The Effects of Calcium Gluconate Administration on Potassium Levels of Post Packed Red Cell (PRC) Transfusion Patients with More Than Three-Day-Stored Blood at RSUP Haji Adam Malik, Medan

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KEYWORDS

PRC, Pottasium, Ca gluconate

ABSTRACT

Background: Blood transfusion is an important and routine medical treatment, especially in cases requiring surgeries such as trauma. One of the biochemical changes that occurs in PRC due to erythrocyte storage is an increase in potassium levels. Hyperkalemia is the most common complication of stored blood transfusion. Cardiac arrest has been widely reported in transfusion-associated hyperkalemia. Methods : This study used a pre-experimental study with a pretest-posttest group design to determine the effects of Ca gluconate administration on blood potassium levels in patients receiving packed red cell (PRC) transfusions with blood stored for > 3 days at RSUP Haji Adam Malik Medan. Results : The distribution of sample characteristics in this study showed a mean age of 46 ± 13.63. There were 7 (22.6%) male and 24 (77.4%) female patients, with a mean BMI of 23.28 ± 6.44. Based on the hemodynamic profile, the mean systolic BP was 105.87 ± 20.59, diastolic BP 70.41 ± 11.94, RR 23.06 ± 2.39 and MAP 83.31 ± 14.48. The mean value of potassium levels before an administration of Ca gluconate was 5.84 ± 0.89, while the mean value after the administration was 5.43 ± 0.90. There were no statistically significant changes in the potassium levels after the administration of Ca gluconate in any samples. Conclusions : There are effects of Ca gluconate administration on the potassium levels of post Packed red cell (PRC) transfusion patients with blood stored for > 3 days at RSUP Haji Adam Malik Medan.

1. Introduction

Blood transfusion is the process of transferring blood or its components from a donor to another person (the recipient). The implementation of the transfusion, in addition to transferring blood cells, could also transfer: glucose, lactate and potassium to the recipient. There are several types of blood transfusions based on the length of storage, namely: fresh, new and stored blood. Termed fresh, as the blood has just been taken from the donor, which is up to six hours after collection. New blood is stored between six hours and six days after being drawn from the donor. Stored blood is Blood transfusion is an important and routine medical treatment, especially in cases that require surgery such as trauma. This procedure is generally relatively safe, yet the procedural risks cannot be completely avoided. In addition, blood transfusion is a difficult procedure. It is due to standard operating procedures related to the collection, storage, supply, and use of blood products as well as post-operative care, either with or without complications. Blood transfusion has become an important part of health services. One of the instances in which it is needed comprises emergency situation.[2]Packed Red Blood Cell (PRC) is a blood component obtained after most of the plasma is separated from Whole Blood (WB) by various methods and contains a hematocrit value of 80%. PRC still contains leukocytes, platelets and a small amount of plasma.

One PRC unit with a volume of 150-300 mL has a blood cell mass of about 100-200 mL. Erythrocyte transfusion aims to replace or restore the capacity of blood to carry oxygen, therefore erythrocytes of good quality are necessary.[3]PRC may be stored from the time of collection at 2-6°C in certain media until it is transfused to the recipient. The purpose of PRC storage is to maintain the viability and function of erythrocytes by reducing the metabolic activity of cells. Proper storage is one way to maintain the quality of erythrocytes. Current regulatory standards require the recovery of more than 75% of blood cells in circulation following 24 hours after transfusion.[4]During the storage of erythrocytes, there are various changes related to the quality and quantity of erythrocytes. The changes include biochemical and structural changes which will affect the viability and function of erythrocytes after transfusion. These changes are known as erythrocyte storage lesion. During storage, blood cells undergo metabolic changes, thus in vitro storage must be considered in an effort to reduce changes that occur in blood cells during storage as in vitro environment is very different from that of in vivo. Changes that occur during storage are decreased levels of Adenosine 5'-triphosphate (ATP) and 2,3-diphosphoglycerate (2,3-DPG), declined blood pH, increased potassium and lactate levels, changes in erythrocyte cell shape, loss of erythrocyte viability, and hemolysis.[5]

