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Randomized Clinical Trial to Evaluate the Safety of Avoiding Pre-operative Transfusion in Sickle Cell Anemia

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Background: Patients with sickle cell anemia have an increased chance of undergoing surgical procedures with higher morbidity. The practice of pre-operative blood transfusion for such patients is still controversial.

Objective: The aim of the study was to evaluate and assess the safety of avoiding pre-operative transfusions in patients with sickle cell anemia.

Design: Prospective randomized clinical trial.

Setting: Surgical departments, King Abdulaziz University Hospital and King Fahed Armed Forces Hospital in Jeddah.

Method: A randomized clinical trial of 369 sickle cell anemic patients with a median age of 16 years old (range: 1-35 years old), underwent surgical procedures between November 1996 and November 2001. Surgical procedures included adenoidectomy, tonsillectomy, total hip arthroplasty, cholecystectomy, splenectomy, and Obstetric and Gynecological surgeries. Patients with stable clinical and hematological state were randomized into two groups: Group I (n=181), received no pre-operative transfusion and Group II (n=188) received simple or partial exchange transfusion pre-operatively. All patients were carefully hydrated and good oxygenation was maintained.

Result: None of the patients developed major intra or postoperative complications in both groups. Fourteen percent of the pre-operative transfusion group developed postoperative complications versus 7% in non-transfused group with a significant P value (0.002).

Conclusion: Avoidance of pre-operative transfusion is a safe practice in properly selected steady state sicklers. On the contrary, it is believed that the risks associated with transfusion were avoided.

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It is generally recommended that patients with sickle cell anemia (SCA) receive red blood cell (RBC) transfusions before undergoing general anesthesia and surgery[1-11].

Recently, a great deal of controversial data has accumulated regarding transfusion management of such patients who require surgery.

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In 1988, Bishoff RJ, concluded that there is no evidence that pre-operative transfusion therapy to patients with SCA decreases morbidity, while there is some evidence to the contrary[11].

In Jamaica, it is a common practice to have major surgery with no pre-operative transfusion for stable SCA patients[12-14].

There are few recent studies in which transfusions were not given routinely prior to surgery; the studies in question enrolled pediatric and adult sicklers[15-17].

The SCA is a common hereditary blood disease seen in this area; the disease is associated with severe clinical manifestations[18, 19]. The aim of this prospective study was to assess the role of pre-operative transfusion practice in patients with SCA, and to assess the new trends and recommendations that hemoglobin concentration is not the sole parameter that should guide transfusion pre-operatively[20-22].

METHOD

This prospective, randomized clinical trial was conducted in King Fahed Armed Forces Hospital (KFAFH) and King Abdulaziz University Hospital (KAUH), over a period of 60-months, from November 1996 to November 2001. Ethics Committee approval was obtained at each participating institution and written informed consent was obtained from all patients prior to participation in any study procedures. Admission protocols were followed as seen in Table 1. The study enrolled 369 sickle cell anemic patients. The patients were randomized in to two groups. Group I: no pre-operative transfusion was given and transfusion was given only as compensation for blood loss during surgery; Group II: patients received either simple or partial exchange transfusion pre-operatively.

Table 1: Randomized studies for admission protocol between 1996 and 1998

Hospitals	Saturday	Sunday	Monday	Tuesday	Wednesday	Weekend
KAUH	T	NT	T	NT	T	NT
KFAFH	NT	T	NT	T	NT	T
Alternating Protocols (Next Week)						
KAUH	NT	T	NT	T	NT	T
KFAFH	T	NT	T	NT	T	NT
Randomized studies for admission protocol on alternative weeks between 1998 to 2001						
Hospitals	Saturday	Sunday	Monday	Tuesday	Wednesday	Weekend
KAUH	T	NT	T	NT	T	NT
KAUH	NT	T	NT	T	NT	T

NT = Non-Transfusion Group (Group I)
T = Transfusion Group (Group II)

The management protocol for both groups, pre and postoperative was similar in both hospitals. All patients were carefully hydrated and good oxygenation was maintained during and after surgery. All patients were evaluated prior to surgery and were clinically and hematologically stable in the immediate pre-operative period. Hematologically stable meant that their Hb was similar to the steady state (Hb 6-9 g/dl); these were confirmed from the outpatients' clinic records. The pre-operative hemoglobin S concentration was routinely checked only in Group II.

In this clinical trial, all types of surgical procedures were performed except cardiac surgery. Surgical procedures included fractures, fixation, eye surgery, functional endoscopic sinus surgery, endoscopies, appendectomies and abdominal surgeries etc.

