Prevention of overwhelming postsplenectomy infection in thalassemia patients by partial rather than total splenectomy

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Objective: We aimed to evaluate the protective role of partial versus total splenectomy against sepsis in patients with thalassaemia when other preventive measures are not available. Overwhelming postsplenectomy infection is a serious complication of splenectomy in these patients, and most present with pneumococcal septicemia. Pneumococcal vaccine given before surgery is a well-established preventive measure. **Methods:** In this study, we compared 2 populations of patients from Iraq and Saudi Arabia, both of whom underwent splenectomy for thalassaemia. All patients from Saudi Arabia were given a preoperative pneumococcal vaccine and underwent total splenectomy after about 4 weeks. Unfortunately, this vaccine was not available for the Iraqi patients. Partial splenectomy was offered to many of these patients as a protective measure against this fatal complication. **Results:** A significant difference was found between the total splenectomy fatalities in the 2 groups. There were 5 deaths in the 30 enrolled Iraqi patients over 4 years. One death over a 12-year period was reported in the 22 patients from Saudi Arabia. Partial splenectomy was associated with a dramatic reduction of mortality in the Iraqi patients. None of the 12 patients died during a follow-up period of 4 years. **Conclusions:** Pneumovax is a powerful prophylactic tool against overwhelming postsplenectomy infection in patients with thalassaemia and should be used whenever available. In poor or problematic countries with limited health resources, partial rather than total splenectomy could offer an alternative measure to avoid this fatal complication.

Objectif : Nous voulions évaluer le rôle de la splénectomie partielle par rapport à la splénectomie totale comme mesure de protection contre la septicémie chez les patients atteints de thalassémie lorsque d'autres mesures préventives ne sont pas disponibles. L'infection postsplénectomie irrépressible est une complication grave de la splénectomie chez ces patients et elle est conjuguée le plus souvent à une septicémie à pneumocoque. Le vaccin antipneumococcique administré avant l'intervention chirurgicale est une mesure préventive bien établie. **Méthodes :** Au cours de cette étude, nous avons comparé deux populations de patients de l'Irak et de l'Arabie saoudite qui ont tous subi une splénectomie à cause d'une thalassémie. Tous les patients de l'Arabie saoudite ont reçu un vaccin antipneumococcique préopératoire et ont subi une splénectomie totale après environ quatre semaines. Malheureusement, le vaccin n'était pas disponible pour les patients irakiens. On a offert une splénectomie partielle à beaucoup de ces patients comme mesure de protection contre cette complication mortelle. **Résultats :** On a constaté une différence importante entre les splénectomies totales mortelles chez les deux groupes. On a enregistré cinq décès chez les 30 patients irakiens inscrits en quatre ans. On a signalé un décès en 12 ans chez les 22 patients de l'Arabie saoudite. On a établi un lien entre la splénectomie partielle et une réduction spectaculaire du taux de mortalité chez les patients irakiens. Aucun des 12 patients n'est mort au cours d'une période de suivi de quatre ans. **Conclusions :** Le pneumovax est un outil prophylactique puissant contre l'infection postsplénectomie irrépressible chez les patients atteints de thalassémie et il faudrait l'utiliser chaque fois qu'il est disponible. Dans les pays pauvres ou ceux où les ressources sanitaires limitées posent des problèmes, la splénectomie partielle plutôt que totale pourrait offrir une solution de rechange afin d'éviter cette complication mortelle.

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Thalassemia is a group of genetic diseases that is common in the Mediterranean, Middle Eastern, Indian and Southeast Asian countries.[1] Health resources are scarce in most of the countries where the disease is common. There are only 600 patients registered in the United Kingdom, with an undiscounted lifetime cost estimated at more than £800 000 for each patient.[2] In most of the countries where thalassemia is common, such a provision for these patients is unrealistic. In 3 metropolitan cities of the Iraqi Kurdistan, 1050 patients are registered with the thalassemia centres. Most of these patients were born during the 3 wars that incapacitated the Iraqi health system. Blood transfusion supply was primitive at best, and desferrioxamine supply was erratic. Most of the patients showed full facial and clinical features of the disease from ineffective bone marrow expansion. Patients became hypersplenic early in their lives and needed splenectomy at a relatively young age.

