

Atrial septal defect closure on cardiopulmonary bypass in a sickle cell anemia : role of hydroxyurea and partial exchange transfusion

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Abstract

Complications associated with Cardiopulmonary bypass such as, hypothermia, risk of hypoxia, stress in a patient with high levels of sickle haemoglobin can cause life threatening consequences. The picture may be worsened by post operative ventilatory problems because of painful sternotomy and depressant effect of narcotics. We managed a case of 16 years female of Turner's syndrome having sickle cell anaemia for closure of Arterial septal defect on cardiopulmonary bypass with partial exchange transfusion and without hypothermia. Summary Sickle cell anaemia is a disorder of haemoglobin structure in which shape of RBC changes to sickle in hypoxic environment and can cause vascular occlusion and ischaemia of multiple organs. Hypothermia, stagnation of blood and acidosis are other factors which can precipitate it and can cause multiple infarcts. When subjected to cardiopulmonary bypass for cardiac surgery, these cases need special management to prevent such episodes. Though exchange transfusion is one of the commonly used methods in perioperative period, we used intraoperative partial exchange transfusion to reduce the concentration of HB- ss. Along with this we insisted on use of hydroxyurea and hematenics for optimization of the patient in preoperative period and TENS for analgesia in post operative period.

CASE REPORT

A 16 year female was admitted to medicine department of the hospital with complains of Pain in right thigh and abdomen for 6 days. This young female a known case of sickle cell anaemia was apparently alright 3 years back when she started getting breathless (grade 1) along with recurrent attacks of common colds which progressed to NYHA grade 3 over last 3 yrs. It was accompanied by generalised dull aching bone pain which used to be precipitated by cold. She was transfused three times in last three years. Last whole blood transfusion was given 1 month before admission. Both parents having sickle cell traits were leading a normal life.

She was pale with pulse rate = 110/ min, BP = 110/ 70 mm Hg and respiratory rate = 24/ min. There was splitting of second heart sound with soft systolic murmur. Per abdomen examination revealed splenomegaly with 3cm below left costal margin. Anthropometry done showed weight of 34 kg and height of 4.7”(short statured). Hemogram on admission showed haemoglobin = 7.6 gm% (PCV = 33%), leucocyte count = 7800/mm³, reticulocyte count = 6% and peripheral smear showed microcytes, macrocytes, target cells, poikilocytosis, anisocytosis. Hemoglobin electrophoresis

finding was suggestive of homozygous sickle cell anemia with HbSS= 71%, HbA2 = 5.6%, HbF = 20%. X-ray chest showed moderate cardiomegaly and ECG had features of right ventricular strain pattern. Two-dimensional echocardiography findings showed: three pulmonary veins draining into left atrium, ostium secundum type ASD of 24 mm size with LIR shunt and moderately dilated right atrium and ventricle, ejection fraction = 36%, right ventricular end-diastolic diameter = 36 mm, Pulmonary arterial pressure=35mm Hg. As the patient also had history of primary amenorrhea and undeveloped secondary sexual characters USG abdomen was done which showed an enlarged spleen with rudimentary uterus with streak ovaries. Turner syndrome was kept as possibility and hormonal assay with karyotyping was done. Serum FSH level was < 0.10 mIU/ml (very low), LH < 0.1 mIU/ml (very low), prolactin = 4.67 ng/ ml (high). Karyotype (45XO) confirmed diagnosis of Turner syndrome.

As the patient presented in sickle cell crisis standard management included i.v. hydration, oxygen supplementation and pain relief (tramadol). She responded well to this and after that started on hydroxyurea (500

mg/day), hematinics supplements and antibiotics. Surgery for ASD closure was planned after 2 months. Hydroxyurea and hematinics were continued upto day of surgery. Patient's Hb was 11.6 gm% ,PCV=36%,on day before surgery. Preoperative Hemoglobin electrophoresis showed HbSS=60%.HbA2=8.6%,HbF=26%.

