ORIGINAL ARTICLE

Effect of automated red cell exchanges on oxygen saturation on-air, blood parameters and length of hospitalization in sickle cell disease patients with acute chest syndrome

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ABSTRACT

Background: Red cell exchanges (RCEs) lead to improvement in tissue oxygenation and reduction in inflammatory markers in sickle cell disease (SCD) patients who present with acute chest syndrome (ACS). The aim of this study is to evaluate the effects of automated-RCE (auto-RCE) on oxygen saturation (SpO_2) on-air, blood counts, the time to correct the parameters and length of hospitalization after the exchange in SCD patients presenting with ACS. **Subjects and Methods:** This was 2 years study involving five SCD patients; the time for SpO_2 on air to increase to ≥95% and chest symptoms to resolve, postprocedure, as well as the length of in-patient hospitalization was recorded. All data were entered into Statistical Package for Social Sciences Version 20.0 (SPSS Inc., Chicago, IL, USA) computer software for analyses. **Results:** The study involved 4 (80%) hemoglobin (Hb) SS and 1 (20%) HbSC patients. The median time of SpO_2 recovery was 24 h, ranging from 6 to 96 h. About 60% (3/5) of patients achieved optimal SpO_2 within 24 h post-RCE, while discharge from intensive care unit was 24 h after auto-RCE in one patient. The Hb concentration was significantly higher, while the total white cell and absolute neutrophil counts were significantly lower at the time of resolution of symptoms, compared to before auto-RCE ($P < 0.05$). The average post auto-red cell transfusion symptoms duration was 105.6 (24–240) h while mean inpatient stay was 244.8 (144–456) h. **Conclusion:** Auto-RCE could reverse hypoxia in ACS within 24 h.

Key words: Acute chest syndrome, auto-red cell exchange, oxygen saturation, sickle cell disease

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INTRODUCTION

Sickle cell disease (SCD) is an autosomal recessive genetic disorder in which there is the homozygous inheritance of the sickle hemoglobin (HbS) or in association with any other abnormal Hb.[1] The hallmarks of this disorder include recurrent acute events known as crises which interrupts steady chronic anemia. Repeated crises and persistent anemia have been shown to predispose to significant end-organ dysfunction, particularly in the homozygous (HbSS) state of the disease.[1,2] Sickle red cells when exposed to reduced oxygen tension assume an abnormal, rigid (sickle) shape that adhere together with platelets and white blood cells (WBCs) to the endothelial wall, leading to vascular occlusion, ischemia, and endothelial dysfunction.[2,3]

Acute chest syndrome (ACS) is a potentially fatal pulmonary complication of SCD, characterized by intravascular pulmonary red cell sickling. The clinical spectrum spans

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from a mild pneumonic illness to life-threatening acute respiratory distress syndrome and multi-organ failure. It is commonly heralded by a fall in alveolar oxygen tension, leading to polymerization of sickle red cells, vaso-occlusion, decreased pulmonary blood flow, and hypoxia. Cytokines, such as vascular cell adhesion molecule 1 are critical in the development of ACS, as it enhances the adherence of red cells to the pulmonary endothelial cells, thus exacerbating vaso-occlusion and hypoxia.[4] Some identified risk factors for the development of this condition include splenectomy,[5] abdominal surgery,[6] asthma,[7] infection,[8] fat emboli, and sickle vaso-occlusive pain.[9]

If untreated, severe cases of ACS may progress to persistent hypoxemia and hypercapnia, resulting in respiratory failure and invariably death.[9] It has been estimated that up to 50% of patients with SCD could have at least one episode of ACS in their lifetime.[10]

Red cell exchange (RCE) (erythrocytapheresis) is an effective important component of the management of sickle-related complications.[11] Common indications include ACS, stroke, multi-organ failure syndrome, and priapism.[11,12] RCE is superior to simple transfusion in that it reduces the percentage of circulating sickle cells while increasing the red cell oxygen carrying capacity, without causing a corresponding increase in blood viscosity and body iron. Increased blood viscosity alters blood rheology and predisposes to ischemic adverse events such as vaso-occlusive crises and stroke while iron overload causes marked organ tissue damage, with an increase in disease morbidity and mortality.[13-16]

