HOMOZYGOUS β-THALASSAEMIA: A REVIEW OF PATIENTS WHO HAD SPLENECTOMY AT THE ROYAL ALEXANDRA HOSPITAL FOR CHILDREN, SYDNEY

T S Hoe, A Lammi, B Webster

ABSTRACT

Twenty-four patients with homozygous β-thalassaemia who had been splenectomised and currently on treatment were studied retrospectively. They were divided into two groups. Group A: who had splenectomy prior to commencement of any regular blood transfusion. The mean haemoglobin for this group rose from 5.5 gm/dl pre-splenectomy to 7.7 gm/dl post splenectomy (p<0.001). Group B: who were on regular blood transfusion when they had their splenectomy and the mean blood transfusion requirement dropped from 317 ml/kg/yr to 230 m/kg/yr of packed red cells following splenectomy (p<0.001). Three patients who were on regular blood transfusion and desferrioxamine developed Yersinia enterocolitica infection. They presented with fever and signs of an acute abdomen. At laparotomy, 2 of the patients had acute appendicitis. All 3 appendices grew Yersinia enterocolitica and one patient also had a Yersinia enterocolitica septicaemia. If a patient develops fever and enteritis, desferrioxamine should be stopped temporarily and cotrimoxazole started as prophylaxis against systemic Yersiniosis. No cases of pneumoccocal sepsis was reported.

Keywords: *homozygous β-thalassaemia, splenectomy, Yersinia enterocolitica.*

SINGAPORE MED J 1994; Vol 35: 59-61

INTRODUCTION

β-thalassaemia is a genetic defect resulting in inability to correctly synthesise the β-globin of the haemoglobin molecule. The clinical manifestations of the thalassaemic syndromes have been reviewed by Weatherall and Clegg[1]. Patients with β-thalassaemia major usually require blood transfusions on a regular basis[2,3]. This results in a cumulative iron load and most of these patients eventually develop some degree of hypersplenism that increases the transfusion requirement which also increases the iron load. In these patients, splenectomy dramatically reduces the transfusion requirement[2,4]. Patients post-splenectomy have been reported to be susceptible to overwhelming infection[5-7] and pneumococcal vaccination and chemoprophylaxis have been recommended. The purpose of this paper is to retrospectively review the patients with homozygous β-thalassaemia who had been splenectomised at the Royal Alexandra Hospital for Children, Sydney, where patients with homozygous β-thalassaemia are initially managed conservatively without blood transfusion and are commenced on hypertransfusion regime if their haemoglobin level remains persistently low (<5 gm/dl), if their growth is affected, or if they are unwell without transfusions. Patients who are splenectomised are given pneumococcal vaccinations but generally no chemoprophylaxis is given.

The Royal Alexandra Hospital for Children
Sydney
Australia

T S Hoe, MRCP (UK), M Med (Paeds)
Lecturer

A Lammi, FRACP, FRCPA
Head of Haematology

B Webster, DCP, FRCPA
Haematologist

Correspondence to: Dr T S Hoe
Department of Paediatrics
Faculty of Medicine
National University of Malaysia
Jalan Raja Muda Abdul Aziz
Kuala Lumpur
Malaysia

METHODOLOGY

Twenty-four patients with homozygous β-thalassaemia who had been splenectomised and who were on treatment at the Royal Alexandra Hospital for Children, Sydney, were studied retrospectively. The medical, blood transfusion and laboratory records were reviewed. Parents and patients were also interviewed regarding any infectious episodes that might not have been in the hospital records.

The patients were divided into 2 main groups, Group A: who had splenectomy prior to commencement of blood transfusion (these patients were maintaining a haemoglobin level of 6-8 gm/dl without blood transfusion when hypersplenism developed and splenectomy was then carried out). Group B: who were already on regular blood transfusion when they had their splenectomy.

