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Open-heart surgery in sickle-cell haemoglobinopathies: report of 15 cases

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ABSTRACT Fifteen cases of open-heart surgery in patients with sickle-cell haemoglobinopathies are reported; 13 had sickle-cell trait, one had SC haemoglobinopathy, and one had β-thalassaemia sickle-cell disease. All patients except one were operated on with moderate hypothermia, aortic cross-clamping, topical hypothermia, and cold cardioplegia. A bloodless priming solution was used in nine patients and five did not receive any blood throughout their hospital stay. Arterial and venous blood gas analysis and a search for sickle cells and haemolysis were carried out during and after cardiopulmonary bypass. The data were compared with the findings in a group of 29 patients without haemoglobinopathy operated on without blood transfusion. Two patients died from low cardiac output, unrelated to the haemoglobinopathy. All other patients recovered uneventfully. Sickling occurred during and after bypass in only one case, and the percentage of sickle cells was considerably lower during and after surgery than before. Haemolysis occurred only once during cardiopulmonary bypass and twice after surgery (the two deaths from low cardiac output). There was no acidosis or hypoxia. There was no difference in the loss of haemoglobin between the 13 survivors and the control group. Our data suggest that adequate oxygenation and avoidance of acidosis and dehydration during surgery are important. On the other hand, we do not believe that preoperative transfusion or exchange transfusion, a blood prime, normothermia, and the avoidance of aortic cross-clamping or topical hypothermia are essential precautions. We believe that transfusion should be used during cardiopulmonary bypass only for severely anaemic patients. The technique used in our cases adds to the safety of the procedure and improves the protection of the myocardium.

The potential dangers to patients with sickle-cell haemoglobinopathies during operations requiring cardiopulmonary bypass have been emphasised by several authors.[1–6] There have been only 11 reported cases; one of these patients died from sickle-cell thrombosis.[7] Recommendations for precautions at cardiopulmonary bypass based on these patients include the use of exchange transfusions, preoperative transfusions, and blood in the priming solution and the avoidance of acidosis, hypoxia, hypothermia, aortic cross-clamping, and mechanical valvular prostheses. More recently, however, a case of successful cardiopulmonary bypass in a patient with sickle-cell trait was reported where aortic cross-clamping, cardioplegia, and topical hypothermia were used.[8] We report our experience with 15 patients from the Ivory Coast with various sickling disorders who required open-heart surgery. We also show that several previously accepted precautions are not necessary. We have developed a technique for safer cardiopulmonary bypass with improved myocardial preservation that does not increase the risks inherent in these patients' condition.

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Methods

The patients in this study were 15 black Africans aged 3–40 years (mean 18·6 years). Thirteen had sickle-cell trait and two a more complex sickling disorder—one SC haemoglobinopathy and one β-thalassaemia sickle-cell disease (table 1). All patients had their cardiac diagnosis confirmed by echocardiography, cardiac catheterisation, and left or right heart cineangiography. None had an obvi-

Table 1 *Details of patients with sickle-cell haemoglobinopathies undergoing open-heart surgery*

Case No	*Sex*	*Age*	*Class*	*Haemoglobin electrophoresis (% abnormal Hb)*	*Preoperative sickling*	*Diagnosis*
1	M	24	II	A S_{48}	0	Ostium secundum
2	F	3	III	A S_{34}	0	Ostium secundum
3	F	8	II	A S_{35}	0	Pulmonary stenosis
4	M	38	IV	A S_{37}	0	Mitral stenosis
5	F	22	IV	A S_{38}	0	Mitral insufficiency
6	M	16	III	A S_{38}	+	Mitral insufficiency
7	M	13	III	A S_{44}	0	Double-outlet right ventricle, dextrocardia, pulmonary stenosis
8	M	28	III	A S_{40}	0	Left ventricular subannular aneurysm, mitral insufficiency
9	M	40	IV	A S_{27}	0	Annuloaortic ectasia
10	F	14	III	A S_{40}	0	Right-heart endomyocardial fibrosis
11	M	23	III	A S_{38}	0	Mitral insufficiency
12	F	21	IV	A S_{33}	0	Aortic insufficiency (endocarditis)
13	M	6	III	S_{55} C_{45}	+	Ventricular septal defect
14	M	5	IV	A S_{40}	0	Tetralogy of Fallot
15	F	11	III	S_{75} $F_{9\cdot6}$ $A_{11\cdot5}$	++	Mitral insufficiency

ous history of sickle-cell crisis and only one patient (case 10) had splenomegaly. No patient had evidence of preoperative haemolysis. Haemoglobin concentrations ranged from 7·4 to 24·9 g/dl (mean 11·8 g/dl when two cyanotic patients with a high haemoglobin concentration are excluded). Only one patient (case 15) had a reticulocytosis—11%. Three patients had preoperative circulating sickle cells: patient 13 had 3% sickle cells in the venous blood and patient 15 had 27·5%—the latter received one unit of packed cells before operation.