In preoperative period she was kept on i.v. ringer lactate to avoid dehydration. Patient was explained about the procedure, anaesthesia, and the recovery. An informed valid consent was obtained.

Intraoperatively, she received dexamethasone, midazolam, fentanyl premedication in standard doses. After preoxygenation the patient was induced with, propofol and vecuronium. Anaesthesia was maintained with N₂O and O₂ (50:50) on circle absorber system with sevoflurane intermittently. Intraoperative continuous CVP, arterial pressure, urine output and temperature monitoring was done. The cardiopulmonary bypass circuit: venous reservoir of 3000 ml capacity was used along with a hollow fibre oxygenator attached to it. A heat exchanger and air filter were installed with it.

Cardiopulmonary bypass circuit was primed with ringer lactate (1.5L), whole blood (1L), sodium bi carbonate (70 ml), 20% mannitol (70 ml), heparin (3400 IU), methyl prednisolone (500 mg). After thoracotomy, pericardial patch was obtained for closure of the defect. After administering heparin 10200 units aortic cannulation was done followed by superior and inferior venacava cannulation. Before initiating bypass, 1000ml of autologous blood was drained via a side port in the venous line and discarded. At the same time priming fluid was infused to maintain the hemodynamic status. Bypass was initiated with flows 2.5 L /min. Mean perfusion pressure was maintained near 65 mm of Hg. After aortic cross clamping warm blood cardioplegia was delivered. The temperature was carefully maintained near 37oC. Blood collected by the suckers was not passed to reservoir and was discarded. The level in reservoir was maintained by addition of fresh blood to it while maintaining the hematocrit near 26% by addition of crystalloids. pH was strictly maintained above 7.4 by addition of sodium bicarbonate. The details of cardio-pulmonary bypass were: total bypass time = 81 mins, total cross clamp time = 35 mins, rest time of 12 mins was given, urine output = 150 ml.

Figure 1

Table 1: Details of cardioplegia

Cardioplegia number	Time (am)	Volume (ml)	K+ (mEq)	Temperature (°C)
CP – 1	11.16	700	16	38.0
CP – 2	11.32	700	08	37.2

Figure 2

Table 2: Perioperative Arterial Blood Gas analysis

Time	9.42 am	11.18 am	11.46 am	12.02 am
Event	Induction	Post Cardioplegia 1	Cross Clamp Off	Post Bypass
pH	7.414	7.441	7.484	7.362
PCO ₂ mmHg	38.3	30.6	27.0	39.2
PO ₂ mmHg	289.4	471.5	438	377.8
Na+ mEq/ L	139	140.2	143.6	142
K+ mEq/ L	3.31	3.84	3.72	3.41
BE	- 0.6	- 3.8	-3.6	-3.7
SO ₂ %	99.6	99.7	99.0	99.4
Hb	11.0	9.1	9.3	9.8
Hct (%)	32.8	25.3	26.7	27.0

The patient was started with dopamine 10 µg/kg/min after which she was easily separated from cardio-pulmonary bypass. Heparin was reversed with 150 mg (1.5 mg per 100 units of heparin) of protamine sulphate which was injected very slowly through the arterial monitoring line to avoid fall in systemic blood pressure and rise in pulmonary vascular resistance. At the end of bypass, blood contained in the reservoir was not returned to the patient and was discarded. Instead, the patient was transfused one unit of fresh blood and ringer lactate to maintain the CVP near 10 cm. After surgery the patient was shifted to the critical care unit (CCU) and put on SIMV mode of ventilation.