Overwhelming postsplenectomy infection (OPSI) is a serious complication of splenectomy and is usually caused by encapsulated bacteria. More than 70% of all cases of OPSI are due to *Streptococcus pneumoniae*, while only 5% of other septic episodes are due to this encapsulated pathogen.[3,4]

Pneumococcal vaccination has been found to be effective in preventing OPSI.[5,6] Unfortunately, none of the Iraqi patients had access to Pneumovax, and total splenectomy was associated with a notable mortality. Partial splenectomy, in the absence of Pneumovax, was found to have survival advantage and was offered to a group of patients.

In Abha, capital of the Asir region of Saudi Arabia, all hypersplenic thalassemic patients with increasing transfusion requirements underwent total splenectomy. They all received Pneumovax 4 weeks before surgery.

In this study, we compared the effect of partial rather than total splenectomy with Pneumovax. This option could be more available in war-torn and poor countries with limited access to health resources.

Methods

In this analysis, we compared 2 studies from Iraq and Saudi Arabia. A prospective plan that lasted 4 years from the Iraqi Kurdistan compared partial and total splenectomy as a preventive measure against OPSI. Thirty patients were initially subjected to total splenectomy. Twenty-five patients had thalassemia major and 5 had thalassemia intermedia. When the mortality from OPSI was found to be high, patients were offered partial rather than total splenectomy. Twelve patients in total (10 thalassemia major and 2 thalassemia intermedia) underwent partial splenectomy (Table 1).

In a retrospective analysis of patients with thalassemia from Abha, 22 (19 thalassemia major and 3 thalassemia intermedia) were found to have undergone splenectomy over a 12-year period. Almost all of them had received the 23-valent pneumococcal polysaccharide vaccine, Pneumovax, usually 4 weeks before surgery. They were all subjected to total splenectomy (Table 1).

Complete information about age group distribution is provided in Table 2. For a more visual comparison, see Figure 1 for the percentages of different age groups.

All of the splenectomies (total and partial) in Iraq were performed by a single surgeon. In Saudi Arabia, many surgeons were involved; this was attributed to the separation of adult and pediatric surgery. Standard procedure was followed for total splenectomy in both countries. An innovative method was used for partial splenectomies in Iraq. The procedure was performed by ligating the

Table 1

Mortality from overwhelming postsplenectomy infection after total and partial splenectomy

Type of surgery	No. of patients	Thalassemia		Deaths	Follow-up, yr	Average age, yr
		Major	Intermedia			
Iraq*						
Total splenectomy	30	25	5	5	4	14.5
Partial splenectomy	12	10	2	NA	4	16.0
Saudi Arabia†						
Total splenectomy	22	19	3	1	12	17.0

*No patients received pneumococcal vaccination.
†All patients received pneumococcal vaccination.
NA = not applicable.

Table 2

Age group distribution of patients who underwent splenectomy for thalassemia

Type of surgery	Age group; no. (and %)					
	< 5 yr	5–10 yr	11–15 yr	16–20 yr	21–25 yr	> 25 yr
Saudi Arabia						
Total splenectomy (n = 22)	NA	5 (22)	4 (18)	9 (40)	1 (4)	3 (13)
Iraq						
Total splenectomy (n = 30)	NA	11 (36)	12 (40)	4 (13)	2 (6)	1 (3)
Partial splenectomy (n = 12)	2 (16)	1 (8)	4 (33)	2 (16)	NA	3 (25)

NA = not applicable.

splenic vessels at the main pedicle. Time was allowed for the ischemic changes to ascend toward the upper pole. The upper pole of the spleen remained normal in colour because it is also supplied by the short gastric vessels. When the ischemia became well-established with a visible demarcation line, the ischemic part of the spleen was excised. The cut surface of the remnant spleen was sutured using absorbable material.

Overwhelming postsplenectomy infection (OPSI) is a fatal complication of total splenectomy in thalassemia patients. Pneumococcal septicemia is the most common presentation of this complication. Pneumovax has been found to be effective in abrogating this problem.[5,6] Pneumococcal vaccine was not available for the Iraqi patients, and none of them received this effective prophylaxis. As mentioned, almost all the patients from Saudi Arabia were given Pneumovax (Table 1).

