Newborn screening for cystic fibrosis – Polish four years’ experience with CFTR sequencing strategy

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Objective: Newborn screening for cystic fibrosis (NBS CF) in Poland is a public health policy program started in September 2006. Summary from four years’ experience is presented in this study.

Patients and Methods: The IRT/DNA strategy was implemented. DNA analysis was performed using direct sequencing of selected CFTR regions. The group of 1,212,487 newborns were screened for cystic fibrosis during the programme.

Results: A total of 221 CF cases were identified during this period. In addition, four CF cases were reported to be omitted by NBS CF programme. Disease incidence in Poland based on the programme results was estimated as 1/4394 and carrier frequency as 1/33. The frequency of the p.Phe508delCTT was similar (62%) to that in the Poland based on the programme results. This strategy allowed to identified twenty-nine unaffected carriers of CF. A subset of infants with borderline sweat chloride results (n = 24) were being followed to investigate the possibility of late onset CFTR-related disease. Follow-up data is pending on 96 infants.

Conclusions: Sequencing assay seems to be adequate method for screening programme using blood spots in Polish population.

Newborn screening for cystic fibrosis in Ontario, Canada: the first three years

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Objective: To present the first three year’s experience of NBS for Cystic Fibrosis (CF) in Ontario.

Methods: Dried blood spot specimens from infants were assayed for immunoreactive trypsinogen (IRT) via radiimmunomassay. Infants with IRT >96 centile had CFTR mutation analysis using the TM Biosciences Tag-It CFTR 39–3 mutation kit. Newborn Screening Ontario (NSO) created a categorical system to stratify positive results by risk: Category A: high IRT and two CFTR mutations, high risk (>100%); Category B: high IRT and one CFTR mutation, moderate risk (~2.5%); and Category C: elevated IRT above the 99.9 centile and no CFTR mutations, low risk (~1%). All infants with a screen positive result were referred for follow-up diagnostic testing at a regional NBS treatment centre. Approximately 428,762 infants have been screened for CF; of those, 1257 were screen positive. NSO has identified 77 confirmed cases of CF. Eight hundred and seventy-one infants with a Category B screen positive have been confirmed to be unaffected carriers of CF. A subset of infants with borderline sweat chloride results (~1%) are being followed to investigate the possibility of late onset CFTR-related disease. Follow-up data is pending on 96 infants.

Conclusions: After three years of screening, the screen positive rate for CF in Ontario is 0.29%. The positive predictive value of the test varies by screen positive result: 100% for Category A, 4.49% for Category B, and 1.29% for Category C. Infants with CF identified through NBS will be followed prospectively to determine if early detection improves the clinical course of disease.

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Background: NBS program was established in Tuscany in 1982. In 2011 DNA mutation analysis was introduced to improve accuracy, taking into account costs and genetic background in our region.

Aims: To assess the performance of the NBS protocol in the period 2000–2010.

Methods: We reviewed the NBS data-base. Our three-stage protocol included: 1. an initial immunoreactive trypsin (IRT) measurement (99th centile cut-off – Delifia™ and AutoDelifia™); 2. meconium lactase dosage and a second IRT blood sample taken at 4 weeks of age; 3. the sweat test (ST).

Results: There were 347,815 babies screened in Tuscany in the period 2000–2010. Of these, 82 were diagnosed with CF and 9 (0.0026%) were known false negative cases. 12 infants were diagnosed by meconium ileus in this period and 10/12 were IRT-positive. Incidence of CF was 1 in 3,443 newborns. 12/92 (13%) had borderline ST at the diagnosis and 2 CFTR mutations. The median (IQ7) age at the diagnosis was 46 (37, 57) days in the last 5-year period compared with 54 (48, 62) days in the previous years (p < 0.05). Considering the false negative cases, the median (IQ7) age at diagnosis was 0.6 (0.3, 1.4) years; 3/9 had pancreatic insufficiency and respiratory symptoms, 5/9 had only salt loss as clinical features consistent with CF. Considering the 2006–2010 period, IRT-1 was positive in 0.91%; sensitivity, specificity, positive and negative predictive values were 92.98, 99.82, 13.80 and 99.99%, respectively.

Conclusions: Critical points in our program were a relatively late diagnosis age and the low positive predictive value. An IRT cut-off reassessment and the introduction of DNA analysis should improve the performance of our program.