Measuring the effects of genetic testing: studies on thrombophilia, sickle cell trait, recurrent miscarriage and male subfertility
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Chapter 5

Sickle cell disease in neonatal screening. Identification of sickle cell trait

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ABSTRACT

Aim
Evaluation of the first year (2007) of the neonatal screening program for sickle cell disease (SCD) and the disclosure of sickle cell trait within primary care in the Netherlands.

Methods
Description of number of children identified through the neonatal screening program as carrier of SCD. Identification from two clinical genetics departments of the Academic Hospitals in Amsterdam and Rotterdam of the number of referrals from general practitioners following identification of sickle cell trait.

Results
In 2007 sickle cell trait was found in 806 children (0.4%). Only 20 families were referred to the two clinical genetics departments, whereas none of these parents were at risk of having a child with SCD.

Conclusion
Among primary care providers, there is a lack of knowledge about both SCD itself as well as about their role in the process. More research is needed to investigate why so few families were referred to clinical genetics departments. More information and coaching for primary care providers is urgently needed.

INTRODUCTION

The neonatal screening (NBS) program in the Netherlands is a nationwide universal screening program, offered to all newborns, obtained by a heel prick and preserved as a dried blood spot on a filter paper (Guthrie spot). In 2007 the neonatal screening program in the Netherlands was expanded with sickle cell disease (SCD). Testing for SCD is performed by High Performance Liquid Chromatography (HPLC). This technique not only identifies children with SCD, but also identifies carriers of SCD (sickle cell trait), through the analysis of the screening sample. With the introduction of the expanded neonatal screening program, the Health Council has advised that sickle cell trait should be disclosed. At this moment only carrier ship of HbS is reported, whereas reporting carrier ship of other hemoglobin variants, such as HbC or HbD, is being considered. The objective of disclosing sickle cell trait is to assist parents in making informed decisions about subsequent pregnancies. Carriers of SCD are healthy, not anaemic and do not experience any other symptoms related to SCD. If both parents are carriers, and thus form an at-risk couple, there is a 25% chance in each subsequent pregnancy that the child will be born with SCD and a 50% chance that it will have sickle cell trait. At the moment over 1.6 million people live in the Netherlands whose origins can be traced back to Africa, Asia, the Caribbean or Mediterranean countries. If we assume that 10% of this population has sickle cell trait, then this would mean that there are approximately 160,000 carriers of SCD, or other forms of hemoglobinopathy (Hb-pathy), in the Netherlands.

The disclosure of sickle cell trait through population screening is unique in the Netherlands, since for the first time there is disclosure of healthy carriers and furthermore because SCD is a disease that is particularly prevalent within specific communities of immigrants. Neighbouring countries such as England, Belgium and France also disclose sickle cell trait identified during the heel prick screening test. At the time of testing, parents are given the choice of opting out, which means they can choose not to be informed if their child is a carrier. This choice can be recorded on the heel prick card.

Since disclosure of sickle cell trait in the neonatal screening was introduced, general practitioners have been given an important role in informing parents about the hereditary nature of SCD and the risks of having further children with the disease. In addition, general practitioners are required to identify at-risk couples, refer them to a clinical genetics department and point out
potential risk factors for family members. We evaluated the year 2007, which was the first year that sickle cell trait was disclosed. How many children were found to be carriers of SCD in 2007? And how many parents were subsequently referred to a clinical genetics department?

METHODS

If a newborn is suspected of having sickle cell trait as a result of the neonatal screening, the general practitioner and the parents are informed in writing by the medical advisors of the vaccination administration. The suspected sickle cell trait is not further confirmed by a second test. By way of this letter, parents are advised to contact their general practitioner to organise a blood test for sickle cell trait or other Hb-pathies that, in homozygote or compound heterozygote form, can lead to SCD in their offspring. If both parents test positive, this means they are an at-risk couple and must be referred to a clinical geneticist for genetic counselling. Based on the national neonatal registration of the RIVM (Dutch National Institute for Public Health and Environment) and the experiences of the clinical genetics departments of the Erasmus Medical Center (EMC) in Rotterdam and the Academic Medical Center (AMC) in Amsterdam, the prevalence and geographical spread in 2007 of carriers of SCD have been documented.

RESULTS

The neonatal screening was performed on 182,303 newborns in 2007. Sickle cell trait was found in 806 children (0.4%). The sensitivity and the specificity of the HPLC test are 100% and 99.99% respectively (source TNO 2008). In figure 1 we present the number of children with sickle cell trait per province in the Netherlands. The cities Amsterdam and Rotterdam are separately shown.