One of the biochemical changes that occur in PRC due to erythrocyte storage is an increase in potassium levels in PRC plasma. The activity of the Na+/K+ATPase pump is strongly influenced by temperature. The pump becomes inactive at 4°C causing potassium to leave the cell and sodium to enter the cell. During blood storage, potassium leaks into the plasma due to failure of the Na+/K+ATPase pump, this process occurs slowly and continuously. Potassium levels in PRC plasma may increase by 0.5-1 mmol/L per day. Potassium leaks progressively from erythrocytes after three days of storage and the extracellular levels may rise to 50 mmol/L with peak plasma potassium levels as high as 90 mmol/L after two weeks of storage.[6]In a study conducted in Minnesota, it was concluded that potassium increased with PRC storage time, up to 77.0 mmol/L on day 14. A study conducted by Monica et. al. stated that PRC had been better to administer under 7 days of storage, since the longer PRC was stored, the more significant the increase in potassium levels was.[7]Smith et. al., analyzed that the potassium content of PRC increased with storage time, i.e. initially 7.3 mEq/L (1 mEq/L=1 mmol/L) and averagely 19 mEq/L in the first week (0−7 days) of storage, 31.5 mEq/L in the second week (8–14 days), and 39.9 mEq/L between 15–28 days of storage. The research by Uvizl et. al. in 2011 reported changes in potassium levels in stored PRC, which increased gradually from 4.0 mmol/L on the first day to 40.5 mmol/L on day 35.[8,9]

According to a previous study by the authors, an increase in potassium levels after transfusion with blood stored for > 3 days was discovered. Meanwhile, there was no increase in potassium levels after transfusion with blood stored for < 3 days. It was acquired from potassium profile examination performed before (4.01 ± 0.79, within normal limits) and after (4.01 ± 0.79, increased) transfusion with blood stored for > 3 days.[10] Hyperkalemia is the most common complication of stored blood transfusion. Cardiac arrest has been widely reported in transfusion-associated hyperkalemia. Several studies suggest that the clinical impact of storage lesion becomes significant after two weeks of storage. A study by Koch CG in 2008 stated that in 6,002 cardiac surgery patients who received PRC transfusions for either 14 days or >14 days, there was a significant association between mortality and blood storage time. A study in Australia by Yap CH in 2008 reported that transfusion of long stored PRC units (more than two weeks) was associated with an increased risk of postoperative complications and mortality.[5,11,12]

The main goals of treatment of acute hyperkalemia are to prevent life-threatening cardiac conduction and neuromuscular disorders, potassium shift into cells, to eliminate excess potassium, and to correct the underlying disorder. The indications for intervention with Ca gluconate are symptomatic hyperkalemia, ECG changes, severe hyperkalemia (more than 6.5 mEq/L), and hyperkalemia with rapid onset, or heart disease, cirrhosis or renal impairment.Calcium antagonizes the effects of potassium on the cardiomyocyte membrane without affecting potassium levels.

If abnormalities are found on ECG or plasma potassium level exceeds 6.5 mEq/L, an intervention is indicated to prevent potentially life-threatening arrhythmias, namely 10 cc of Ca gluconate is given intravenously with a concentration of 10% over 5-10 minutes. The patient should be on close cardiac monitoring, and the ECG is to be repeated after administration of Ca gluconate. If the ECG persists after 5-10 minutes, a second administration should be performed within 5 minutes.With the preceeding reasonings and no research has been conducted on the comparison of PRC potassium levels based on storage time so far, the researchers are interested in conducting a study on the effects of Ca gluconate administration to potassium levels in post Packed red cell (PRC) transfusion patients with blood stored for > 3 days at RSUP Haji Adam Malik, Medan.

2. Methods

This study used a pre-experimental study with a pretest-posttest group design which was conducted on all patients undergoing elective and emergency surgery requiring PRC blood transfusion at RSUP Haji Adam Malik Medan.The sample of this study comprised the entire study population that met the inclusion and exclusion criteria, as well as the dropout criteria with consecutive sampling technique, which acquired a number of samples of 30 people. The inclusion criteria in this study were all patients undergoing elective and emergency surgery requiring PRC blood transfusion, grade 3-4 bleeding, aged 18-64 years, potassium levels of 3.5 mmol – 5.5 mmol, ASA physical status (American Society of Anesthesiologists) 2-3, patients undergoing elective and emergency surgery requiring PRC blood transfusion of more than 2 bags (units).Exclusion criteria in this study were patients who refused to participate in the study, had a history of allergy to blood transfusions, pregnancy, kidney disorders, and patients who received whole blood and/or platelet transfusions. Whereas the dropout criteria were patients who experienced allergies during blood transfusion, patients who did not receive 2 bags of blood transfusion, patients with bleeding grade of < 3, and cardiovascular and respiratory emergencies in forms of: MAP <50 and persistent, pulse rate <60 or >150 times per minute and persistent, arrhythmia, respiratory rate <12 times per minute or apnea, oxygen saturation <90% and not increasing with oxygen administration.This study uses primary data which will then be analyzed using SPSS and tested with dependent T test.

