

Heart valve surgery in patients with homozygous sickle cell disease: A management strategy

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ABSTRACT

Background: Patients with the homozygous sickle cell disease have increased perioperative mortality. Some indications like heart valve surgery, may justify an exchange blood transfusion to reduce the proportion of hemoglobin S (HbS) and complications. **Subjects and Methods:** We report two female cases aged 20 and 27, of African origin with homozygous sickle cell anemia who underwent heart valve surgery to treat mitral valve regurgitation. This presentation describes the perioperative considerations including anesthesia and postoperative care. **Results:** A partial exchange blood transfusion decreased HbS levels from respectively, 90% and 84%, 9% to 27% and 34%, and simultaneously treated the anemia. Neither sickling crisis nor acidosis occurred in any patient, and no special postoperative complication occurred. Average hospital stay was 10 days. Currently, the two patients remain alive and free of cardiac symptoms. **Discussion:** Although the presence of sickle cell disorders is associated with increased risk of sickling and thus vaso-occlusive complications, they should not be taken as a contraindication for heart valve surgery. Nevertheless, monitoring of certain parameters such as venous, arterial oxygen content, pH, and body temperature is mandatory for a better outcome. Furthermore, preoperative exchange transfusion has a positive influence on the outcome of surgery and on the survival of patients undergoing heart valves surgery. Avoiding intraoperative hypoxia, hypothermia, and vaso-constrictive agents, minimizing HbS levels with preoperative exchange transfusion, and ensuring a stress-free environment with the judicious use of sedatives made surgery relatively safe in these cases.

Key words: Exchange transfusion; Heart valve surgery; Hemoglobin; Sickle cell disease

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INTRODUCTION

Hemoglobinopathies mainly sickle cell anemia and thalassemia, are autosomal-recessive inherited disorders. Approximately 5% of the whole world population carries a potentially pathological gene.

Sickle cell disease (SCD) is frequently seen among Africans but is also found in Southern Europe, the Middle East, and India.^[1] Patients with SCD who require cardiac surgery, especially homozygous forms are at risk of a potentially fatal sickling crisis, which may be induced by hypothermia, hypoxia, acidosis, or low-flow states.^[2]

Modification of the routine perioperative management strategies with special

considerations is required for a successful outcome in patients with SCD, who undergo heart valve surgery.

Because it is a rare clinical entity, the aim of our present study was to report a simplified

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management strategy that can be used by cardiac surgery teams in patients undergoing heart valves surgery in the presence of SCD to reduce perioperative complications in this population of patients.

SUBJECTS AND METHODS

We evaluate two female adult patients of African origin aged 20 and 27 with homozygous sickle cell hemoglobinopathy who underwent open heart surgery for the heart valve disease at our institution.

The two patients received exchange transfusion before surgery, to decrease hemoglobin S (HbS) concentration to about 30%.

We do not perform any exchange transfusion during cardiopulmonary bypass (CPB).

Analyzed parameters were exchange transfusion, length of surgery, CPB time, and cross-clamp time, duration of Intensive Care Unit, hospital stays, and complications. Perioperative changes in temperature, hemodynamics, respiratory, and metabolic parameters were recorded [Table 1].

Standard Hb electrophoresis was performed to detect the concentrations of HbS, HbC, and HbA [Figure 1a and b].

Alterations in Hb and hematocrit, blood loss, and transfusion requirement were documented [Table 2].

The two patients were followed up in the postoperative period for 10 and 2 years.