Documented effects of RCE in the setting of ACS include improved tissue oxygenation, changes in Hb oxygen affinity and blood oxygen pressure, increase in transcutaneous oxygen saturation (SpO_2), increased HbA content with reduced HbS fraction and reduced WBC count and inflammatory markers.[17-21]

There is a paucity of literature on the timelines for resolution of parameters (such as SpO_2 and blood counts) in SCD patients with ACS, who had received RCE, particularly automated-RCE (auto-RCE). The aim of this study was, therefore, to evaluate the spectrum of changes in the blood counts and SpO_2 in SCD patients with ACS, post auto-RCE, with a view to highlighting changes in counts at symptom resolution and the timelines for saturation to become optimized.

SUBJECTS AND METHODS

This was a retrospective study, carried out at the red cell unit of the University College London Hospital, involving confirmed SCD patients aged ≥18 years who presented to the emergency room with ACS between the months of January 2014 and January 2016. Diagnostic features considered in keeping with ACS included fever, cough, chest pain, shortness of breath, reduced SpO_2, hemoptysis, and suggestive chest X-ray findings with or without preceding history of acute pain crisis.[22] Other inclusion criteria were hospitalization on account of ACS ≥24 h and at least one session of auto-RCE in the index admission.

The data of individual patients were retrieved from the departmental paper medical notes as well as the hospital's patient data program. Sociodemographic information, date and time of admission, symptoms at presentation, date and time of auto-RCE procedures, serial recordings of SpO_2 on room air (from the point of admission till resolution of chest symptoms and discharge from hospital), time of resolution of chest symptoms post-RCE and length of hospitalization were extracted. The results of serial blood counts: WBC count, Hb concentration, platelet count, absolute neutrophil count (ANC), absolute lymphocyte count, platelet count and the neutrophil-lymphocyte ratio (NLR) were similarly retrieved from the electronic patient data program of the unit. All data were entered into Statistical Package for Social Sciences version 20.0 (SPSS Inc., Chicago, IL, USA) computer software for further analyses.

The time for SpO_2 (in room air) to increase to ≥95%,[22] was noted for each patient, and this was taken as the time for significant improvement in SpO_2 to have taken place, post auto-RCE. The means of blood counts before auto-RCE were compared with values recorded at the point of symptom resolution using the Student's *t*-test while the level of statistical significance was set at $P \leq 0.05$ (at 95% confidence interval).

RESULTS

A total of 5 patients, with mean age of 40.40 ± 5.12 years, including 4 HbSS and 1 HbSC; two males and three females were studied.

The mean of Hb concentration was significantly higher in all patients at the point of resolution of symptoms compared to the value recorded before auto-RCE (105.40 ± 7.90 g/L vs. 81. 80 ± 8.53, $P = 0.01$, Table 1).

Correspondingly, the means of total white and ANCs were significantly lower at the point of symptom resolution in all patients, compared with values before auto-RCE (9.47 ± 3.52 × 10^9/L vs. 14.03 ± 2.41 × 10^9/L; 5.21 ± 3.44 × 10^9/L vs. 8.26 ± 4.88 × 10^9/L, *P* values 0.03 and 0.04, respectively, Table 1).

The means of platelet count and NLR were lower at the point of symptom resolution in all patients compared with values before auto-RCE. However, these differences were not statistically significant ($P > 0.05$, Table 1).

The median time of SpO_2 recovery in all patients was 24 h (6–96 h); 60% (3/5) of all patients achieved optimal

Table 1: Comparison of means and standard deviation of haematological indices before automated red cell exchange and at symptom resolution

Hematological indices	Before automated red cell exchange	At symptom resolution	*P*
Hb concentration (g/L)	81.80±8.53	105.40±7.90	0.01*
WBC (×10⁹/L)	14.03±2.41	9.47±3.52	0.03*
Platelet count (×10⁹/L)	261±41.92	247.00±131.75	0.85
ANC (×10⁹/L)	8.26±4.88	5.21±3.44	0.04*
ALC (×10⁹/L)	2.12±1.32	1.52±1.14	0.31
NLR	3.35±2.30	2.90±1.79	0.50

*Significant *P* values. Hb – Hemoglobin; WBC – White blood cell; ANC – Absolute neutrophil count; ALC – Absolute lymphocyte count; NLR – Neutrophil to lymphocyte ratio

SpO_2 within 24 h post auto-RCE, whereas 80% (4/5) achieved this within 48 h. Only one patient was admitted to the intensive care unit (ICU) at presentation; discharge from ICU occurred 24 h after auto-RCE.