CARDIOPULMONARY BYPASS

A bubble oxygenator was used in all patients (Travenol 6 LF, Temptrol Q100, Q110, and BOS 10). Table 2 shows data concerning the conduct of cardiopulmonary bypass and the procedures performed. Ten patients had a bloodless priming solution and nine of these received no blood during surgery. Arterial and central venous blood gases were measured before cardiopulmonary bypass, every 20 minutes during the operation, immediately after the operation, and on return to the intensive

Table 2 *Methods used in the open-heart surgery on patients with sickle-cell haemoglobinopathies*

Case No	*BSA (m^2)*	*Priming solution (ml)*	*Postoperative transfusion (ml)*	*Aortic cross-clamping time (min)*	*Lowest temperature (°C)*	*Cold cardioplegia and topical hypothermia*	*Procedure*
1	1·95	Ringer's, 1500 blood 800	400	0	35	–	ASD closure
2	0·42	Ringer's, 200 blood 250	150	57	30	+	ASD closure
3	0·82	Ringer's, 800 blood 200	0	27	30	+	Pulmonary valvotomy
4	1·50	Ringer's 2000	2000	72	32	+	MVR (xenograft)
5	1·56	Ringer's 1300	0	64	29	+	MVR (xenograft)
6	1·49	Ringer's 1200	0	90	28	+	MVR (xenograft)
7	1·15	Ringer's 900 (+ 100)	1600	125	27	+	Correction
8	1·56	Ringer's 1100	1400	135	28	+	Plication of aneurysm and MVR (xenograft)
9	1·72	Ringer's 1200 (+ 300)	1800	148	28	+	Bentall procedure (xenograft)
10	1·38	Ringer's 1200	0	92	28	+	Endocardectomy and TVR (xenograft)
11	1·72	Ringer's 1300	0	79	30	+	MVR (xenograft)
12	1·50	Ringer's 800 (+ 125	0	111	28	+	AVR (xenograft)
13	0·79	Ringer's, 300 blood 600	650	53	29	+	Patch closure
14	0·68	Ringer's 800 (plus blood) 600	500	88	28	+	Correction
15	1·01	Ringer's, 200 blood 800	650	47	28	+	Mitral valvuloplasty

ASD: atrial septal defect; AVR: aortic valve replacement; BSA: body surface area: MVR: mitral valve replacement; TVR: tricuspid valve replacement.

care unit. Care was taken to correct any acidosis or hypoxia.

A search for sickle cells was made on the samples drawn for blood gas analysis, with the use of a May-Grunwald-Giemsa stain and microscopic examination of blood smears. Simple signs of haemolysis were also looked for—that is, the colour of the serum and urine was noted and serum bilirubin and lactate dehydrogenase concentrations were determined—in the early postoperative period and seven days after surgery. The serum-free haemoglobin was not measured. Haemoglobin concentrations were measured daily after cardiopulmonary bypass so that the loss of haemoglobin and the percentage change after surgery could be calculated.

POSTOPERATIVE CARE

After operation care was taken to avoid any acidosis or hypoxia and blood transfusions were kept to a minimum. Postoperative fluid replacement was with 500 ml/m² on the first day and 750 ml/m² on the second day. All patients received iron supplements. Except for patient 4, who had atrial fibrillation with left atrial thrombosis, they did not receive anticoagulants.

COMPARISON WITH A GROUP OF PATIENTS WITHOUT HAEMOGLOBINOPATHY

Haemoglobin concentrations, before and after operation and at discharge, and blood gases were measured in a control group of 29 patients without haemoglobinopathy. These patients had undergone cardiopulmonary bypass without blood transfusion during their hospital stay. The patients were subjected to the same protocol of priming, temperature control, aortic cross-clamping, topical hypothermia, and cold cardioplegia. The results were compared with the group of five patients with haemoglobinopathy undergoing cardiopulmonary bypass without blood tranfusion during their stay in hospital (cases 5, 6, 10, 11, 12).