Of all children born with sickle cell trait, 59% were born in the provinces of North Holland and South Holland. Based on the previously mentioned carrier prevalence of 10%, about 1 in 10 parent couples of a child with sickle cell trait is an at-risk couple. If 806 children have sickle cell trait, then approximately 40 at-risk couples can be identified. In our calculation we have assumed that most parent couples have the same ethnic background.

Because we have no records from general practitioners as to how many parents were actually informed about the sickle cell trait, we also do not know what further action parents took. In other words, it is unknown if further testing was done for Hb-pathies or not. From records available from the clinical genetic departments of both the EMC and the AMC, it appears that in 2007 a total of 20 parent couples were referred for genetic counselling as a result of their children having sickle cell trait. None of the parents had been tested for Hb-pathies by their general practitioners prior to the referral. Further investigation revealed that none of the parents was part of an at-risk couple. One parent was found to have a form of SCD that had not previously been diagnosed.

DISCUSSION

The prevalence of sickle cell trait among newborns was 0.4% in 2007. It is unknown exactly how many parents were informed about the sickle cell trait in their children by their general practitioner and we also do not know how many parents were tested for Hb-pathies. The number of referrals to the two clinical genetics departments in the areas with the highest percentage of sickle cell trait affected children was extremely low and did not include any at-risk couples.
Since the introduction of the neonatal screening for SCD in the Netherlands on the first of January 2007, primary care providers (general practitioners and midwives) are expected to play a key role in providing information to parents about the risks of SCD or other forms of Hb-pathy in high-risk population groups.

Informed choice
The disclosure of sickle cell trait as a result of the neonatal screening test offers at-risk couples the opportunity to make an informed decision about a subsequent pregnancy when assessing the risks of having a child with SCD. This disclosure offers parents the option of primary prevention. In order to make an informed decision it is important that parents are properly informed about sickle cell trait and SCD, taking into account their level of education, language and culture. This implies that primary care providers must receive adequate information and training to optimise their methods of communication. Because of the relatively short period between the decision to expand neonatal screening and the actual implementation of said test, insufficient research was conducted as to how and whether general practitioners would fulfil the new role assigned to them. In addition, it is not clear what the most efficient method of disclosure of sickle cell trait is and whether the neonatal screening test is the right point in time for parents to receive information about sickle cell trait and the risks of having further children with SCD.

Primary care providers’ experiences
Based on an exploratory survey amongst 353 primary care providers (94 general practitioners, 60 paediatricians and 199 midwives) who attended a seminar on the expanded neonatal screening program, we found that many doctors and midwives had a lot of unanswered questions and uncertainties about SCD itself, and also about the role thrust upon them as a result of the expanded neonatal screening. This is possibly one of the reasons behind the low percentage of referrals to clinical genetics departments. This lack of clarity concerning the role of primary care providers appears to be an issue in other countries as well. In the meantime, a professional development program has been launched for primary care providers and the Centre for Population Studies will shortly release a DVD with more information. The information provided to primary care providers must be plain and clear and outline the concrete steps that the general practitioner is expected to take. A system whereby general practitioners report back on the actions they have undertaken will also provide a clearer picture of the effectiveness of disclosing sickle cell trait. A study will be started in 2009 to investigate the experiences general practitioners have with disclosing sickle cell trait.

Information for parents
A number of obstacles have also been identified in parents themselves. For example, it is known that parents have difficulties understanding the information given to them, especially concerning the difference between a child with SCD and one with sickle cell trait, which can lead to unnecessary anxiety. The Centre for Population Studies is planning on evaluating this situation in the near future. In addition to unfamiliarity with SCD, misconceptions about the disease and heredity and a possible language barrier, there may also be cultural and religious reasons as to why parents do not want to have themselves tested as possible carriers of SCD. It is therefore very important in the future that information content and the timing of when such information is given is more suited to the at-risk population groups concerned.

Whether at-risk couples will ultimately choose to undergo prenatal testing remains a question. In other countries where neonatal screening of sickle cell trait has been in place for longer, the percentage of prenatal testing during pregnancy varies from 22% in England to almost 100% in Cyprus. Research conducted in the Netherlands prior to the introduction of expanded neonatal screening indicated that the intention to terminate a pregnancy of an affected child ranged from 16% of the Moroccan population to 68% of the Suriname Hindustan population.

In order to evaluate the ultimate effect of disclosing sickle cell trait it is crucial to understand the extent to which parents use this information when choosing to undergo diagnostic tests in subsequent pregnancies.

Conclusion
Evaluation of the disclosure of sickle cell trait, as a result of the expanded neonatal screening program in 2007, illustrates that the procedures concerning disclosure to primary care providers is not yet optimal. The timing and impact of sickle cell trait disclosure, identification of at-risk couples and the ensuing decision making process requires a more comprehensive evaluation. There is currently a clear need for more information and guidance, both to primary care providers as well as to parents.
REFERENCES