For Group A, the mean haemoglobin level over the one-year period immediately pre-splenectomy as well as post-splenectomy was noted. For Group B, the transfusion requirement pre and post-splenectomy was expressed as the volume of packed red-blood cells (haematocrit 56%) used for transfusion in one year divided by the weight of the patient in mid-year and expressed as ml/kg/year. Each unit of packed red blood cells was assumed to have a volume of 245 ml. With only occasional exceptions, the pre transfusion haemoglobin level was >9 gm/dl. One patient in Group B was excluded in the analysis for blood transfusion requirement as her transfusion records at the time of splenectomy were unavailable.

Statistical analyses were performed using the student t-test for independent samples and paired samples.

RESULTS

There were 13 males and 11 females. Their ages at the time of study ranged from 4 years 2 months to 19 years 10 months (mean: 97 months). There were 10 Greeks, 4 Lebanese, 4 Cypriots, 3 Italians, one Maltese, one Pakistani and one Indonesian. The mean age at diagnosis was 1 year 7 months (range: 3 months to 5 years). The mean age at splenectomy was 6 years 1 month (range: 15 months to 17 years 6 months). The mean age at the start of blood transfusion was 4 years 8 months (range: 3 months to 11 years 1 month).

For patients in Group A, the mean age at splenectomy was 4 years 3 months (range: 2 years 1 month to 8 years 6 months) and the mean age at starting blood transfusion was 6 years 3 months

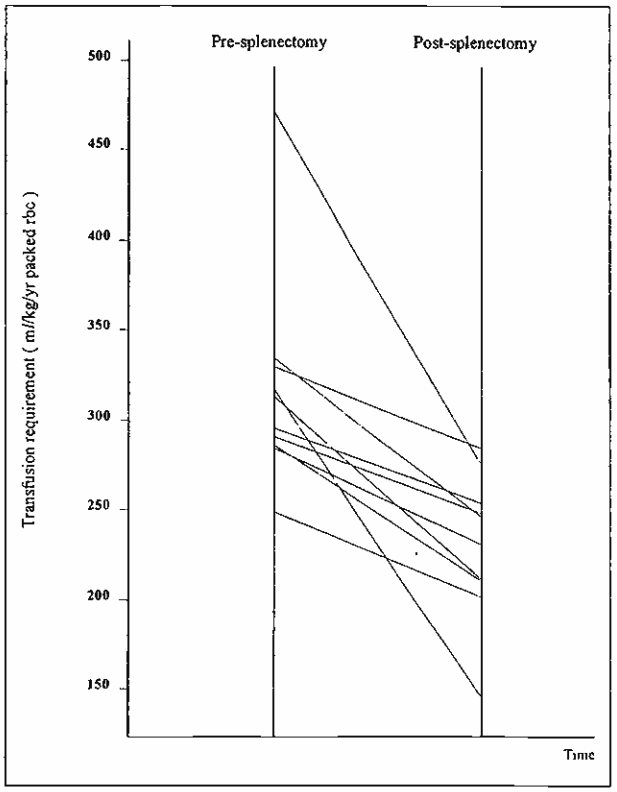
(range: 3 years 9 months to 10 years). Three patients in this group were classical β-thalassaemia intermedia and have not been transfused at the time of study (age range: 4 years to 14 years 2 months). The mean pre-splenectomy Hb level was 5.5 gm/dl (C.I.95 = 5.5 ± 0.5) and the mean post-splenectomy Hb level was 7.7 gm/dl (C.I.95 = 7.7 ± 0.73) (Table I). The rise in haemoglobin resulting from splenectomy was significant (p<0.001).

Table I – Mean haemoglobin levels (gm/dl) in Group A patients (pre and post-splenectomy).

Patient	Mean haemoglogbin levels gm/dl	
	Pre-splenectomy	Post-splenectomy
1	5.1	6.5
2	6.0	8.0
3	5.5	6.6
4	5.5	8.0
5	4.6	7.9
6	5.4	6.2
7	4.7	7.5
8	6.0	6.0
9	4.3	7.7
10	7.6	9.0
11	6.0	7.2
12	6.2	10.4
13	4.5	9.5

For patients in Group B, the mean age at splenectomy was 9 years (range: 1 year 3 months – 17 years 6 months) and the mean age at start of blood transfusion was 3 years 1 month (range: 3 months – 11 years 1 month). The pre-splenectomy blood requirement ranged from 243-469 ml/kg/yr (mean 317 ± 59) and the post-splenectomy blood requirement ranged from 144-283 ml/kg/yr (mean 230 ± 40). There was a significant decrease in transfusion requirements (p<0.001) (Fig 1).