Results

Two patients died after operation. Patient 7, who had a double-outlet right ventricle, remained in a low cardiac output state, with acidosis and haemolysis requiring high doses of catecholamines after cardiopulmonary bypass, despite an apparently satisfactory surgical correction with normal arterial oxygen saturation. He died in ventricular fibrillation after several episodes of ventricular tachycardia. Necropsy was not performed. In retrospect, on the basis of the postoperative angiogram, the size of the left ventricle was felt to have been inadequate. Patient 8, who had a left ventricular subannular aneurysm and mitral insufficiency, had a very difficult postoperative course. He was weaned from bypass with difficulty and required high doses of catecholamines; the low cardiac output persisted, with acidosis and haemolysis, and he died 12 hours after operation. At necropsy two aneurysms of the sinus of Valsalva impinging on the left ventricular wall were found. They had not been apparent at cardiac catheterisation. The remaining 13 patients had an uncomplicated postoperative course with a mean hospital stay of 16 days.

Table 3 shows the results of investigations done

Table 3 *Results of open-heart surgery in patients with sickle-cell haemoglobinopathies*

Case No	*Lowest venous PO_2 (kPa)*	*Lowest venous pH*	*Lowest venous O_2 saturation (%)*	*Peroperative and postoperative sickling*	*Haemolysis*		*Result*
					At operation	*After operation*	
1	4·5	7·40		0	0	0	Good
2	3·2	7·29	21·8	0	0	0	Good
3	5·5	7·27	58	0	0	0	Good
4	4·7	7·42		0	0	0	Good
5	5·7	7·35	40	0	0	0	Good
6	5·5	7·27	40·4	0*	0	0	Good
7	4·9	7·43	42	0	+	++	Died: low cardiac output and arrhythmia
8	4·4	7·30	43	0	0	++	Died: low cardiac output
9	4·9	7·36	48	0	0	0	Good
10	5·5	7·36	65	0	0	0	Good
11	4·9	7·40	70	0	0	0	Good
12	4·9	7·31	69	0*	0	0	Good
13	5·3	7·42	35	0*	0	0	Good
14	7·3	7·26	69	0	0	0	Good
15	5·6	7·26	61	+*	0	0	Good

*Patients with oval-shaped red cells (see text).
Conversion: SI to traditional units—Oxygen tension (Po_2): 1 kPa = 7·5 mm Hg.

during cardiopulmonary bypass. Sickle cells were identified in only one patient (case 15); they were 0·1% of the red-blood-cell count during operation and 5% the day after surgery when the patient was extubated. A repeat haemoglobin electrophoresis showed 30% haemoglobin S at that time. In four patients some oval-shaped red cells were found—2% of red blood cells in patient 13 and 1% in patient 6. They disappeared after surgery. In patient 15, in addition to sickle cells, 2% of oval-shaped cells were found during cardiopulmonary bypass. Only one patient (case 7) had slight haemolysis, inferred from the colour of the urine and serum, during operation. Patients 7 and 8, both of whom died, had postoperative haemolysis associated with severe low cardiac output and acidosis. The serum bilirubin and lactate dehydrogenase concentrations were within the normal range seven days after operation in all surviving patients.

In the five patients who did not receive blood during their hospital stay the mean haemoglobin concentration was 11·9 ± 1·61 g/dl before operation; after a mean hospital stay of 17·6 days it was 9·92 ± 0·94 g/dl, a fall of 1·98 g/dl. The group of 29 patients without haemoglobinopathy, who had similar procedures, the same cardiopulmonary bypass operation without blood transfusion, and the same hospital stay (mean 16·41 days), had a mean haemoglobin concentration of 12·78 g/dl before operation and of 10·75 g/dl at discharge, a fall of 2·03 g/dl.