Preoperative exchange transfusion

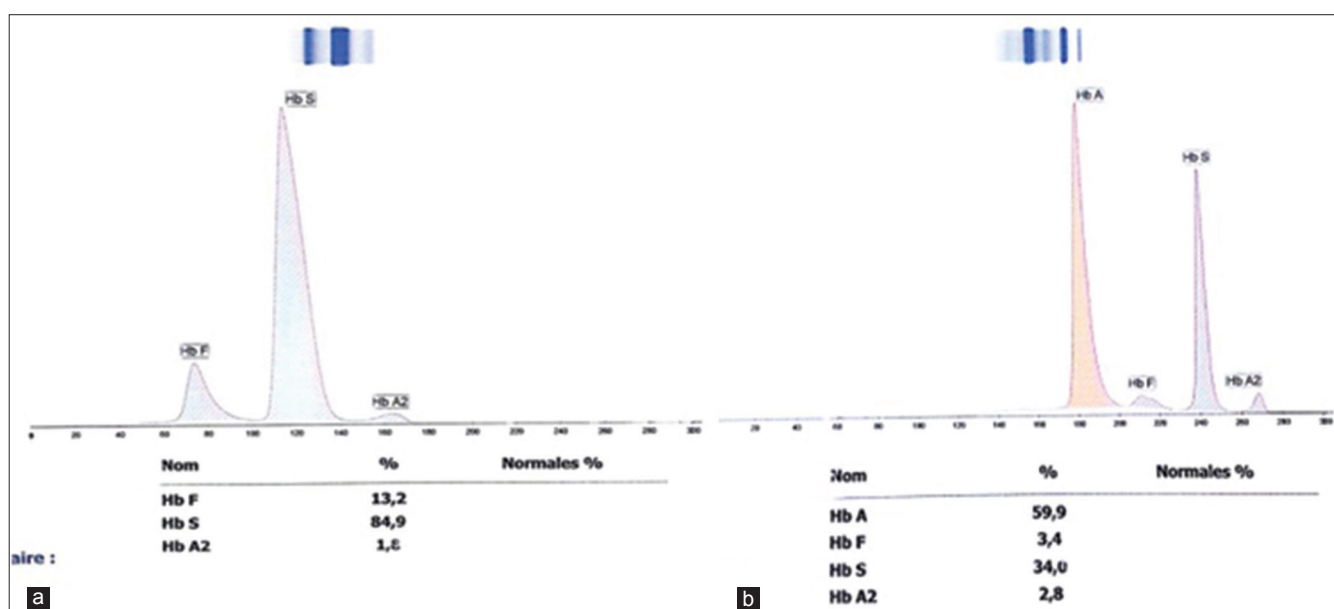
Exchange transfusion was performed preoperatively in the two patients to decrease HbS concentration and to increase hematocrit.

One-third to one-fourth of the calculated blood volume was drained from a central vein (internal jugular vein) using a blood component collector of red blood cells and plasma (Haemonetics® MCS® + 8150 – Haemonetics Corporation, 400 Xood Road, Braintree, MA 02184, USA) [Figure 2] in order to separate different blood cells by a centrifugation procedure. Red blood cells are recuperated into a blood bag then plasma and other cells are restituted to the patient.

During this procedure, and to avoid blood coagulation into the extracorporeal circuit, an anticoagulant like: Anticoagulant citrate dextrose solution, solution A is used.

Concomitant transfusion is performed into a peripheral vein. Red blood cells were replenished with packed red blood cells from healthy individuals obtained from the hospital blood bank.

Five to six blood bags were sufficient on each patient to decrease HbS concentration and to increase hematocrit.



Figures 1: (a and b) Standard hemoglobin electrophoresis before and after exchange transfusion on patient two (MINCAP SEPIA capillary method)

Table 1: Demographic characteristics of the two patients

| Patients | Age (years) | Sex | Weight/height (kg/m) | Diagnosis | Procedure | Cross clamp/CPB (min) | CPB temperature (°C) | Hospital stay (days) | Status |
|----------|-------------|--------|----------------------|-----------------------------------|--|-----------------------|----------------------|----------------------|------------------|
| 1 | 20 | Female | 47/1.67 | MV regurgitation | MV repair (Seguin ring 30 mm) | 55/90 | 37 | 15 | Alive (10 years) |
| 2 | 27 | Female | 37/1.60 | Rheumatic MV and TV regurgitation | MV replacement (St. Jude mechanical valve 33 mm)+ TV repair Carpentier Edwards ring 32 mm | 67/123 | 37 | 14 | Alive (2 years) |

CPB: Cardiopulmonary bypass, MV: Mitral valve, TV: Tricuspid valve

Table 2: Preoperative biological data of the two patients

| Patients | Preoperative | | | | | |
|----------|-------------------------------------|---|---|---|---------------------|--|
| | HbS before exchange transfusion (%) | Hct/Hb before exchange transfusion (%/g/dl) | Red blood cells centrifuged volume (ml) | Red blood cells transfused volume (ml/bags) | %HbS after exchange | Hct/Hb after exchange transfusion (%/g/dl) |
| 1 | 90 | 30/9.5 | 700 | 1000/5 | 27 | 38/13 |
| 2 | 84.9 | 26/8.5 | 600 | 1200/6 | 34 | 45/15 |

Hb: Hemoglobin, Hct: Hematocrit

**Figure 2: Haemonetics® MCS®+ 8150 Multicomponent Collection System**

Anesthesia management

The two patients received their cardiac medications until the morning of surgery. Contraindicated drugs were avoided. Oral intake was stopped 6 h before surgery.

In a heated operating room (25°C), after oxygenation, anesthesia was induced with midazolam, fentanyl, and pancuronium was used for muscle relaxation. After intubation, the two patients were ventilated with 100% oxygen.

