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RED CELL STORAGE: CHANGES AND CONCERN WITH BLOOD TRANSFUSION

Immunohematology

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ABSTRACT

OBJECTIVES - To study the changes associated with red cell storage and risk associated with blood transfusion.

MATERIAL AND METHODS - A total of 31 whole blood units with CPDA-1 as a preservative were studied for markers of storage lesion along with red cell indices on day 0, day 7, day 14 and day 28 of storage.

RESULT- Changes in the levels of total protein, sodium and potassium were statistically significant. There was a gradual reduction in glucose, albumin, and calcium concentration. The overall average daily potassium change of 0.41 mmol/l and sodium change of 0.33 mmol/l over the 28 days period was noticed.

CONCLUSION - During storage red cell undergoes several changes affecting survival and function. Clinical effect occurring due to storage lesion in transfused patient needs more studies to be undertaken to see the in vitro effect of red cell storage changes.

KEYWORDS

Whole Blood, Blood Transfusion, Infants, Storage Lesion

INTRODUCTION

RBCs undergo structural and functional changes that reduce function and viability after transfusion. Critically ill patients and neonates may be especially susceptible to the adverse effects of prolonged RBC storage. Large amount of whole blood and red blood cellular products are transfused annually across the globe, red blood cell concentrates (RBCC) are the most commonly transfused component. Use of SAGM (containing saline, mannitol, glucose, and adenine), ADSOL (a solution consisting of adenine, dextrose, sodium chloride, and mannitol) are the preservative solution used in component therapy in which the storage period increased upto 42 days. Other additive solutions include AS1, AS 2 and AS 3. A whole blood unit is not a commonly transfused product as the clotting factors and thrombocytes reduces within hours of donation. Whole blood is mainly used for patients with massive transfusion or exchange transfusion in neonates. During blood storage, there is a slow but constant leakage of potassium from the cells into the surrounding plasma along a concentration gradient as a result of sodium potassium ATPase pump failure. The plasma level of potassium may increase by 0.5-1.0 mmol/L per day of refrigerator storage (3). There is a notion that the total amount of extracellular potassium in a unit of blood stored for 35 days falls within 7mmol/L to 25mmol/L (4). Other condition which enhances the storage lesion and increased potassium levels are Gamma irradiation. Transfusion guidelines promote best transfusion practices but never eliminate side effect and complication of transfusion.

MATERIAL AND METHODS

The study was conducted in H.B.T. Medical College and Dr. R. N. Cooper Hospital, located in the city of Mumbai, India. A total of 31 whole blood units with CPDA-1 as a preservative were included in the study. All whole blood units were stored at 4 °C for 28 days and samples were withdrawn aseptically on day 0, day 7, day 14 and day 28 of storage. Markers of storage lesion including plasma Na^+, K^+ and other biochemical parameters were studied in all samples on automated biochemistry analyser (Erba analyser XL600). Red cell indices such as Haemoglobin, haematocrit, mean corpuscular volume, and mean corpuscular haemoglobin concentration was measured on automated cell counter (Erma PCE 210, India). Statistical analysis was performed using SSPS software (Version 17.0) using appropriate test and proportion

RESULT

Blood stored at 1° to 6°C decreases the rate of cellular metabolism and energy demand, which allows blood to be stored for 35 to 42 days. It makes the sodium-potassium pump inoperative and consequently allows potassium ions to exit the cell and sodium ions to enter via the semipermeable membrane.

TABLE 1: Distribution of Biochemical Variables on different days:

S. no	Parameters	Day 0	Day 7	Day 14	Day 21	Day 28	F Value	P value
1	Glucose	194.29	199.55	147.35	136.19	146.13	11.30	0.001
2	T. Protein	6.88	6.96	6.81	6.70	7.87	35.46	0.001
3	Albumin	3.36	3.23	3.20	3.15	3.18	3.17	0.02
4	Calcium	10.05	9.26	7.98	7.20	7.02	138.56	0.001
5	SGOT	35.87	42.16	35.74	33.87	44.94	2.89	0.02
6	SGPT	25.19	28.03	26.32	25.35	25.68	0.29	0.88
7	Sodium	144.13	157.26	140.68	131.97	135.00	172.85	0.001
8	Potassium	4.20	7.43	11.10	12.95	15.60	422.38	0.001
9	Chloride	108.16	111.58	104.58	98.87	98.84	50.54	0.005
10	Cholesterol	134.97	162.19	147.87	142.58	139.84	5.45	0.005

The mean of all the biochemical variables levels of all the samples in relation to the various days' readings are shown in table 1. It showed gradual reduction in glucose, albumin, and calcium concentration. There were changes in the levels of total protein, sodium and potassium, which was statistically significant. The potassium levels raised from 4.20 mmol/l on day 0 to 7.43 mmol/l on day 7 and further to 11.10 mmol/l on day 14, after which the rise seemed to have slowed reading 12.95 mmol/l on day 21 and 15.6 mmol/l on day 28. It was observed that there was a change of 0.46 mmol/l during the first seven

days of storage; day 7 to day 14 recorded a daily potassium change of 0.52 mmol/l; day 14 to day 21 recorded a 0.26 mmol/l daily change while day 21 to day 28 recorded daily change 0.37 mmol/l. The overall average daily potassium change of 0.41 mmol/l over the 28 days period was seen in our study. Sodium levels were showing significant changes from 144.13 mmol/l on day 0, 157.26 mmol/l on day 7 and afterwards gradual decrease in the levels upto 135.0 mmol/l on day 28. It was observed that there was a change of 1.87 mmol/l during the first seven days of storage; day 7 to day 14 recorded a daily sodium change of 2.36 mmol/l; day 14 to day 21 recorded a 1.2 mmol/l daily change whiles day 21 to day 28 recorded daily change 0.43 mmol/l. The overall average daily sodium change of 0.33 mmol/l over the 28 days period was noticed.