Discussion

Only 11 patients with a sickle-cell haemoglobinopathy undergoing open-heart surgery have been previously reported.[1 2 4–6 8 9] The main features of these are outlined in table 4. Seven of these patients had sickle-cell trait. All except one[8] were submitted to the same type of treatment before, during, and after bypass. One patient with sickle-cell trait died because of diffuse sickle-cell thrombosis after the procedure.[7]

The danger of sickling provoked by cardiopulmonary bypass has been emphasised by all authors.[1–3 5 7 9] Hypoxia or acidosis initiates the sickling phenomenon, which is initially reversible but then becomes irreversible. Presumably blood viscosity increases under these conditions and capillary stasis occurs. The consequence of this phenomenon is thrombosis, with tissue ischaemia and necrosis. The capillary stasis enhances tissue acidosis and hypoxia, thereby initiating a vicious circle. According to some authors,[2 9] sickle cells are mechanically more fragile, leading to additional haemolysis. Cardiopulmonary bypass may be a contributing factor by causing hypoxia or acidosis or both. Moreover, a decrease in body temperature provokes an increase in blood viscosity and thereby augments sickling.[2 9] Haemolysis may occur as a result of trauma when blood is exposed to a mechanical prosthesis. The presence of haemoglobin C adds appreciably to the risk of thrombosis and tissue anoxia.[10] These potential dangers during cardiopulmonary bypass can exist even in the absence of a history of sickling crises.[7]

The possible dangers of the sickle-cell haemoglobin states have led to many recommendations concerning the conduct of cardiopulmonary bypass in such patients.

(1) Optimal oxygenation must be maintained during and after surgery. Sickling may occur in the homozygous SS patient at oxygen tensions (P_{O_2}) below 5·3 kPa (40 mm Hg)[5] to 6·0 kPa (45 mm Hg).[11] It can occur in the heterozygous state at a P_{O_2} of 2·7 kPa (20 mm Hg)[5] to 3·3 kPa (25 mm Hg).[11] It is therefore important to assure optimal oxygenation before, during, and after anaesthesia[11] and surgery and to avoid respiratory or metabolic acidosis. Although acidosis was thought to be the major triggering factor of sickling, this theory has

Table 4 *Previously reported cases of open-heart surgery in sickle-cell haemoglobinopathy*

Date	*Age*	*Sex*	*Haemoglobin electrophoresis*	*Diagnosis*	*Operation*	*Result*
1963[3]	9	M	SS	ASD primum	Patch closure	Good
	4	M	SS	Pulmonary valvar stenosis	Valvotomy	
1964[4]	4	M	SS	Tetralogy of Fallot	Correction	Tricuspid insufficiency, increased sickling
1967[7]	58	M	AS	Aortic stenosis	AVR	Died: sickle-cell thrombosis
1970[9]	30	F	AS	Mitral insufficiency	MVR (homograft)	Good
1972[5]	14	M	AS	Mitral insufficiency	MVR (Starr)	Good
1972[2]			AS	Aortic stenosis	AVR	Good
			AS	Tetralogy of Fallot	Correction	Good
1976[5]	5	F	S-Thal	Tetralogy of Fallot	Correction	Good
1978[6]	53	F	AS	Aortic insufficiency	AVR (Björk)	Good
1981[8]	13	F	AS	Mitral insufficiency		

ASD: atrial septal defect; AVR: aortic valve replacement; MVR: mitral valve replacement.

been questioned[5]; but prevention and treatment of acidosis are important measures during any cardiac operation.

(2) The reduction of the percentage of haemoglobin S before operation has been advocated by some authors[3] to decrease the risk of sickling during or after surgery. This can be accomplished by preoperative transfusion[5] or by partial exchange transfusion immediately before bypass,[1 8 9] and would necessitate the use of blood in the priming solution.[1-3 5 9] For some authors[2] the latter would be sufficient to decrease the percentage of haemoglobin S.

(3) In the postoperative course, donor blood with haemoglobin S should be avoided. An electrophoresis of haemoglobin should therefore be performed on all donors.

(4) Systemic hypothermia increases blood viscosity and augments sickling and therefore on a theoretical basis has not been recommended.[2 5]

(5) Theoretically, aortic cross-clamping and the use of topical hypothermia was felt to cause in situ sickling. These techniques were therefore not recommended[2 5] but more recently have been used successfully.[8 12]

(6) It has also been suggested that the use of prosthetic valves should be avoided because of potential mechanical trauma to erythrocytes.[2 5] A Starr-Edwards-type prosthesis,[1] however, and a Björk-Shiley prosthesis[6] have been used without problems in two patients. Tricuspid insufficiency, which occurred after correction of one case of tetralogy of Fallot, led to mechanical trauma of red blood cells, haemolysis, and increased sickling after surgery.[4]