By the time of symptom resolution, the WCC and platelet counts had returned to normal in 60% (3/5) of study patients. The average duration of chest symptoms, post auto-RCE, was 105.6 (24–240) h while mean in-patient stay was 244.8 (144–456) h.

DISCUSSION

The median time for SpO_2 to increase to ≥95% post auto-RCE in this study was 24 h. The SpO_2 cut-off of ≥95% was chosen as it conforms to the British Committee for Standards in Haematology guidelines on ACS; it is believed to represent the point of optimal oxygen-carrying capacity of the red cells.[22] Increasing hypoxemia and hypercapnia have been shown to be important hallmarks of ACS and in severe cases can progress to death from acute hypoxic respiratory failure.[10] Auto-RCE for ACS with HbAA red cells can provide a rapid and dramatic improvement in oxygen carrying capacity which reverses hypoxaemia and hypercapnia, commonly reflected as an increase in SpO_2.[23] The timelines required for this to take place has however not been sufficiently studied.[18]

In this study, 60% (3/5) and 80% (4/5) of patients achieved optimal tissue oxygenation in 24 h and 48 h, post auto-RCE, respectively. The above timelines demonstrated in this study could well indicate the times expected to achieve management goals in patients with ACS on auto-RCE. Physicians could, therefore, find this information handy in making management decisions as well as during counseling of patients/relatives on clinical recovery and possible length of hospital stay. Further study of larger subjects is suggested to confirm our finding and generate more data on auto-RCE in SCD patients with ACS. Interestingly, one of the patients was observed to have achieved optimal SpO_2 (96%) by 96 h post auto-RCE but desaturated over the next 5–9 days, subsequently stabilizing over the next 11–12 days. It is important to note that persistent desaturation post-RCE could, in fact, be a "red flag" for further investigation for documented conditions such as unresolved chest infection, and other co-morbidities such as asthma, pulmonary hypertension and the presence of chronic sickle lung disease.[22] These conditions influence SpO_2 and may require specific interventions as applicable. The index patient had underlying pulmonary hypertension secondary to past episodes of ACS, which probably explains the pattern of SpO_2 observed.

In this study, we observed that the WBC and ANC showed a uniform decrease in patients post auto-RCE and remained significantly lower at the point of resolution of symptoms compared to the values obtained before the exchange. Our finding is in agreement with the earlier report of Marques *et al*., who observed a reduction in WBC count post-RCE.[21] This could be as a result of the reported post-RCE blunting of inflammation;[20] white cells, particularly neutrophils tend to increase in inflammation, as part of the acute phase response.[24] The Hb concentration increased progressively in all the patients, postprocedure and remained significantly higher than preexchange levels at the point of symptom resolution, this is consistent with the documented increase in Hb content which occurs post-RCE.[19]

The average length of inpatient hospitalization in this study is similar to that reported by Vichinsky *et al*. in adults patients (10.2 days vs. 10.5 days, respectively) but higher than observed by Sprinkle *et al*. in children (10.2 days vs. 7 days, respectively).[9,25] The average time for resolution of chest symptoms post auto-RCE (4.4 days) was shorter than the total inpatient hospitalization time in this study. Some of our patients had extended hospital stay due to concurrent co-morbidities such as renal impairment and pulmonary hypertension. It is, therefore, likely that the in-patient hospitalization, post auto-RCE could be similar to that observed in children (and may parallel the time of resolution of chest symptoms), in the absence of significant co-morbidities. There is a need to investigate for concurrent co-morbidities in SCD patients with ACS, who may need extended hospitalization post auto-RCE.

Limitations of this study

The small sample size could have affected the power of our conclusions.

CONCLUSION

Auto-RCE continues to show tremendous benefit in the setting of ACS, particularly with regards to prompt restoration of SpO_2 and timely resolution of presenting chest symptoms. It, therefore, has remarkable potential in significantly reducing lengths of ICU and hospital stay in SCD patients with this life-threatening complication.

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Conflicts of interest
There are no conflicts of interest.

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