed red blood cell storage conditions such as oxygen, temperature, pH, and storage time is crucial to minimise lipid peroxidation and the release of F2-isoprostanes, which in turn can reduce the risk of erythrocyte damage and the release of free haemoglobin. By understanding these mechanisms, proper management of packed red blood cell (RBC) storage can improve the success and safety of blood transfusions.[5]

The analytical test results of this study obtained a p-value of 0.00 ($p < 0.05$) for Statistical Relevance. A p-value of 0.00 indicates that the test results show a significant difference between the tested groups, in accordance with the hypothesis tested. Therefore, it can be concluded that the Ha hypothesis is accepted, namely there is a significant difference in haemoglobin levels on Day 1, Day 7, and Day 15.

Storage loss is characterised by the rupture of the erythrocyte membrane followed by the release of free haemoglobin into the plasma, a process known as hemolysis. If hemolysis occurs, the released free haemoglobin can increase the haemoglobin level in stored blood samples or packed red blood cells. 2 Increased haemoglobin (Hb) in packed red blood cells due to hemolysis can be a concern because it can affect the quality of stored blood products and can lead to potential complications if used in transfusions. Therefore, strict monitoring of the packed red blood cell storage process is crucial to minimise the risk of hemolysis and maintain red blood cell integrity.[6]

An increase in the haemoglobin index in packed red blood cells stored for 15 days or more can be an indicator that the red blood cells have undergone significant structural and functional changes. However, it is important to note that although the haemoglobin index may increase, the quality of red blood cells for transfusion may be reduced due to a decrease in 2,3-DPG and affected red blood cell function. Although

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the anticoagulant CPDA (1) is added to packed red blood cells to preserve the blood, changes still occur in blood components, especially red blood cells that change shape and become abnormal over time. In addition, during storage, there is a decrease in the level of Adenosine Tri Phosphate (ATP), which functions as an energy source for red blood cells. This effect will cause many red blood cells to lyse due to lack of energy. The large number of lysed red blood cells causes haemoglobin to leave the red blood cells, so that the haemoglobin level in packed red blood cells will increase.[7 8]

CONCLUSION

Based on the results of the ANOVA test, there is a Sig of 0.00, which means there is a significant difference between the haemoglobin levels and the storage period of PRC on Day 1, Day 7, and Day 15 at the Pirngadi Medan UTD.

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