3. Result and Discussion

There were 30 patients who underwent elective and emergency surgery requiring PRC blood transfusion according to the inclusion, exclusion, and dropout criteria at RSUP Haji Adam Malik Medan. Table 1. shows that the distribution of sample characteristics in this study had a mean age of 46 ± 13.63. There were 7 (22.6%) male patients and 24 (77.4%) female patients, with a mean BMI of 23.28 ± 6.44. Based on the hemodynamic profile, the mean systolic BP was 105.87 ± 20.59, diastolic BP 70.41 ± 11.94, RR 23.06 ± 2.39 and MAP 83.31 ± 14.48.

Table 1. Sample Characteristics

Characteristic	Subject
Age	46 ± 13,63
Gender Female Male	 24 (77,4%) 7 (22,6%)
BMI	23,28 ± 6,44
Systolic BP	105,87 ± 20,59
Diastolic BP	70,41 ± 11,94
MAP	83,31 ± 14,48
RR	23,06 ± 2,39

Based on Table 2, the mean value of potassium levels before transfusion was 3.79 ± 0.54, whereas the mean value after transfusion with blood stored for > 3 days was 5.84 ± 0.89. The mean value declined to 5.43 ± 0.90 after the administration of Ca gluconate. The values were then tested statistically and a p-value = 0.43 was obtained, showing no significant difference among the mean values of potassium levels before and after the administration of Ca gluconate.

Tabel 2. Potassium levels before and after transfusion, and after Ca gluconate administration

Characteristic	Potassium levels before transfusion	Potassium levels after transfusion	Potassium levels after Ca gluconate administration	p-value
Blood stored for > 3 days	3,79 ± 0,54	5,84 ± 0,89	5,43 ± 0,90	0,43

As seen in table 3, there were changes in potassium levels after blood transfusions with blood stored for > 3 days and after Ca gluconate administration.

Table 3. Distribution of potassium levels before and after transfusion, and after Ca gluconate

administration

Potassium levels before transfusion	Potassium levels after transfusion	Potassium levels after Ca gluconate administration
3.13	5.7	5.32
4.08	5.8	4.9
3.8	5.5	5
4.02	6	5.5
3.15	5.56	5.12
3.45	5.65	4.98
3.33	5.67	5
3.8	6.12	6.12
3.13	6.22	5.76
4.14	6.34	5.87
3.08	5.54	4.7
3.33	5.89	5.89
3.23	5.92	5.92
3.14	5.84	5.12
4.01	6.23	6.23
4.1	5.6	5.1
3.8	5.5	5.12
3.45	5.62	5.12
4.13	6.12	5.66
3.13	6	5.3
4.14	5.53	4.97
3.08	5.92	4.96
3.33	6.11	6.11
3.23	5.68	5.33
4.33	6	5.43
3.23	5.8	5.8
3.14	6.25	6.25
4.01	5.56	5.11
3.23	5.85	5.85
4.66	5.6	5.2
3.89	6	5.67

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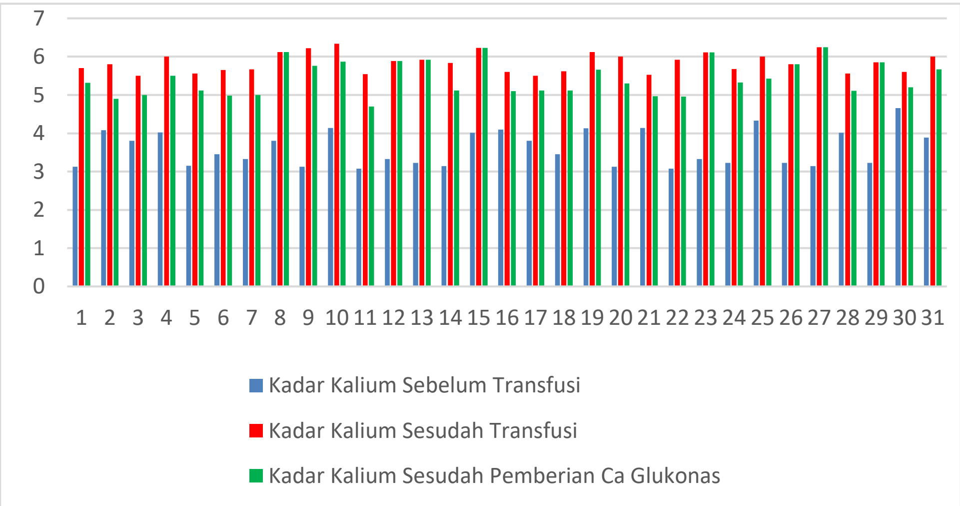
Figure 1 presented an insignificant change in potassium levels before and after administration of Ca gluconate. The average potassium levels before the administration was above 5.5, while there was no significant change in any sample after the administration.

