Chronic intravascular haemolysis after aortic disc valve replacement

Comparative study between Lillehei-Kaster and Björk-Shiley disc valve prostheses

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A randomized series of 64 patients was studied haematologically one year after single aortic valve replacement either with a Lillehei-Kaster pivoting disc valve or a Björk-Shiley (Delrin) tilting disc valve. Patients had haemoglobin concentrations, red blood cells counts, serum bilirubin, serum iron, total iron-binding capacity, serum haptoglobin, and serum lactate and hydroxybutyrate dehydrogenase performed. All patients had normal haemoglobin values and normal red blood cells counts. Haptoglobin was absent or reduced in 80 per cent, while raised values for serum lactate dehydrogenase were found in 75 per cent. The increase in serum lactate dehydrogenase activity was moderate and indicated a normal or only slightly reduced red cell lifespan in most patients. The incidence and severity of haemolysis were of the same order of magnitude in patients with a Lillehei-Kaster prosthesis as in patients with a Björk-Shiley prosthesis. For both models, intravascular haemolysis was of little clinical significance, and was of less severity than previously reported after replacement with aortic ball valve prostheses.

Paravalvular leakage or pronounced valvular regurgitation were not found to be main determinants of the haemolysis, neither did the valve size seem to be of importance in this connexion. In this respect, our data with the new disc valves differ from the results usually found in patients with ball valves.

The reasons for the haemolysis in patients with disc valves are briefly discussed.

Increased destruction of red blood cells is a known complication in patients after insertion of aortic valve prostheses (Bell, Petuoglu, and Fraser, 1967; Eyster, Mayer, and McKenzie, 1968; Myhre, Dale, and Rasmussen, 1970a). Most studies in this field, however, have been based on examination of patients with ball valve prostheses of different types, while information about the haemolytic activity after aortic valve replacement with the modern Lillehei-Kaster pivoting disc valve (Lillehei *et al.*, in the press) or Björk-Shiley tilting disc valve (Björk, 1971) is scanty. This is in particular true in respect of the new Lillehei-Kaster prosthesis. Data from a clinical trial providing a direct comparison between the incidence and severity of haemolysis with

these two modern valve prostheses therefore should be of considerable interest.

The purpose of the present study is (1) to assess the incidence and severity of chronic haemolysis in patients with aortic disc valve prosthesis; and (2) to determine if there is any difference between patients with the Lillehei-Kaster or the Björk-Shiley prosthesis.

Subjects and methods

The present study is based on re-examination of 66 unselected patients with aortic valvular heart disease, consecutively operated upon with insertion of an aortic valve prosthesis in 1970-71. In most patients, the valvular lesions appeared to be of rheumatic or congenital origin; in a few patients, there was a history of acute or subacute bacterial endocarditis. Associated

TABLE 1 Age, sex, and clinical diagnosis

Type of aortic prosthesis	Age (yr)	Sex M	F	Diagnosis		
				Aortic stenosis	Aortic regurgitation	Aortic stenosis and regurgitation
Lillehei-Kaster (n=31)	52.1	24	7	1	17	13
Björk-Shiley (n=33)	51.5	22	11	4	11	18

mitral valve disease was observed in 12 patients, but none of them was treated with concomitant mitral valve surgery. There were 48 men and 18 women. The pre-operative diagnosis together with age and sex distribution are given in Table 1. The patients were randomized into two groups, and a Lillehei-Kaster pivoting disc valve or a Björk-Shiley (Delrin) tilting disc valve was inserted alternately. The re-examination took place 12 months after the operation. During the observation period, all patients were on maintenance treatment with digitoxin and diuretics, while none of them, apart from one exception, received iron supplements.

To assess anaemia and possible haemolysis, the following laboratory tests were performed: haemoglobin concentrations by cyanmethaemoglobin, red blood cells by Celloscope counting, serum bilirubin by Jaffe's reaction, serum iron and total iron-binding capacity by Technicon methods on an Auto-Analyzer, haptoglobin by saturation with haemoglobin and measuring of the peroxidase activity, and lactate dehydrogenase activity in serum using Kabi's reagents. In addition the serum activity of aspartate aminotransferase (SGOT); alanine aminotransferase (SGPT), and hydroxybutyrate dehydrogenase (SHBDH) were determined by Kabi reagents. Reticulocyte counts and urine tests for haemosiderin were not performed.

