Comments on 'Clinical course of 63 children with hereditary spherocytosis: a retrospective study' – with the particular question: 'Should HS be treated the same way throughout the world?'

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The authors describe a retrospective study of 63 children with hereditary spherocytosis (HS) in Minas Gerais, Brazil.[1] HS is generally a mild and benign disease which is found in all areas of the world, but most commonly in peoples of Northern European origin. In this study, as elsewhere, more severe forms of the disorder were diagnosed earlier in life. The classification of Eber et al.[2] has been useful in defining the severity and children at risk of complications and those in whom splenectomy is indicated. The principles of diagnosis and management, as outlined in recent guidelines,[3] can be applied in all locations and populations. It is important to make a correct diagnosis; this is usually straightforward when there is a positive family history and typical physical findings of splenomegaly with spherocytes seen on the blood smear. It is important to review the blood smear carefully and to consider alternative diagnoses if the findings are not typical. Congenital dyserythropoietic anaemia type II can be missed, and if the red cell morphology is not typical, other red cell membrane disorders must be considered. Anaemia may or may not be present (many individuals have compensated haemolysis with a normal haemoglobin) but reticulocytosis is usual. Jaundice is variable. Both anaemia and jaundice are increased under stress, particularly in the face of any type of infection. Aplastic crises are most commonly attributable to parvovirus B19 infection (as in other types of haemolysis). This may precipitate the first presentation of the child and it is important not to assess severity of the HS until the child is fully recovered. It is often not necessary to perform the osmotic fragility (or any other diagnostic) test when other features are typical as this is a laborious and time-consuming test, that can give false negative results.[3]

The management of people with HS is supportive; folate supplements are indicated certainly in moderate and severe HS but not necessarily in mild HS if the diet is adequate. Red cell transfusions may be needed in severe cases but children tolerate anaemia well, even with Hb 6-8 g/dL and transfusions should not be based on the Hb level alone as this may lead to unnecessary transfusions with increased risk of iron overload.[3] The level of transfusions at 35 (55% of patients) in this survey[1] is surprisingly high given that only 13 had severe disease. Iron supplementation should not be given unless there is additional evidence of deficiency. People with anaemia of any cause will have increased iron absorption, and those with congenital haemolysis are at risk of iron loading. Generally HS is diagnosed in childhood and it is important to encourage a normal level of activity and lifestyle. Most people with HS have splenomegaly; this is not an indication by itself neither for splenectomy nor for any reduction in activity. Follow-up, particularly in children, is important to check adequate growth and development especially in those with severe and moderate HS; checkups should generally be at 6 to 12 month intervals rather than 3-monthly as suggested by these authors unless there are other medical problems. For children with mild HS, annual follow-ups are adequate and adults with mild and stable HS often need no regular appointments.

An important question is when and whether to do splenectomy. It is clear that the spleen removes spherocytic red cells and this is responsible for the decreased red cell survival. Splenectomy results in an increase in red cell survival and in most cases, a normal Hb, and is thus very effective treatment. It is clearly indicated in severe (Hb 6-8 g/dL, reticulocytes > 10%) and some moderate HS (Hb 8-12 g/dL, reticulocytes > 6%),[2] but not in mild HS where the risks usually outweigh the benefits. The main risk is of overwhelming sepsis with encapsulated organisms, typically pneumococcus (the most common culprit), haemophilus influenza and meningococcal species. Splenectomy should be deferred until after 6 years of age if possible because of infection risks. Prior to splenectomy, all individuals should be vaccinated against these organisms. There may be local variations in vaccination practice related to national guidelines and predominant microbiological species. Although post splenectomy penicillin prophylaxis is often

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advised, the evidence for this is scanty.[4] It may be more important to advise patients carefully about the need for urgent medical attention for fever, and to keep a course of appropriate antibiotic at home to start when a suspected infection starts. These are not the only organisms with risk; the spleen gives some protection against malaria and this might affect the balance when considering whether to perform splenectomy in malaria areas.

The high incidence of splenic sequestration reported in this survey (14 cases – 22.2%) is surprising. This is not a common complication of HS and is rarely reported in the literature and is not generally among the indications for splenectomy in this condition. Could these cases have been precipitated by intercurrent viral infections? In HS the indications for splenectomy must be carefully weighed up. There is increasing recognition of additional long term risks associated with thrombosis and vascular disease.[5] The clinical picture of HS may be modified by co-inheritance of haemoglobinopathies (sickle cell trait, thalassaemia) which show considerable geographical variations. These can affect the degree of anaemia and the risk of cholelithiasis, and need to be taken into consideration in the overall management strategy.

Gall stones are a recognised complication of HS due to increased bilirubin turnover and the risk is reduced considerably by splenectomy. It is not clear whether regular ultrasonographic evaluations is cost-effective in the asymptomatic patient[3] and it is not clear whether asymptomatic stones should be treated surgically. The recent guidelines[3] recommend that, in children undergoing splenectomy, the gallbladder should be removed at the same time if there are symptomatic gallstones. If the gallbladder is left *in situ*, including cases when a cholecystostomy with stone extraction is done, close follow-up using ultrasound is necessary. In children who require cholecystectomy for symptoms of gallstones, the use of concurrent splenectomy is controversial. It may be associated with a decreased future risk of common bile duct stones, but is associated with a risk of post-splenectomy sepsis. The laparoscopic route is recommended, but this depends upon local facilities and an experienced surgeon.

It is important to make the correct diagnosis, to provide the patient and family with good information and to encourage normal activity and lifestyle. Careful assessment should be made before proceeding to surgery and older affected relatives treated by splenectomy in the past may need advice and immunisations in relation to their risk of infection.

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