NEONATAL SCREENING FOR SICKLE CELL DISEASE

Spanish full text

SUMMARY

Introduction. Sickle-cell anaemia is a systemic disease caused by a genetic haemoglobin disorder that is transmitted by autosomal recessive inheritance. It appears most frequently in geographical areas in which malaria is endemic, though this geographical pattern has varied with recent migratory flows. The estimated incidence of sickle-cell anaemia is low in Spain. Although the clinical manifestations depend on genotype and age, in its most severe forms clinical disease onset may occur in the first months of life and lead to elevated mortality, due principally to infections caused by encapsulated bacteria. Neonatal sickle-cell anaemia screening aims at initiating early prophylactic antibiotic treatment, so as to reduce the incidence and mortality of pneumococcal infection in children with sickle-cell anaemia.

Objective. To assess the efficacy/effectiveness and safety of neonatal sickle-cell disease screening.

Methods. Systematic review of the scientific literature (Updating a health technology assessment report conducted by Galician Agency for Health Technology Assessment in 2004). Electronic search was conducted in databases specialised in systematic reviews, general databases and databases of ongoing research projects. A supplementary search on preventing pneumococcal infection in children (antibiotic prophylaxis and vaccination) was performed. Critical appraisal of scientific literature was conducted by a single reviewer.

Results. Two systematic reviews on neonatal sickle-cell disease screening were found, which concluded that screening is supported by evidence from observational studies and indirect evidence from one randomised clinical controlled trial. The need for further research on alternative screening methods to identify only clinically relevant hemoglobinopathies and on counselling practices to minimize the negative effects of communicating carrier status has been highlighted. In the assessment on prevention of

pneumococcal infection in sickle-cell disease, in a meta-analysis on antibiotic prophylaxis a significantly lower incidence of pneumococcal infection in children under 5 years old has been found in the intervention group.

Conclusions and recommendations

- The aim of a neonatal screening programme for sickle-cell disease is to detect the disease in a presymptomatic stage, to establish early treatment aimed at reducing morbidity and mortality caused by sickle cell disease in childhood. This proposed early treatment is based on two pillars: prevention of pneumococcal infection (with antibiotic prophylaxis and pneumococcal vaccination) and health education of parents in order to identify acute complications in its early stage.
- There is no direct evidence, based on comparative studies, of the efficacy of neonatal screening programmes in reducing morbidity or mortality among children with sickle cell disease.
- There is evidence, based on good quality studies, showing that prophylactic penicillin reduces incidence of pneumococcal infections in children with homozygous sickle cell anaemia, which provides indirect evidence to indicate that children diagnosed during the presymptomatic stage are benefited by early administration of prophylactic antibiotics.
- The long-term effect of neonatal screening on chronic multiorganic complications of sickle-cell anaemia is not known.
- In population registers, a significant reduction over time in mortality among children with sickle-cell anaemia has been described but the contribution of newborn screening to this improvement in prognosis cannot be formally established.
- Current techniques for detecting haemoglobin disorders have demonstrated their validity, with a very high sensitivity and specificity, but they detect major drepanocytic syndromes, such as sickle cell trait carrier status, as well as other haemoglobinopathies of no clinical relevance or whose clinical relevance is unknown.

- Sickle cell disease is a hereditary disease, with a clear ethnic pattern, which mainly affects people originally from regions where malaria was endemic, though, as a result of migrations, incidence has risen in other regions, such as Europe and North America.
- In Spain there are no data on the real prevalence of sickle cell disease. There is an overall estimation, based on migratory flows, which classifies Spain in the group of countries with low risk of incidence of sickle-cell anaemia, but the distribution of immigrants is very variable throughout the country's regions (Autonomous Communities).
- The effectiveness and the cost-effective ratio of sickle cell disease screening depend on the prevalence of the disease.
- Universal newborn screening is not cost-effective in regions with low prevalence of sickle cell disease. Selective screening of risk populations by ethnic origin is a cost-effective screening strategy in regions with low prevalence but it reduces the effectiveness of screening due to misclassification of newborn risk.
- In Spain, there are four universal neonatal screening programmes for sickle-cell disease which form part of newborn blood spot screening programmes.
- Before deciding to implement a neonatal screening programme, the expected incidence of sickle cell disease in newborns in the respective autonomous communities must be properly known or estimated.
- Conducting cost-effectiveness studies in the context of the autonomous communities is recommended to define the most appropriate screening strategy (universal, selective). Furthermore the feasibility and acceptability of each screening strategies must be weighed.
- Neonatal screening programmes must establish a quality-assurance protocol that would enable their results to be monitored and assessed, to ensure the early introduction of preventive measures and follow-up of all children diagnosed in the screening programme.