Institutionen för Klinisk Vetenskap, Intervention och Teknik, Enheten för Pediatrik

Studies as a basis for a possible introduction of newborn screening for cystic fibrosis in Sweden

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ABSTRACT

Background: Cystic fibrosis (CF) is the most common life-shortening autosomal recessive disease in Caucasians. It is a multi-organ disease that results from mutations in the gene that encodes the CF transmembrane conductance regulator (CFTR) protein, which regulates ion transport at epithelial surfaces. The main clinical characteristics are progressive pulmonary disease and pancreatic insufficiency. Not long ago most affected patients died in childhood. The outlook for patients with CF has improved steadily over the years, as a result of more aggressive therapy and care in specialised centres. Current understanding of the molecular-biological defect that underlies CF will lead to new treatments. To benefit from these new treatments, patients should have as few irreversible lesions as possible. An early CF diagnosis by newborn screening is therefore highly desired. The overall aim of this thesis was to provide a basis for discussion of whether CF should be included in the national newborn screening programme in Sweden.

Paper I is a multi-centre study in which we analysed the *CFTR* mutation in 75% of the Swedish CF population (331 patients). The three most common *CFTR* mutations were deltaF508 68.3%, 394delTT 8.5% and 3659delC 7.9%, comprising 84.6% of the CF alleles in the material. This result shows that newborn screening for CF with an IRT/DNA approach is possible in Sweden.

Paper II is a questionnaire study of parental attitudes towards newborn screening for CF in which the parents of 143 CF patients and parents of children in two age-matched control groups participated. A majority of the parents, 70-86% in the different groups of parents, supported screening for CF. The parental attitude of CF parents was independent of the age of the child, the delay of diagnosis as experienced by the parents, and the well-being of the CF child at the time of diagnosis.

Paper III is a questionnaire study to the parents of the same 143 CF patients as in Paper II to investigate their experiences after the clinical CF diagnosis of their child, and to find out the effects of the diagnosis on the family. The parental experiences on receiving a clinical CF diagnosis were intense and emotional. The parents stated that the CF diagnosis greatly influenced other family members, such as siblings and grandparents. A majority of the CF families had not experienced any change in relationships within the family, or in the social life of the family, one year after the diagnosis.

Paper IV is a register study of 119 CF patients born between 1974 and 2001 in which we studied disease progression over time for lung, liver, nutritional and overall morbidity with Kaplan-Meier curves and proportional hazards regressions. The median age at diagnosis of the patients was 5 months. The patients with overall morbidity at diagnosis showed a slow decline of symptoms, with half of the patients becoming free of overall morbidity after 4.8 years; however, the patients who were older than 24 months at diagnosis had a lower probability of becoming free of morbidity (crude hazards ratio 0.14 [95% confidence interval 0.04, 0.45]) than those with an earlier diagnosis, at the age of 2-12 months ($p < 0.01$).

Paper V is a register study of all patients in the Stockholm CF Centre register with the diagnosis of CF and two verified *CFTR* mutations, in total 220 patients. *CFTR* mutations or larger deletions were found in all patients with classic CF. There was no statistical difference in lung function using the mixed model analysis for the different mutation groups studied. Patients born after 1985 had better lung function (FEV_1 and FVC) than those born earlier.

Conclusion: Our studies show that the conditions for a newborn screening programme for CF in Sweden are good and that a majority of parents in Sweden support the inclusion of CF in the newborn screening programme.

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