Of the 66 patients, 2 patients with raised serum transaminase activity indicating liver disease had to be omitted, leaving 64 patients to be included in the present

study. There were 31 patients with a Lillehei-Kaster pivoting disc valve prosthesis, and 33 patients with a Björk-Shiley tilting disc valve prosthesis.

Tests of the statistical significance of differences in laboratory findings between the two groups of patients was made using Student's t-test (Snedecor, 1956). P values higher than 0.05 were not considered to be significant.

Results

Laboratory data obtained from patients with the two types of aortic disc prosthesis are summarized in Table 2. In both groups the values for haemoglobin concentration and red blood cell counts remained within the normal ranges, with only minor exceptions.

Serum lactate dehydrogenase levels were above the normal range in 80 per cent of patients with Lillehei-Kaster prosthesis (exceeding 500 U in one patient), and in 64 per cent of patients with Björk-Shiley prosthesis (less than 500 U in all cases). The mean serum lactate dehydrogenase activity was above the normal mean, with no significant difference between the two groups.

Absent or reduced serum haptoglobin was found in 77 per cent of patients with Lillehei-Kaster prosthesis and in 82 per cent of patients with

TABLE 2 Comparison between laboratory data in patients with Lillehei-Kaster or Björk-Shiley aortic disc valve prosthesis (mean value and range)

Type of prosthesis	Hb (g/100 ml)	Red blood cells (ml/mm ³)	Serum bilirubin (mg/dl)	Serum iron (µg/dl)	Total iron-binding capacity (µg/dl)	Hapto-globin (mg/dl)	Serum lactate dehydro-genase (U/l.)	Serum hydroxy-butyrate dehydro-genase (U/l.)	SGOT (U/l.)	SGPT (U/l.)
Lillehei-Kaster (n=31)	15.14 13.0-18.2	4.850 3.85-5.64	0.89 0.4-1.9	116.6 65-190	339.8 250-530	25.7 0-197	211.8 128-580	162.1 99-267	11.4 9-18	11.6 4-26
Björk-Shiley (n=33)	15.19 13.3-16.6	5.005 4.24-5.70	0.78 0.4-2.2	115.2 75-180	322.5 185-475	21.1 0-111	195.2 100-385	168.0 108-341	11.5 7-19	10.9 5-25
Normal range	13.5-18.0	4.50-6.50	0.2-1.0	85-125	270-390	30-180	75-160	60-130	5-17	4-17

Björk-Shiley prosthesis. Mean values for haptoglobin were lower than in normals in both groups, again with no significant group difference.

The values of serum iron and total iron-binding capacity were within the normal range in the majority of the patients. Two patients had only 65 μg per 100 ml of serum iron, they also showed pathological results in all other tests, with the exception of the total iron-binding capacity. In 4 more patients the values were just below the lower limit of normal, and in a few patients they were above normal. Ten patients had raised bilirubin values. In this group, 7 patients had additional signs of haemolysis, while 3 patients (bilirubin 1.1, 1.4 and 1.9 mg/dl) showed no other indications of haemolysis.

Fig. 1 shows the relation between serum lactate dehydrogenase activity and haptoglobin values. The plot demonstrates that raised SLDH values were always associated with reduced or absent haptoglobin, but there is no linear relation between the two variables. Furthermore, haptoglobin may be reduced or even absent in spite of normal SLDH values, showing that haptoglobin is by far the most sensitive indicator of haemolysis and that it is probably too sensitive for practical clinical use.

FIG. 1 Plot diagram showing the relation between SLDH and haptoglobin values in patients with prosthetic aortic disc valves. Horizontal interrupted line marks upper normal range for SLDH, and vertical interrupted line marks lower normal range for haptoglobin.

With the great majority of haemoglobin values within the normal range any correlation between serum lactate dehydrogenase activity and haemoglobin values could not be expected, and this was so, as shown in Fig. 2. In this figure 5 patients with low serum iron concentration are tagged, but no relation between iron deficiency estimated in this way and the degree of haemolysis can be demonstrated.

Fig. 3 shows the relation between SLDH increment and valve size. The size of prosthesis is indicated by the valve number given by the manufacturer. The degree of haemolysis apparently had no direct relation to the valve size in any of the two prostheses evaluated. In the diagram, patients with paravalvular leakage or pronounced valvular regurgitation are tagged. Our data do not indicate that such circumstances enhance haemolysis. However, it should be emphasized that the regurgitation was only slight or moderate in all these patients with one exception who had to be reoperated.