Fig 1 - Transfusion requirements in Group B patients



The main indications for splenectomy were large spleens and hypersplenism.

The mean splenic size at splenectomy was 10 cm (range: 3-17 cm) below the left costal margin. All patients had pneumococcal vaccination and all but 2 patients had no chemoprophylaxis with penicillin (one patient had penicillin prophylaxis because she had frequent tonsillitis pre and post-splenectomy and the other had 2 years of penicillin prophylaxis following splenectomy).

Complications

Five patients had pathological fractures secondary to medullary hyperplasia (3 were never transfused and two had their fractures 8 months and 18 months after the start of blood transfusion respectively). One patient with β-thalassaemia intermedia had a gallstone and one patient had a right cerebral infarct with a resultant transient left hemiparesis.

Table II shows the presenting symptoms and organisms involved and the serum ferritin at the time of infection. Patients LH, PM and JA presented with fever and signs of an acute abdomen and laparotomy were performed in all 3 patients. JH was noted to have an appendicular abscess, 2 of the cases (LH and JA) had acute appendicitis on histopathological examination. All 3 appendices grew *Yersinia enterocolitica* on culture. A search through the microbiological records of all homozygous β-thalassaemia patients on treatment at The Royal Alexandra Hospital for Children from 1982-1989 showed that one other patient had a *Yersinia entercolitica* infection and she too presented with fever and signs of an acute abdomen and an appendicectomy was done. The appendix culture grew *Yersinia entercolitica*, her serum ferritin was 3100ng/ml and she too was on desferrioxamine. Histopathological examination showed acute appendicitis. This same patient developed another episode of *Yersinia entercolitica* septicaemia and osteomyelitis of the right humerus 2 months later.

Table II – Infection in Homozygous β-thalassaemia patients (post-splenectomy)

Patient	Presenting symptoms	Culture	Serum ferritin ng/ml	Desferrioxamine*
SD	Fever	– ve	–	–
LH	Fever, abdominal pain	Blood & Stool: Y. entero-colitica	> 2500	+
FJ	Fever	Blood: E. coli	265	–
PN	Fever, abdominal pain	Appendix: Y. entero-colitica	2300	+
JA	Fever, abdominal pain	Peritoneal Y. entero-colitica	2400	+
FS	Fever	–ve	2000	+
VN	Frequent episodes URTI **	–ve	–	–

* : + denotes on Desferrioxamine, – denotes not on Desferrioxamine.
** : URTI denotes upper respiratory tract infections.

DISCUSSION

In Group A, there was a rise in the mean haemoglobin level from a mean of 5.5 gm/dl pre-splenectomy to 7.0 gm/dl after splenectomy. Thus by removing the spleen, we have been able to delay the onset of regular blood transfusions in these patients.

In Group B, we find that there is a significant drop in transfusion requirements as was reported in other series[2,4,7,8] after splenectomy.

Our patients were not on chemoprophylaxis because in Sydney there is ready access to medical care and the patients' personal physicians have been advised to give prompt treatment should they develop fevers. Despite the non usage of chemoprophylaxis, we did not have any case of pneumococcal sepsis. However, 3 of the patients had *Yersinia enterocolitica* infection and there was also one patient amongst those homozygous β-thalassaemics who were not splenectomised having 2 episodes of infection by the same organism. All 4 patients had high serum ferritin and were on desferrioxamine. It is a well-known fact that *Yersinia enterocolitica* infection is associated with high serum ferritin and desferrioxamine therapy because the desferrioxamine are siderophores which bind iron from transferrin[9] and *Yersinia entercolitica* produce no detectable siderophores but have receptors for them and can use ferrioxamine as a growth promoter[10,11]. Schametzky[12] recommended that patients with β-thalassaemia who become febrile with enteritis or pharyngitis should have their desferrioxamine therapy discontinued temporarily and cotrimoxazole administered immediately as prophylaxis against systemic Yersiniosis.

