Newborn Screening for Cystic Fibrosis in Genetically Heterogeneous Populations

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Received date: April 13, 2021; **Accepted date:** April 27, 2021; **Published date:** May 04, 2021

Citation: Teper A, Rodríguez V (2021) Newborn Screening for Cystic Fibrosis in Genetically Heterogeneous Populations. Neonat Pediatr Med 7: 212.

Abstract

Cystic fibrosis is the most frequent autosomal recessive disease in Caucasians. Survival improves with the implementation of newborn screening programs that enable early detection and rapid initiation of treatment to reduce the effects of the disease. Not all available algorithms for newborn screening are suitable for all populations. IRT/PAP is the algorithm of choice in genetically heterogeneous populations.

Keywords: Cystic fibrosis; Newborn screening; Immunoreactive trypsinogen; Pancreatitis-associated protein

Introduction

Cystic Fibrosis (CF) is the most frequent autosomal recessive disease in Caucasians [1] Recent studies in the United States report improved survival of patients with CF and a projected median survival of 56 years for children born today [2]. The figure falls to under 15 years in low-income countries [3]. While CF affects various organs (pancreas, exocrine glands, male reproductive system, and, in particular, the respiratory system), progressive lung disease accounts for 90% of morbidity. The key causes of progressive decline in lung function are bacterial colonization from an early age, which causes lower airway inflammation followed by chronic endobronchial infection and impaired mucociliary clearance [4]. Longer survival depends on timely prevention of respiratory complications [5]. Results from clinical research studies show that children with CF have normal lung function at birth but develop abnormalities after 6 months of life; these in lude airflow limitation, inhomogeneity lung ventilation, and increased airway resistance [6]. Importantly, disorders of this type are not reversible, even in patients treated in specialized CF centers [7]. These findings are relevant, because prevention of respiratory complications and impaired lung function is a key objective of treatment. Consequently, early intervention is necessary.

Literature Review

Newborn Screening (NBS) for CF is widely agreed to be beneficial, and extensive use of this approach can facilitate the early diagnosis and treatment necessary to prevent severe complications (mainly respiratory and nutritional), which arise during the course of the disease [8]. Of note, 62.5% of newly diagnosed cases in United States were detected by NBS in 2019 [9], and 74% of all children aged 5 years or younger registered in the ECFSPR in 2017 were screened at birth [10]. In Argentina, according to the National Cystic Fibrosis Registry, newly diagnosed cases detected by NBS represented 69% of all patients with CF in 2017 [11].

NBS as a component of public health initiatives involves Presymptomatic Administration of Preventive Medicine in order to reduce morbidity in patients with specific biochemical or genetic disorders [12]. Initial experiences with NBS for CF date back to the early 1970s, when pioneering programs analyzed the albumin content of meconium [13]. In 1979, Crossley et al. reported that increased Immunoreactive Trypsinogen (IRT) could be measured in neonates with CF based on the dried blood spots used to screen for other diseases (Sensitivity, 100%) [14]. During the following decade, determination of IRT levels in heel blood was implemented in Australia [15] and some European countries. The first NBS program for CF was initiated in 1982 in Colorado, USA [16].

A suitable screening program can detect the highest possible number of affected cases, guarantee a minimum number of missed cases, identify the lowest number of non-affected carriers, take ethnicity into account, and generate the least anxiety for families. The

the second sample to be taken. After 15 years of experience in the City of Buenos Aires, we found that 20% of children with an initially high IRT level did not return for a second sample, thus necessitating performance of a sweat test. Non-attendance was particularly noticeable in vulnerable populations.

Identification of the CF Transmembrane Conductance Regulator (CFTR) gene facilitates the inclusion of genetic analysis in the NBS algorithm [23]. Molecular analysis is feasible in children with high IRT levels, as long as the gene panel is appropriate for the population, ie, covering more than 98% of mutations in that region. Detection of a culprit mutation in its homozygous form confirms the diagnosis and enables referral to a tertiary institution for follow-up. A sweat test should be requested in cases of a heterozygous mutation in order to differentiate between affected children and carriers. This strategy, known as IRT/DNA, is highly sensitive, does not require a second sample, and reduces parental anxiety. The main disadvantage is its high cost [24] and the detection of carriers, whose management is not envisaged in most screening protocols.

Another weakness of screening based on genetic analysis is the legal implications. In France, for example, laws on bioethics require parental consent for DNA analysis. The Ethics and Genetics Committee of the French Association of Neonatal Screening requires parental informed consent. In one study, a low percentage of parents refused to provide their informed consent (0.8% at the start of the pare wfs

Conclusion

Latin America is a very diverse and heterogeneous region in terms of its geography and also in terms of demographics, ethnicity,

39. Teper A, Smithuis F, Rodríguez V, Salvaggio O, Macallini G, et al. (2020) Comparison between two newborn screening strategies for cystic fibrosis in Argentina: IRT/IRT vs. IRT/PAP. Pediatr Pulmonol. 56: 113-119.
40. Sarles J, Barthellemy S, Férec C, Iovanna J, Roussey M (1999) Blood concentrations of pancreatitis associated protein in neonates: Relevance to neonatal screening for cystic fibrosis. Arch Dis Child Fetal Neonatal Ed 80: F118–F122
41. Merelle ME, Huisman J, Alderden-van der Vecht A, Froukje Taat, Dick Bezemer, et al. (2003) Early versus late diagnosis: psychological impact on parents of children with cystic fibrosis. Pediatrics 111: 346-50.
42. Baroni MA, Anderson YE, Mischler E (1997) Cystic fibrosis newborn screening: I mpact of early screening results on parenting stress. Pediatr Nurs 3:143--51.
43. Parsons EP, Bradley DM (2003) Psychosocial issues in newborn screening for cystic fibrosis. Paediatr Respir Rev 4:285-92.