All of the Iraqi patients were Kurdish. The Saudi cohorts were Saudi, Palestinian, Egyptian, Jordanian and Bengalese. The age range of the Iraqi patients was younger than that of the patients from Saudi Arabia. None of the patients from Saudi Arabia who had undergone splenectomy were younger than 8 years, whereas the Iraqi patients had an age range starting at 3.5 years. The average age of the Saudi patients who underwent splenectomy was 17 years. The Iraqis who underwent total splenectomy had an average age of 14.5 years, while the partial splenectomy group had an average age of 16 years. Details of the different age groups are provided in Table 2 and illustrated in Figure 1.

Results

Data are tabulated in Table 1. Table 2 and Figure 1 show age group distribution of all the patients both in real years and in percentage form for a better graphic comparison. Of the 30 patients who underwent total splenectomy in Iraq, 5 died from OPSI over a 4-year study period. None of the 12 patients who underwent partial splenectomy died from OPSI. In Saudi Arabia, there was 1 OPSI fatality over a period of 12 years.

Patient–year breakdown of the above data seems appealing for statistical analysis, because the patients in Saudi Arabia were observed for 12 years while the Iraqi patients were observed for only 4. This does not seem justifiable, since the mortality of OPSI is known to be more marked in the early years after splenectomy and a lesser proportion of patients die in later years.

In Iraq, most patients died from a rapidly fulminant form of a hyperpyrexic illness that was followed by multiorgan failure and disseminated intravascular coagulation. The 1 patient who died in Saudi Arabia (4 years after splenectomy) was a 14-year-old Palestinian. He was admitted with fever and pulmonary symptoms. He did not respond to aggressive antibiotic and supportive cover and died 2 days after admission from multiorgan failure. Blood and other body fluid cultures did not grow any microorganism. Microbiological investigation of the Iraqi patients was primitive and noncontributory.

None of the partial splenectomy group in Iraq needed a follow-up total splenectomy over the 4-year period. This could be explained by the better access to health resources currently available to the Iraqis.

Although the average age of the patients was slightly lower in the Iraqi cohort, compared with the Saudis (14.5 and 16 v. 17 yr), the age distribution was unpredictable and did not reveal a pattern (Fig. 1). The only 2 patients who were in the risk group and who were supposed to be highly vulnerable to OPSI (aged under 5 yr) had undergone partial splenectomy; none of them succumbed to OPSI.

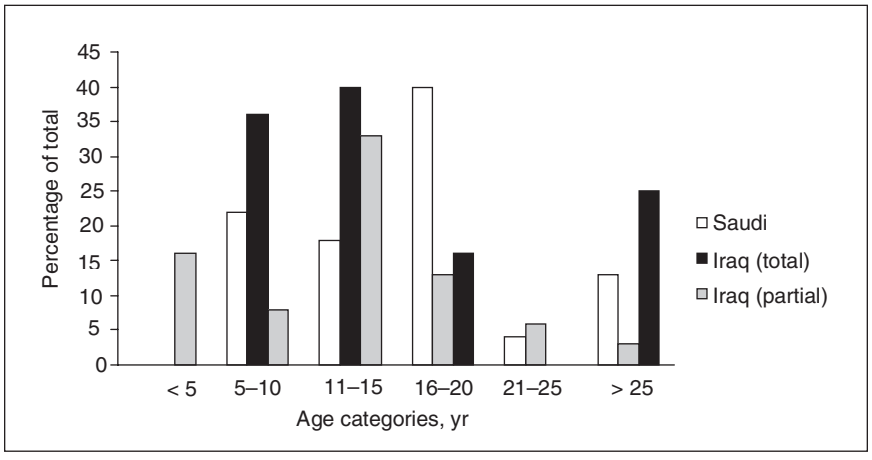

FIG. 1. Age group distribution (%) of patients who underwent splenectomy for thalassemia.