All invasive procedures were performed while the patients were under deep anesthesia: After tracheal intubation, arterial, and central venous lines were inserted. Further incremental doses of fentanyl were administered during the operation.

Tranexamic acid was used routinely to prevent bleeding complications.

Arterial blood pressure, central venous pressure, electrocardiogram, saturation with pulse oximetry, and rectal temperature were routinely monitored during and after surgery. Anesthesia was maintained with an infusion of propofol.

Fast-track anesthetic management was not performed, and the two patients were transferred to the intensive care unit while still under sedation with propofol. Tracheal extubation was performed once optimal cognitive, hemodynamic, and respiratory functions were achieved.

For postoperative pain management, morphine, and paracetamol were administered.

Cardiopulmonary bypass

CPB was performed in a routine manner. The bypass circuit volume was adjusted according to the age, weight, and body surface area of each individual patient to reach a hematocrit value of average 30% during CPB. Additional crystalloid, colloid, or red blood cells were added to the CPB circuit as needed according to the desired hematocrit levels.

Throughout the bypass, venous oxygen saturation was kept at >80%. To avoid the risk of sickling, rectal temperature was maintained >36, 5°C. pH of the serum during CBP was maintained between 7.35 and 7.45 by

correction of acidosis with sodium bicarbonate. The flow was adjusted as a body surface area times cardiac index (2.2–2.4). We avoided using of exchange transfusion during CPB. Myocardial protection was performed using a 20 ml/kg of antegrade cold crystalloid cardioplegia. A second or a third shot of crystalloid cardioplegia was given every 20 min with half of initial dose (10 ml/kg).

RESULTS

Operations were performed to treat valvular pathologies [Table 1]. Baseline Hb and hematocrit values were 9.5 g/dL to 30% for the first patient and 8.5 g/dL to 26% for the second one.

The preoperative HbS concentration before therapeutic exchange transfusion was about 90% and 84.9%.

After exchange transfusion in the preoperative period, hematocrit was increased to 38% and 45%. Preoperative HbS concentration decreased to 27% and 34% after preoperative exchange transfusion [Table 2].

Mean CPB and cross-clamp times were 123 and 95 min, respectively. None of the patients underwent active systemic cooling and all operations were performed at $>36^{\circ}\text{C}$. The mean flow rate during CPB was 3.5 L/min. On-pump perfusion pressure ranged from 65 to 80 mmHg.

Neither sickling crisis nor acidosis occurred in any patient, and no major postoperative complication occurred. Postoperative biological data of the two patients is reported on Table 3.

Average hospital stay was 10 days. Currently, the two patients remain alive and free of cardiac symptoms.

DISCUSSION

Sickle cell hemoglobinopathy is a recessively inherited genetic disorder seen world-wide. It results from the mutation of the substitution of adenine for thymidine,

which further ends up matching with valine rather than glutamine at the sixth codon of chromosome 11 that is, the β -globin gene.^[3] The condition may present as SCD (homozygous genotype [HbAS]), the severe form in which, the fractional concentration of HbS ranges between 70% and 98%, or it can be manifested as sickle cell trait, which is rather benign and more common among populations as the heterozygous genotype (HbAS), in which the fractional concentration of HbS is $<50\%$.^[4]

The solubility characteristics of HbS are severely impaired, and after the dispersal of oxygen to tissues, the molecule adopts its characteristic sickle shape. Erythrocytes containing high amounts of HbS undergo multiple sickling and desickling events, deforming their conformation and eventually resulting in autolysis and anemia.^[5] Furthermore, these deformed cells have an increased tendency to adhere to the vascular endothelium, frequently leading to occlusion of small-caliber vessels, and causing organ damage.^[5]

The classic precipitating factors for sickling include stress, exposure to cold, dehydration, infections, hypoxemia, inflammatory cascades, and acidosis.^[6-8] Such conditions lead to potassium efflux, causing the formation of insoluble globin polymers. These molecules increase the viscosity of blood and lead to vaso-occlusive phenomena, which include cell sickling, adherence of sickle cells to the endothelium, and vaso-occlusion.^[9,10] Although the risks are accompanying sickle cell pathology before high-risk surgery including orthopedic and cholecystectomy, have been well stated, the literature contains only small series or case reports on sickle cell patients having cardiac surgery.^[6,11,12]

It should be noted that predisposing conditions are more common in patients undergoing cardiac surgery especially during the anesthesia, CPB itself, as well as aortic cross-clamping, low-flow states, topical or whole-body hypothermia, cold cardioplegia, and use of vaso-constrictive agents, may predispose to the crisis state.^[6,12] Hence, special care should be taken in sickle

Table 3: Postoperative biological data of the two patients

| Patients | Postoperative | | | | |
|----------|---|-------------------------------|--|---------------------|-------------------------|
| | Peroperative red cells bag transfused volume (ml) | Postoperative blood loss (ml) | Postoperative red cells transfused volume/bags (ml/bags) | % Hct postoperative | Hb postoperative (g/dl) |
| 1 | 0 | 900 | 400/2 | 34 | 10.5 |
| 2 | 0 | 500 | 200/1 | 36 | 11.8 |

Hb: Hemoglobin, Hct: Hematocrit

cell patients who require cardiac surgery to avoid or at least to minimize those risk factors.