RESULT

The mean age of patients in this study was 16 years (range 1 – 35 years old). Table 2 illustrates the characteristics of patients in both groups including different types of SCA, age, sex and types of transfusion given to the patients. Table 3 shows the types of operations in both groups.

The results showed none of the patients developed major intra or postoperative complications in both groups. Almost 24% of the patients had delayed surgery in the transfused group to fulfill the criteria of HbS concentration $\leq 40\%$ (Table 4).

Table 2: Characteristics of patients with SCA in both groups.

Characteristics		Group 1 (n=181)	Group II (n=188)
PHENOTYPE:	HbA Level		
HbSS	0	137	135
HbSâ^{0} thalassemia	0	35	39
HbSâ$^{+}$ thalassemia	3 – 5%	5	9
HbSC	0	4	5
SEX:			
Male		76	78
Female		105	110
AGE (yr)			
1 – 4		15	16
> 4 – 12		46	42
> 12 – 18		40	38
> 18 – 35		80	82
PREOPERATIVE TRANSFUSION			
Simple Transfusion		0	90
Partial Exchange Transfusion		0	98

Table 3: Different types of surgeries in both groups.

Type of Surgery	Number of Surgeries	
	Group I	Group II
Adenotonsillectomy	52	45
Total hip arthroplasty	28	21
Cholecystectomy	27	30
Splenectomy	28	20
Obstetrics / Gynecological Surgeries	23	35
Miscellaneous	16	28
Emergency	07	9
Total	181	188

Table 4: Complications in both groups.

Complications	Group I	Group II	P. Value
Painful Crises	3	5	
Neurological Complication	0	4*	
Minor Respiratory Complication	5	4	
Moderate to Severe Respiratory Distress	0	3*	
Circulatory Overload or Heart failure	0	5*	
Infection	3	3	
Others	2	3	
Total (Percentage)	13 (7.0%)	27 (14.0%)	0.002
Delay of Surgery	1	45*	> 0.001

* Hemoglobin raised $\geq$ 10.5 g/dl
To fulfill the criteria of HbS concentration < 40% pre-operative

The majority of the transfused group has been exposed to multiple donors. In total 27/188 (group II) (14%) patients from the transfused group developed complications in the postoperative period, while 13/181 (7%) patients had complications postoperatively in group I, with a statistical significance between the two groups, P value was 0.002.

DISCUSSION

The pattern of transfusion practice for patients with SCA is changing. In certain situations, blood transfusion can be life-saving to SCA patients. Transfusion of red cells can dilute sickle hemoglobin, suppress endogenous erythropoiesis, correct severe anemia and improve oxygen-carrying capacity.

We still do not understand all of the mechanisms that contribute to clinical complications occurring in some of the transfused sicklers[8, 23-25]. It is probably the combination of increased blood viscosity with decreased efficiency of oxygen delivery to the tissues[1].

The viscosity of blood is determined by the total hematocrit (Hct) and the deformability of the RBCs. As erythrocytes are transfused; therefore, the Hct rises resulting in a significant increase in blood viscosity. In anemic patients, oxygen transport increases as blood is transfused until the Hct reaches 40%. Once the Hct has risen above 45%, the viscosity increases dramatically and oxygen transport starts to fall. Unfortunately, in patients with SCA (Hb SS), the viscosity of RBC suspension at full oxygenation is already higher than that of a healthy non-sickler patient with normal hemoglobin (Hb AA) and the viscosity of the sickle cell RBC rises progressively with deoxygenation.

When a patient with SCA receives a simple blood transfusion, the increase in Hct with a constant sickle crit (Sct) leads to an increase in viscosity, thus limiting the improvement of oxygen delivery, despite the improved oxygen carrying capacity[26, 27]. It appears that Hct of ≥25% causes disproportionate increase in whole-blood viscosity related to increasing Hct, as compared with Hb AA patients.

HbS by nature has more potential to deliver oxygen to the tissue due to its low oxygen affinity, making SCA a unique disorder with adequate oxygen delivery to the tissues in the stable state, despite the lower hemoglobin level.

This randomized clinical trial showed that there were no major differences in the mortality, morbidity and disease complications postoperatively between the two groups. Recent studies confirmed these findings[28,29].

CONCLUSION

Avoidance of pre-operative transfusion is a safe practice in patients with SCA in a stable state.

The study showed no evidence that pre-operative transfusion decreases morbidity and there was some evidence of an increase of postoperative complications.

Transfusions in sickle cell patients need a justified indication and it is recommended not to raise the hemoglobin level above 10.5 g/dl.

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