Children with a late diagnosis of CF despite a long-established newborn screening programme

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Objectives: Neonatal screening for CF has been continuous in New Zealand (NZ) for 30 years. Initially this was by two blood immunoreactive trypsinogen (IRT) levels until 1996 when a three gene detection replaced the second IRT measurement.

Aim: To determine the number of children with a late diagnosis and why they were not detected despite our long term newborn screening programme.

Methods: Retrospective review of all children with CF under full care at Starship Children’s Hospital, Auckland, NZ from 2003–2012 which includes patients up to 18 years of age to therefore determine missed on screening from 1985–2012 in the greater Auckland region with a general population of 800,000 to 1.2 million over this time.

Results: In the last decade 100 children with CF were in this clinic of whom 18 had a late diagnosis, mean age 14 months (range 6 weeks to 11 years). Eight of them were born overseas in regions without a newborn screening programme at that time. Ten were born in NZ, 4 were pancreatic sufficient and 6 were pancreatic insufficient. Nine were missed as the IRT level was not in the highest 1% and therefore the gene determination was not undertaken, or they had “uncommon” gene, undetectable on screening. One child’s parents refused newborn screening. All ten had recurrent pneumonias, 2 had established bronchiectasis, 4 FTT and 1 had severe liver disease leading to the diagnosis.

Conclusion: Even with an established newborn screening programme in place, cystic fibrosis should be considered in the appropriate clinical setting.

Clinical outcomes of cystic fibrosis patients during their first year of life after neonatal screening implementation

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Objectives: To assess the diagnostic and clinical outcomes of infants in their first year of life, followed up after cystic fibrosis newborn screening (NS).

Methods: A transversal and descriptive study including 24 infants followed up from 2010–2012 that were screened by immunoreactive trypsinogen (IRT) tests in 2 measurements in the first month of life with the cut-off value >70ng/ml and positive sweat chloride test (SCT). The clinical outcomes were assessed in the months 0, 3, 6, 9, 12. All received similar treatment. Among 24 infants: 16 were male and 21 Caucasian. 3 died. IRT was realized during the first week and in the 3rd or 4th week of life. The mean values were: IRT1 = 191 ng/ml and IRT2=207 ng/ml. The mean values of SCT were 100.3% and 110 mEq/l. 90% presented respiratory manifestations and 33.33% had pulmonary colonization by P. aeruginosa. All 24 patients had digestive manifestations with 21% of steatorrhea mean values. In the first month of life, 16.66% and 12.5% of them had already been hospitalized for respiratory disorders and meconium ileus respectively. The most critical clinical health condition happened between 3 and 6 months of life, in which 45.83% were hospitalized (20.83% and 25% with metabolic and respiratory disorders).

Conclusion: The NS contributed for a good nutritional status, improvement of metabolic and respiratory conditions and lack of hospitalizations after 6 months of age.

Neonatal screening for cystic fibrosis – A new experience for genetic counseling

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Neonatal Screening for Cystic Fibrosis (NS CF) has been introduced in the Czech Republic (CR) since October 2009. For the Moravia region, CF Center of University Hospital Brno performs examinations (IRT/DNA analysis and comprehensive care for patients with 1 and or 2 mutations in the CFTR gene). Every year we examine IRT level from dry blood spot in around 40,000 newborns, a positive result and DNA analysis of 50 CFTR mutations (Elacigene) is indicated in about 1% of newborns and in about 1% of the analyzes we confirm the newborn with CF.

As part of comprehensive care for families of newborns with one and/or two mutations in the CFTR gene, we noted certain facts, that we further analyzed:

- Lower prevalence of CF in the study population compared to the statistics.
- New spectrum of CFTR mutations in the Moravia population.
- Detection of CF at an older still untreated siblings.
- A false negative IRT result.
- Non-cooperation of the family.
- Incorrect reset of DNA analysis due to contamination of blood spot.
- Detection of a part of healthy heterozygotes in the population.
- Psychological stress of parents.
- Adoption as a result of diagnosis CF in the newborn.

Conclusions: NS CF in CR definitely met expectations and leads to early detection of CF patients. NS CF but also brings some unexpected findings and situations to be applied within the comprehensive care and genetic counseling. Detection of patients with CF with NS is not 100%. Detection of heterozygotes is irrelevant – unsolicited finding that brings stress situations, but also allows the family genetic counseling and targeted CF prevention. Efforts to minimize the psychological stress of parents will never be completely successful.

Comparison of two sweat test systems (Macroduct versus Nanoduct) for the diagnosis of cystic fibrosis in the newborn screening program in Switzerland

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Background: Newborn screening for CF, based on an IRT-DNA-IRT protocol, was introduced in Switzerland in January 2011. In the 2-years pilot phase, we compared the performance of two sweat test methods for diagnosing CF.

Methods: All children with a positive screening result were referred to a CF center for a sweat test with:

- Macroduct (measuring chloride, at least 15 ml sweat required); and
- Nanoduct (conductivity, at least 3 ml sweat required).

If sweat test results were positive, borderline or inconclusive, an extensive DNA analysis was performed.

Results: Within two years, 162 children were screened positive and further investigations in a CF center were needed. In 49 the diagnosis CF could be confirmed, and in 12 an equivocal CF was made; 88 children had negative investigations, and 13 children were not yet fully investigated. At the time of writing the abstract, details of the investigations were only available for 141 children. They were seen in a CF center at a median age of 25 days. Macroduct was attempted in 121 (86%), Nanoduct in 136 (96%). A reliable result was available in 74% (89/121) for Macroduct and 86% (117/136) for Nanoduct. In 81 children both sweat tests could be performed, while in 36 only Nanoduct and in 8 only Macroduct was feasible. In 16 (9.8%) children none of the two sweat tests could be performed at the first assessment. Sensitivity and specificity data will be presented at the conference when all investigation details will be available.

Conclusions: In this pilot study, Nanoduct showed a better feasibility for use in newborns compared to the Macroduct, mainly because it needs a lower sweat volume.