The abdominal pain syndromes associated with *Yersinia entercolitica* infections include mesenteric lymphadenitis, acute terminal ileitis and the clinical entity of Right Iliac Fossa Syndrome. All our cases of *Yersinia entercolitica* infection presented with abdominal pain and fever and on presentation had signs of an acute abdomen with tenderness and guarding. Three out of the 4 homozygous β-thalassaemia patients had acute appendicitis on histopathologic examination. A review of the literature revealed that Attwood[13] reported that 31% of acute appendicitis was associated with Yersiniosis though only 3% was associated with *Yersinia enterocolitica*. In 1976, Jepsen et al[14] reported that 12% of acute appendicitis was associated with *Yersinia enterocolitica* and Gutman[15] reported 5 of 16 children during an outbreak of infection with *Yersinia enterocolitica* who had appendicectomy were found to have acute appendicitis due to this organism. Although no figures have been reported regarding the incidence of *Yersinia enterocolitica* in acute appendicitis in patients with homozygous β-thalassaemia, in view of the high incidence of *Yersinia entercolitica* in acute appendicitis in normal patients coupled with the increased susceptibility to *Yersinia enterocolitica* infection in patients with β-thalassaemia on regular blood transfusions and desferrioxamine, any β-thalassaemia patient on regular blood transfusions and desferrioxamine who presents with fever, abdominal pain and who has abdominal signs that closely resemble that of an acute appendicitis should have a laparotomy.

REFERENCES

1. Weatherall DJ, Clegg JB. The thalassaemia syndrome. 3rd ed. Oxford: Blackwell, 1981.
2. Modell B. Total management of thalassemia major. Arch Dis Child 1977; 52: 489-500.
3. Graziano JH, Piomelli S, Hillgartner M, Giardina P, Karpatkin M, Andrew M, et al. Chelation therapy in beta-thalassaemia major III. The role of splenectomy in achieving iron balance. J Pediatr 1981; 99: 695-9.
4. Cohen A, Markenson AL, Schwartz E. Transfusion requirement and splenectomy in thalassaemia major. J Pediatr 1980, 97:100-2.
5. Smith CH, Erlandson ME, Stern G, Hilgartner MW. Post splenectomy infection in Cooley's anemia. Ann NY Acad Sci 1964; 119: 748-57.
6. Eraklis AJ, Kevy SV, Diamond LK, Cross RE. Hazard of overwhelming infection after splenectomy in childhood. N Engl J Med 1967; 276: 1225-9.
7. Engelhard D, Cividalli G, Rachmilewitz EA. Splenectomy in homozygous beta thalassaemia: A retrospective study of 30 patients. Br J Haematol 1975; 31: 391-403.
8. Piomelli S, Hart D, Graziano J, Grant G, Karpatkin M, McCarthy K. Current strategies in the management of Cooley's anemia. Ann NY Acad Sci 1985; 445; 256-67.
9. Neilands JB. Microbial iron compounds. Ann Rev Biochem 1981; 50: 715-31.
10. Perry RD, Brubaker RR. Accumulation of iron by Yersinia. J Bacteriol 1979; 137: 1290-8.
11. Robins-Browne RM, Prpic JK. Desferrioxamine and systemic Yersinosis. Lancet 1983; ii: 1372.
12. Schametzky M, Konig R, Lakomek M, Tillmann W, Schroter W. Prophylaxis of systemic Yersinosis in thalassaemia major. Lancet 1984; i:791.
13. Attwood SEA, Cafferkey MT, West AB, Healy E, Mealy K, Buckley TF. Yersinia infection and acute abdominal pain. Lancet 1987; i:529-33.
14. Jepsen OB, Koener B, Lauritsen KB, Hancke AB, Andersen L, Hendrichsen S. *Yersinia enterocolitica* infection in patients with acute surgical abdominal disease. A prospective study. Scand J Infect Dis 1976; 8:189-94.
15. Gutman LT. *Yersinia enterocolita* and *Yersinia pseudotuberculosis* In: Gorbach SL. ed. Infectious diarrhoea. Boston: Blackwell Scientific Publications. 1986: 65-83.