Discussion

In the present study evidence of a minor degree of intravascular haemolysis was present. The values for haemoglobin and number of erythrocytes were within normal range in all patients. A sensitive method for measuring intravascular haemolysis is to determine serum lactic dehydrogenase activity

FIG. 2 The relation between SLDH activity and haemoglobin concentration in patients with prosthetic aortic disc valves.

FIG. 3 SLDH values related to valve size and type. The shaded area shows the normal range. Patients with pronounced valvular regurgitation or paravalvular leakage are especially marked (/).

(SLDH), since the erythrocytes have a high concentration of this enzyme which is released into plasma by haemolysis. In our patients the average SLDH was slightly raised, but all patients had less than 500 U, with one exception. This means a normal or only slightly reduced life span of erythrocytes in the great majority of patients examined (Myhre, Rasmussen, and Anderson, 1970b). The corresponding slight rise in serum hydroxybutyric acid dehydrogenase seems to support the red cell origin of the SLDH increase. The serum haptoglobin was usually absent or much reduced, but is probably a variable too sensitive to be used as a reliable index for intravascular haemolysis in this connexion. Measurements of reticulocyte counts were not included in the present study, as it has been shown earlier (Myhre, Dale, and Rasmussen, 1971) that this measurement is of minor value, except in cases with more severe haemolysis. Urine haemosiderin was not determined, as this would hardly give any more information than the serum haptoglobin concentration.

The present study thus shows that the severity of erythrocyte destruction in patients with the modern disc valve prosthesis is of little clinical significance. In this respect, our data confirm the promising results previously reported by Björk (1971). In a randomized study, however, we were not able to show any difference in severity or incidence of intravascular haemolysis in patients with Lillehei-Kaster prosthesis compared with patients with Björk-Shiley prosthesis.

From a practical point of view, our results indicate that supplementary iron therapy in most

cases is not necessary after replacement with either the Lillehei-Kaster or Björk-Shiley disc valve prosthesis. Furthermore, these patients most probably run a very low risk of long-term anaemia and renal haemosiderosis.

It is obvious from the data presented above, that both types of disc valve prosthesis presently used by us are less traumatic to blood than the conventional ball valve prosthesis. With all the latter types of prostheses, serum lactic dehydrogenase values have been found consistently twice or more the normal

FIG. 4 Comparison between mean SLDH levels found in patients with Starr-Edwards or Magovern aortic ball valves, and Björk-Shiley or Lillehei-Kaster aortic disc valves. The number of cases in each group is indicated on the columns. Data from patients with ball valves are compiled from Myhre, Rasmussen, and Dale, 1970c.

levels (Eyster, Rothchild, and Mychajliw, 1971; Myhre *et al.*, 1970a; Santinga, Kirsh, and Batsakis, 1973). In particular, significantly higher serum lactate dehydrogenase values have been found in patients with Starr-Edwards prosthesis of the 1200 and 2300 series, while the difference between patients with Magovern prosthesis and our patients is small. This is shown in Fig. 4. Significant haemolytic anaemia has been reported in 5 to 10 per cent after replacement with ball valves but usually limited to the few cases with leakage around the valve prosthesis (Brodeur *et al.*, 1965).

In the present study, increased concentrations of serum lactate dehydrogenase showed no correlation with the valve size. Moreover, we were not able to demonstrate higher enzyme levels in the relatively small group of patients with paravalvular leakage or pronounced valvular regurgitation than in patients without such complications. In this respect, the new disc valves seem to differ from the conventional ball valves. With the latter prosthesis, several studies have shown that the size of the valve as well as malfunction of the valve or paravalvular leakage are important determinants of increased haemolysis (Brodeur *et al.*, 1965; Robinson, Morrow, and Gebel, 1966; Myhre *et al.*, 1970a).

The increased destruction of erythrocytes with haemolysis after insertion of prosthetic heart valves has been related to an increase in shearing stress developed from turbulent jets and from increased diastolic or systolic gradients (Nevaril *et al.*, 1968). The two disc valve models used in the present study are both characterized by a central flow pattern with little turbulence. Furthermore, peak systolic gradients measured after operation have been found significantly lower than usually reported in patients with aortic ball valve prostheses (Björk, Olin, and Rodriguez, 1972; Lillehei *et al.*, in the press). It, therefore, seems justified to conclude that as far as intravascular haemolysis is concerned, the two disc valves have several advantages when compared with other types of heart valve prosthesis used today.

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