Discussion

Unlike the lymph nodes, located in the lymphatic system pathway and able to recognize, immunologically handle and filter pathogens, the spleen is directly interspersed in the blood traffic and is probably the first organ to encounter microorganisms. The spleen is the largest single lymphatic organ in the body and can effectively mount the initial immunological response to pathogens. In children, this primary exposure seems to be essential for future recognition of pathogens by the rest of the immune system, mainly the lymph nodes.[7] In the spleen, an ideal environment is provided for optimal initial handling of pathogens. It filters particulate matter in the bloodstream and generates opsonins and other soluble mediators of phagocytosis through ideal juxtaposition of different elements of the immune system.[7–9]

Splenectomy, especially at a young age, is known to be associated with the possibility of severe and fatal sepsis. Encapsulated bacteria are the most common culprits. *Streptococcus pneumoniae* constitutes 70% to 90% of these OPSIs.[3,4,10] *Haemophilus influenzae* serotype b (Hib) and *Neisseria meningitidis* constitute most of the rest. Effective vaccines are available against each of these pathogens. It is mandatory for every patient undergoing elective splenectomy to have Pneumovax, optimally at about 1 month presurgery.[11] Vaccination against the other 2 encapsulated bacteria usually depends on availability. In addition to this immunoprophylaxis, other measures include chemoprophylaxis with prolonged use of antibiotics and patient education to attend seriously to any impending fever or infection. With prophylaxis, the incidence of OPSI and its mortality could be decreased by 47% and 88%, respectively.[5]

OPSI could present itself as a rapidly progressive fatal febrile illness that can terminate in septicemia and disseminated intravascular coagulation. Multiorgan failure and possible adrenal hemorrhage could follow. Pneumococcal pneumonia or meningitis are common presentations. Prognosis is usually poor. Once sepsis becomes well-established, mortality will be very high. The time interval between splenectomy and OPSI could vary from 24 days to 65 years and overall mortality could reach 50%.[10,12] The incidence of OPSI is related to patient age, as well as the duration since and reason for splenectomy.[13] The risk is highest in children, in patients who had the operation within the previous 2 years and in patients who underwent the procedure for thalassemia or lymphoma.[14] The percentage of patients developing OPSI ranged from 1.5% for those who had trauma to 25% in patients who had undergone splenectomy for thalassemia.[9]

Partial splenectomy aims to retain around 25% of the normal spleen volume by removing as much as 80% to 90% of the enlarged spleen.[15] It is a safe and effective procedure for retaining immune competence in patients with thalassemia.[16]

With super-transfusion care, supported by judicious iron chelation, many patients with thalassemia in developed countries are expected to have minimal splenomegaly and marrow expansion complications. However, massive splenomegaly and hypersplenism with increasing transfusion requirements seem to be universal in most children in developing and underdeveloped countries. Total splenectomy was the norm for decades. Many studies on partial splenectomy emerged when fatality due to OPSI increased.[17,18] Now there is considerable controversy around the value of this procedure in reducing transfusion requirements while maintaining the immunocompetence of patients. While some physicians advocate the procedure,[17,18] most now recommend total rather than partial splenectomy.[19,20] This is based on the fact that many of these patients will need total splenectomy in the future.[21] There seems to be a general consensus that partial splenectomy should be offered to children below the age of 5 years, because that is when the spleen is most needed.[16,18,19,22] The trend toward partial splenectomy in hereditary spherocytosis, especially in younger patients, is much stronger.[23–26]

One should be careful about basing the current trend against partial splenectomy on the future deterioration of the response and recurrence of increasing transfusion requirements. Even after total splenectomy, the relief offered to thalassemia patients is temporary. Although many years of symptomatic improvement and reduced transfusion requirements could be enjoyed by these patients, most of them will return to their preoperative state, with no sustained improvements in baseline pretransfusion hemoglobin levels.[27]

Partial splenectomy should be considered as a major preventive measure against OPSI, especially when access to Pneumovax or compliance with a continued oral antibiotic is not optimal. This comparative analysis of 2 geographically and socially similar countries, one with a stable and sound health system and the other with collapsed resources, supports consideration of partial splenectomy as a management modality.

In conclusion, OPSI should be preventable if appropriate precautions are taken. Pneumovax is an effective and mandatory measure. Partial splenectomy seems to be protective when vaccination is not available.

Competing interests: None declared.

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