TABLE 2: Distribution of Hematological Variables on different days:

S.no	Parameters	Day 0	Day 7	Day 14	Day 21	Day 28	F value	P value
1	WBC	5854.84	6351.61	4925.81	3701.61	3438.71	30.84	0.001
2	LYM %	33.95	36.10	36.19	35.61	34.81	0.36	0.83
3	MON %	6.39	6.26	6.23	6.00	6.26	0.23	0.92
4	GRA%	59.67	57.48	57.52	58.35	59.00	0.34	0.85
5	RBC	4.41	4.35	4.45	4.43	4.42	0.31	0.87
6	HB	12.29	12.56	12.87	12.75	12.67	0.66	0.62
7	HCT	37.06	37.65	38.45	37.48	37.06	0.55	0.70
8	MCV	84.20	84.35	85.00	81.16	82.68	0.83	0.51
9	MCH	27.86	27.87	28.87	27.77	27.68	0.68	0.61
10	MCHC	33.01	32.19	33.03	32.13	31.61	5.31	0.005

When the mean values of WBC on day 0 was compared to day 28, it was assumed that there was rapid deterioration in granulates WBC. Changes in white blood cells are due to the loss of cell characteristics leading to release of bio reactive substance such as histamine, lipids, and cytokines, which may exert direct effects on recipients. Other hematological parameters remained stable during this study period, hence may be considered acceptable for clinical utility. The levels of WBC were changing from 5854.84 on day 0 to 6351.61 on day 7 and then decreasing gradually from 4925.81 on day 14 to 3438.71 on day 28. The changes were statistically significant. The changes in the MCHC levels and platelet levels are also statistically significant.

TABLE 3: Bonferroni's multiple comparison test of variance between the various reading days:

Sr No	Days	Na^+	K^+		
		Mean Difference	P value	Mean Difference	P value
1	Day 0 vs Day 7	-13.1290*	<0.05	-3.2258*	<0.05
2	Day 0 vs Day 14	3.4516*	0.014	-6.8935*	<0.05
3	Day 0 vs Day 21	12.1613*	<0.05	-8.7419*	<0.05
4	Day 0 vs Day 28	9.1290*	<0.05	-11.4000*	<0.05
5	Day 7 vs Day 14	16.5806*	<0.05	-3.6677*	<0.05
6	Day 7 vs Day 21	25.2903*	<0.05	-5.5161*	<0.05
7	Day 7 vs Day 28	22.2581*	<0.05	-8.1742*	<0.05
8	Day 14 vs Day 21	8.7097*	<0.05	-1.8484*	<0.05
9	Day 14 vs Day 28	5.6774*	<0.05	-4.5065*	<0.05
10	Day 21 vs Day 28	-3.0323*	0.048	-2.6581*	<0.05

*The mean difference is significant at the 0.05 level.

DISCUSSION

Infants requiring major surgery or due to hemorrhage may have to be transfused with large quantities of stored red blood cell and transfusions of RBC containing increased levels of potassium have been associated with myocardial hyperkalemia and neonatal arrhythmia (1, 2). It was demonstrated in some studies done in critically ill patients that the sodium levels would revert to their normal levels within 24 hours after transfusion, whereas the potassium levels take about 4 days to stabilize (5,6). Increased potassium levels in red blood cells may lead to arrhythmia when neonates or infants are transfused with large volumes of stored blood (2,6). In a study done by Rutger et al red cells stored for more than 24 days compared with less than 10 days found an almost 2-fold increase in mortality rate after the transfusion of fresh red cells compared with old red cells (7). Pre-storage leucoreduced red cell should be used commonly as it decreases the red cell storage lesion, immunomodulation, CMV transmission risk, reduces the risk of alloimmune platelet refractoriness; the possible avoidance of vCJD transmission; as well as reducing the risk of mortality and organ dysfunction in cardiac surgery patients.(8) In a study done by Spinella et al in trauma patients transfused with ≥5 units of RBCs, transfusion of RBCs ≥ 28 days of storage was associated with increased chance of deep vein thrombosis and in-hospital mortality when compared with a group of patients of similar severity of injury who were transfused RBCs of decreased storage age.(9) Availability of specific therapy (i.e. the use of packed red cell for the treatment of anemia and FFP to treat coagulopathy) contradict the use of whole blood. The use of whole blood when specific component is indicated and available could lead to complications such as volume overload. Transfusion of packed red cell rather than whole blood can reduce the wastage other components such as plasma and platelets, which can provide optimum benefit to neonates and infants requiring other blood component.

CONCLUSION -

During storage, red cell undergoes several changes affecting survival and function. Clinical effect occurring due to storage lesion in transfused patient needs more evidence in associations with mortality, length of stay, (postoperative) infections and organ failure as are largely unknown. Increased potassium level may require special attention in individuals with renal impairment. More new studies need to be undertaken to study the in vitro effect of red cell storage changes.

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