These maneuvers may start with decreasing the amount of HbS concentration in the blood with exchange transfusion.

Exchange transfusion decreases the amount of circulating sickle cells without increasing hematocrit levels or blood viscosity.^[11] On the other hand, in patients with deep anemia, therapeutic exchange transfusion not only is advantageous for decreasing HbS, but also increases the preoperative hematocrit and hence oxygen delivery to the organs, which further facilitates surgery. Exchange transfusion can be done preoperatively as performed in our experience, peroperatively, or both.^[6] Although there is no consensus on absolute safe values of HbS in patients undergoing surgery, it is proposed that the level of HbS should be reduced to average 30% for major surgical procedures or even 5% for cardiac surgery before or at the time of surgery.^[10-13]

Although some authors advocate against blood transfusion for Hb levels >7 g/dL the benefits of a reduction in HbS and an increase in HbA concentrations are obvious for preventing sickling phenomena and providing adequate delivery of oxygen to the tissues.^[14-16] The advantages of preoperative transfusion include increased hematocrit levels and suppressed production of HbS in this particular group of anemic patients. The literature contains reports indicating that the majority of patients with sickle cell hemoglobinopathy scheduled for cardiac surgery receive preoperative transfusion.^[2,7,17,18]

It should be kept in mind that the amount of circulating HbS is only one factor among many (e.g. disorganized endothelial function, cytokine expression, increased number of inflammatory cells) for sickling and vascular occlusion complications.^[12]

Stress is another major factor that may lead to sickling. Cardiac surgery itself constitutes a major stress for the patient, but the preparatory phase for operation including intubation and the insertion of catheters, contributes considerably toward this stress, particularly in pediatric patients, and it is strongly recommended that patients must be kept fully sedated during this phase.^[10,15,19]

Prevention of hypothermia in the operating theater is an easy preventive measure that helps avoiding

sickling phenomena. Warm-air blankets before and after surgery may be helpful to stabilize the patient's body temperature.^[10] On the other hand, systemic cooling via the CPB circuit is commonly applied in cardiac operations to reduce the metabolic rate. Hypothermia carries the risk of sickling, and vascular occlusion in the presence of sickle cell hemoglobinopathy. This can be avoided by applying "topical-only" cooling or achieving moderate hypothermia, but totally warm CPB is another valid option frequently mentioned in the literature.^[2,13,17,18,20,21]

Avoidance of hypoxia is crucial for preventing a sickling crisis. Thus, oxygen delivery to the CPB circuit should be ensured at all times during surgery. In some series, the CPB pump prime was hyperoxygenated to a PO₂ >50 kPa to mediate increased oxygen levels in the patient's own blood after mixing in CPB circuits. The patient's venous oxygen saturation monitoring is a reliable marker for blood oxygenation. Levels >80% during the surgical procedure were advocated as safe.^[2,13,22,23]

Although the presence of sickle cell disorders increases the risk of sickling and thus vaso-occlusive complications in patients, they should not be taken as a contraindication for heart valve surgery. Nevertheless, monitoring of certain parameters such as venous and arterial oxygen content, pH, and body temperature is mandatory for a better outcome. Furthermore, preoperative exchange transfusion has a positive influence on the outcome of surgery and on the survival of patients undergoing heart valves surgery.^[23] Our clinical experience is consistent with the acceptance of patients with sickle cell hemoglobinopathies for cardiac surgical operations requiring CPB. Avoiding intraoperative hypoxia, hypothermia, and vaso-constrictive agents; minimizing HbS levels with preoperative exchange transfusion, and ensuring a stress-free environment with the judicious use of sedatives made surgery relatively safe in these two patients.

CONCLUSION

Heart valve surgery can be performed safely in patients with SCD with the good outcome by modifying the routine perioperative management strategies and by using special considerations. Nevertheless, literature on the evaluation and specific management of these patients remains limited, and further studies are strongly recommended.

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Conflict of interest

There are no conflict of interest.

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