Sickle Cell Disease: Time for a Targeted Neonatal Screening Programme

Abstract:

Ireland has seen a steady increase in paediatric sickle cell disease (SCD) in the past 10 years, mainly due to immigration. An epidemiological study carried out in 2005 identified 100 children with SCD. Unfortunately, only twenty five per cent of these children were being referred to the haemoglobinopathy service (Hb service) in the first year of life. Newborn screening for SCD has been in place in many western countries for the last two decades. Such screening programmes have only been associated with a reduction in infant mortality from eight per cent to three per cent, but also a reduction in the morbidity and mortality risk in the under 5yr age range. This is due to the early commencement of prophylactic antibiotics and appropriate vaccination.

Methods

All children referred to the haemoglobinopathy service between January 2009 and December 2012 were identified using the database held by the haemoglobinopathy service in OLCHC. From this list, all children born in Ireland after 2005 (when screening began) were identified. This list was then cross referenced with laboratory data provided by St James Hospital Dublin and Our Lady's Children's Hospital Crumlin (OLCHC). Once a positive sample is identified the laboratory contacts the Hb service at OLCHC and an outpatient appointment is made with a view to early prophylaxis and education.

The aim of this review was to identify all children with sickle cell disease born within the Republic of Ireland between 2009 and 2012 and compare them to the cohort born before screening commenced. We hoped to see a significant change in identification and management of infants with SCD and also wanted to identify areas for future improvement. Ultimately we hoped to provide a strong case for the instigation of a national targeted haemoglobinopathy screening programme.

Results

Baseline demographics

A total of 109 children were referred to the Hb service from January 2009 to December 2012. 78 of these were born in Ireland and could have been identified by a screening programme. A total of 396 children were attending our service in 2011. An additional 12 children who were born in Ireland were referred but not yet attended our service. These were in the screening programme but were not yet referred to the Hb service. A total of 206 children were referred from the initial database in Table 1. The majority of these children were of Sub-Saharan African origin, the rest were from the Indian subcontinent. Over eighty per cent of all children were referred within the first 12 months of life. Essentially, haemoglobin variants are screened from the birth year for all at-risk infants on the first day of life using High Performance Liquid Chromatography or haemoglobin Iso Electric Focusing. All samples are confirmed in the haematology laboratories of either St James Hospital Dublin or Our Lady's Children's Hospital Crumlin (OLCHC). Once a positive sample is identified the laboratory contacts the Hb service at OLCHC and an outpatient appointment is made with a view to early prophylaxis and education.

Introduction

Sickle cell disease (SCD) is the commonest haemoglobinopathy in man. It is an autosomal recessive condition that leads to to abnormally structured and functioning red cells that have a shortened life span, a poor capacity to carry oxygen and a tendency to occlude microvascular spaces. Significant morbidity and mortality results from organ sequestration, occlusion and sepsis. The risk of hospitalisation during the first three months of life but as the Hb F concentration decreases, sickling begins to occur. SCD has recently been labelled a global public health problem by the WHO, with recent epidemiological evidence pointing to a worldwide neonatal incidence of 294,000-330,000 cases per year. SCD was once isolated to Sub-Saharan Africa, India and parts of the Mediterranean and Middle East, however population migration, particularly in the past 10 15 years, has vastly changed the distribution and range of this disease and currently only fifty per cent of cases originate within the original countries involved.

The aim of this review was to identify all children with sickle cell disease born within the Republic of Ireland between 2009 and 2012 and compare them to the cohort born before screening commenced. We hoped to see a significant change in identification and management of infants with SCD and also wanted to identify areas for future improvement. Ultimately we hoped to provide a strong case for the instigation of a national targeted haemoglobinopathy screening programme.
Table 2 highlights the geographical pattern of screening. Seventy five per cent of children referred over the four-year period were born in areas in which screening occurred. Sixty five per cent of these infants were referred before three months, more than half had a delayed referral between three and six months, with a further twenty one per cent presenting between six and twelve months. The remaining twenty five per cent of infants were born in areas that do not currently screen. An additional twenty one per cent of infants had a delayed referral, nineteen per cent between three and six months and eighty one per cent older than six months at referral.

Discussion

Our study sought to highlight that neonatal screening for SCD in a targeted population within Ireland is a feasible and necessary step for the prevention of significant morbidity and mortality in this population. Both universal and targeted programmes are in use throughout the USA and many African countries. Screening is cost effective and is an acceptable test for most families. Whilst the prevalence of SCD in the Irish population is very small, the prevalence of 200/100,000 children under the age of fifteen of African and Asian origin is 50 times higher than the current prevalence (4/100,000) of Cystic Fibrosis in children under the age of fifteen of Irish origin, a disease screened for in the national newborn screening programme. Screening leads to early referral to a specialist Hb service. We have shown that the single biggest impediment to treatment commencement is the time taken to initiate diagnosis and referral. In hospitals that screen at birth, sixty five per cent of children are referred by three months of age, compared with none of the unscreened children. Early presentation greatly reduces the risk of morbidity and mortality from sickle cell crises, which is highest between the second 6 months and 5 years.14 Early prophylactic penicillin prophylaxis is recommended to commence between 2 and 3 months of life.13 In our study the median age for commencement of antibiotic prophylaxis in the screened group was 56 days compared with over 13 months in unscreened children. The rate of mortality in children born in centres that do not screen was twenty one per cent in the unscreened group compared with just three per cent in the screened population. Based on this data, the number of children needed to screen to prevent one child from presenting with a sickle crisis is 4.

The suggested gold standard of care is that ninety five per cent of children should be referred by the age of 3 months.15 Our figure of sixty five per cent (in the screened group) reflects the fact that there is no funded support for this programme, nor is there a national coordinator or a government supported policy. One of the reasons for delayed referral from hospitals that screen occurred where there was an intermediary step in the processing of samples. The fastest results came from hospitals that utilise the laboratory service based in OLCHC or St James Hospital Dublin. Repeat sampling was not required and appointments for the outpatient clinic were made directly by the Hb service in OLCHC following direct and timely communication of a positive result from the laboratory. In general, there are intermediate steps in the process that ensure that each child's results are seen, correctly interpreted and acted swiftly upon. One of the biggest challenges is contacting parents and ensuring their clinic attendance. As can be seen in Table 1, there was at times a long delay between referral and the first clinic attendance. Once again, the lack of a funded coordinator for the service makes this a difficult task and many of the children had received upwards of four appointments before presentation at clinic. The lack of a national programme and associated antenatal and postnatal education around SCD screening as well as early phone contact, means that parents often do not understand the importance of attending and fail to do so until repeatedly requested. According to the 2011 National Census, there are 869,929, 8,044 and 3,166 people of either African or Asian nationality living in Leinster, Munster, Connaught and Ulster (part of) respectively. Table 2 clearly identifies children from all four provinces presenting with SCD disease. The prevalence of SCD as high as 0.2 per cent in this population, it is difficult to ignore the need for a targeted neonatal national screening programme.

While awaiting the implementation of a neonatal screening programme, we would strongly suggest that at a minimum, all hospitals with maternity units in this state commence screening for newborns at risk of SCD. It is a cheap, cost effective intervention with a number-needed-to-screen of just 4 to prevent one child from a potentially fatal crisis. We also recommend improving local and national awareness regarding the importance of screening, the interpretation of results and encourage medical and nursing staff to always be alert to the possibility of undiagnosed SCD in an unwell child.

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References

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