Post-operatively the patient had spontaneous eye opening started responding to verbal commands after 1 hour. Post bypass urine output was 700 ml. No hematuria. Arterial blood gas and electrolytes were normal. The patient was started one more unit of blood (350 ml). Also, she was given TENS (transcutaneous electrical nerve stimulation) for pain relief. She had 525 ml of urine in next 2 hrs and 40 ml drain. This was replaced by crystalloid. CVP was kept near 10 cm. After 2 hrs ABG and Hb was repeated and was normal. With TOF ratio of 1 the patient was extubated and was put on ventimask with 60% Fio₂. The patient's vital parameters, urine output, CVP drains were monitored closely over next few hours and remained normal. U/O of next 6 hrs was almost 675ml and drains 20ml. She had only mild pain for which TENS was continued and diclofenac suppository was given per rectally. Chest physiotherapy, nebulisation, incentive spirometry was started. Dopamine support was tapered off gradually. The patient started having full diet. Hydroxyurea 500 mg/day was reinstituted after 36 hours.

Her stay of next 20 days in hospital was uneventful. She was discharged from hospital on hydroxyurea, antibiotics and hematinics. During next visit after 15 days all the medications were stopped except hematinics.

DISCUSSION

On our search for management strategies for patient of sickle cell disease on cardiopulmonary bypass without exchange transfusion, we found that, preoperative blood transfusion is indicated in sickle cell disease patient which increases the hematocrit along with decrease in sickle cell Hb levels (1,4). Preoperative sickle cell Hb value of $\leq 30\%$ was recommended but with us the preoperative sickle cell Hb value was brought down to 60% with three units of fresh blood transfusion in combination with hydroxyurea and hematinics preoperatively. Hydroxyurea in a dose of $10\text{--}30\text{mg/kg}$ has been a main stay of treatment in patients with severe symptoms (3). It is known to increase HbF and also exerts beneficial effects on red cell hydration, vascular wall adherence and suppression of granulocytes (3). We were impressed by case study of Sutton et al (1) regarding partial exchange transfusion and platelet sequestration but due to lack of facility in our set up we planned for partial exchange transfusion only using fresh blood (≈ 24 hrs of collection) (5,6). Using simple mathematical calculations as following,

Preop HbSS = 60% . Preop hematocrit = 36% .

Blood volume of patient = $34 \times 85 = 2890\text{ml}$

Estimated RBC volume = $36\% \times 2890 = 1040\text{ml}$.

Patient's blood replaced = 1200ml .

1200ml of patient's blood = 432ml of RBC + 768ml of Plasma

So total RBC volume decreases by $432\text{ml} = 41.5\%$ decrease in RBC volume

So expected decrease in HbSS = 41.5% of total HbSS

So decrease in HbSS after exchange transfusion = $41.5 \times 60 / 100 = 24.9\%$

Final HbSS value after exchange transfusion = $60 - 24.9 = 35.1\%$

It was concluded that with exchange transfusion of 1200ml of fresh blood the HbSS level would be decreased to $35\text{--}36\%$.

Because hypothermia leads to vasoconstriction and stasis of RBCs leading to sickle cell crisis we avoided hypothermia. For the same reason warm blood cardioplegia with high Pao₂ and low hematocrit and hence low viscosity was given (16). Acidosis was prevented intra and postoperatively by avoiding potent opioids which can cause respiratory depression. Instead we used TENS to manage sternotomy pain (8,9) in post operative period with diclofenac suppository. Post operative complications are kept to minimum with early extubation and timely physiotherapy with meticulous fluid input-output monitoring and maintenance of hematocrit using post operative blood transfusion. Methylprednisolone can inhibit activation of endothelium caused by surgical stress and sickling, cytokines and platelet aggregation (15).

CONCLUSION

Managing sickle cell disease patients on Cardiopulmonary bypass is a team work which includes anesthesiologist, physician, surgeon, perfusionist, chest physiotherapist, good blood bank and laboratory support. Partial exchange transfusion with use of fresh blood is an effective tool in the hands of anaesthesiologist to optimise the sickle cell Hb value of the patient in absence of cell saver. Preoperative optimization of the patient, meticulous intraoperative fluid monitoring, with avoidance of respiratory depression and acidosis and use of alternative strategies for pain management have a significant role in patient outcome.

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