In the Ivory Coast haemoglobinopathies are frequent.[13] They affect 20% of the population, 11% having haemoglobin S (9·5% AS, 0·2% SS, 0·25% SC; and 1·07% S-Thal) and 7% having the C haemoglobinopathy. This poses a potential problem for open-heart surgery. The above recommendations for the conduct of cardiopulmonary bypass in these patients are quite contrary to our routine. We try to avoid the use of blood whenever possible, for reasons that include difficulties in procurement (particularly for the rare groups) and the transmission of parasitic disease, hepatitis, etc, which are common in Africa. We therefore use total haemodilution with reduced priming volume, moderate hypothermia (28°C), aortic cross-clamping, local cardiac hypothermia, and cold cardioplegia for myocardial protection.

In our first patient (closure of atrial septal defect) we did use blood, without hypothermia or aortic cross-clamping. In the other patients we have progressively used (*a*) partial then total haemodilution and (*b*) decrease in temperature to 32°C, then 30°C, and finally 28°C. We have also added aortic cross-clamping, with topical hypothermia and cardioplegia. All of these changes were introduced progressively when we realised that they caused no harm. Blood is used in the priming solution only for small children or if the patients are severely anaemic. It is used after operation only for bleeding or when the haemoglobin concentration falls below 8 g/dl. Despite a low preoperative concentration of haemoglobin, a common finding in Africa, blood was not used in five patients. Interestingly, the decrease in haemoglobin concentration between the preoperative period and the time of discharge of these five patients and the 29 patients without haemoglobinopathies who were subjected to the same cardiopulmonary bypass technique was not significantly different. This suggests that the mechanical fragility of the red blood cells in patients with sickle-cell haemoglobinopathies undergoing bypass surgery is not increased. From our data we conclude that the use of blood can be substantially reduced for open-heart surgery in this group. The systematic use of blood for oxygenator priming, preoperative transfusion, and exchange transfusion does not seem necessary.

Moderate hypothermia, aortic cross-clamping, topical hypothermia, and cold cardioplegia have been well tolerated by all our patients. None of the patients developed sickling either during or after the operation. Furthermore, in three patients who had sickling preoperatively (one of them with 27% of circulating sickle cells) sickling disappeared or was considerably reduced during and after bypass. The appearance of a small percentage (1–2%) of oval-shaped red cells requires elucidation. We have interpreted it as a possible transitional phase from normal red cells to sickle cells. Apparently the process was reversible.

The increase in viscosity at 28°C does not seem to be detrimental to tissue oxygenation or to induce sickling (J Lonsdorfer *et al*, paper presented to the Société Biologie Clinique de Côte d'Ivoire, 1979). In none of our patients did we observe a venous Po_2 lower than that measured in the control group of 29 patients. Furthermore, the haemoglobin dissociation curve is directly influenced by temperature and a decrease in the latter increases the oxygen saturation at an equivalent Po_2. The polymerisation of haemoglobin S is directly related to oxygen saturation; so hypothermia should in fact exert a favourable influence (Lonsdorfer *et al*). Moreover, haemodilution decreases blood viscosity and improves capillary perfusion at low temperatures, presumably decreasing the risk of sickling.

In our patients, haemolysis was generally not a

problem. In the two cases where it occurred it was possibly due to the presence of a severe low cardiac output with metabolic acidosis. Since many of our patients live in remote areas we prefer xenograft valves. This avoids the necessity for anticoagulation and prevents the increased haemolysis reported with the use of mechanical valves.

Because of the technical conditions prevailing in tropical Africa for open-heart surgery we felt the need to re-evaluate previous statements in the literature, based mainly on theoretical considerations. We conclude from our experience that for patients with sickle-cell haemoglobinopathies bypass with haemodilution, moderate hypothermia, aortic cross-clamping, topical hypothermia, and cold cardioplegia can be used with no more risk than in patients without haemoglobinopathies. These techniques provide better protection for the myocardium than the use of blood, normothermia, and the absence of aortic cross-clamping advocated by others.[1-4 7]

Addendum

Since January 1981 five more adult patients with sickle-cell trait have undergone cardiopulmonary bypass with the techniques described above. Two of them received no blood at all. No sickling was seen in the samples taken during or after operation. They recovered uneventfully from surgery.

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