Figure 1. Bar Diagram of Potassium Levels Before and After Administration of Ca gluconate



Discussion

In this study, it was discovered that the potassium levels after transfusion with stored blood for > 3 days increased. The result was similar to that of a study conducted by Daulay in 2021, regarding the effect of basic storage time on potassium levels of patients receiving PRC transfusions at RSUP Haji Adam Malik Medan.[10]However, an observation of the potassium levels after administration of Ca gluconate showed a decrease in the levels, in contrast to the research conducted by Lema, et al. in 2019. The study reported no roles of calcium preparations in lowering serum potassium levels. However, intravenous calcium is an urgent therapeutic management in the event of hyperkalemia.[13]Calcium acts by affecting the transmembrane electrical gradient of myocytes in cardiac muscles. This is due to the mechanism of action of Ca gluconate that lowers the membrane potential threshold of cardiac cells, which are easily excited due to the effects of hyperkalemia. Calcium is believed to stabilize the myocardium by lowering the membrane potential of cardiac myocytes. Intravenous calcium acts after 5 minutes of administration, with a short duration of action.Severe hyperkalemia is potentially life-threatening and may cause muscle paralysis and fatal cardiac arrhythmias. Moderate and severe hyperkalemia require prompt management and close monitoring to prevent worsening of cardiac arrhythmias and muscle paralysis. Hyperkalemia with potassium levels higher than 6.5 mEq/L or a discovery of ECG changes is a medical emergency and should be treated as soon as possible. Ca gluconate is given in hyperkalemic states with or without ECG changes. All patients with confirmed hyperkalemia should be undergo ECG immediately in order to look for the possibilities of serious cardiac arrhythmias. Ca gluconate should be given as a first-line agent in hyperkalemic patients with ECG changes and in patients with severe hyperkalemia to protect cardiomyocytes.

Cardiac stabilization by calcium infusion was first introduced in 1964 by Chamberlain, with the findings of a study of ECG abnormality resolution after intravenous calcium administration in 5 patients with potassium levels of 8.6-10mmol. Calcium quickly decreases the effects of increased potassium levels. Hyperkalemia causes membrane instability by increasing the threshold potential of the myoside to 0 mV, calcium could antagonize it by restoring the range of the larger transmembrane voltage gradient. This effect occurs within a few minutes after intravenous calcium administration. Furthermore, treatment with calcium protects the heart from fatal dysrhythmias. Calcium is predicted to stabilize cardiac cellular membranes. It does not cause movement of potassium between cell compartments, nor does it cause excretion of potassium. The short-lived effect and the lack of ability of calcium to lower potassium levels result in the need for administration of other medications.[14]

Calcium preparation which is usually given intravenously is 10cc of Ca gluconate 10%, for over 5-10 minutes. If the ECG changes persist after 5-10 minutes of the first administration, a second injection of Ca gluconate should be repeated in 5 minutes. Ca gluconate works rapidly, with an onset of 1-2 minutes and a duration of 30-60 minutes with an expected decrease of 0.5-1.5 mEq/L in potassium levels. Long-term treatment of hyperkalemia includes diet and potassium modification. The regulation of intra- and extracellular potassium distribution is also known as internal potassium balance. Under normal conditions, insulin and catecholamines play the most important roles in controlling this regulation.Lema et. al. claimed that insulin worked by accelerating the transfer of potassium into cells via receptor binding in skeletal muscle. The administered insulin regimen was a bolus injection of fast-acting insulin. Hollander and Calvert in the American Academy of Family Physician stated that the serum potassium levels decreased rapidly by administering insulin and glucose intravenously, nebulizer beta-2 agonist, or both. 1 unit of insulin should regularly be given intravenously. Insulin worked by moving serum potassium into the intracellular space.[13,15]The limitations of this study include the absence of potassium level examination when massive bleeding occurred, as there hypokalemia would occur at the time of bleeding due to a large amount of wasted blood components.

4. Conclusions

According to the results of this study, the average potassium levels after receiving PRC blood transfusion with blood storage duration of > 3 days was found to be above the normal value, and they will decline after the administration of Ca gluconate, although not statistically significant. Thus, it could be concluded that there is an effect of Ca gluconate administration on potassium levels of post PRC transfusion patients with blood stored for > 3 days.

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