O-015 - AN EXPERIENCE IN MOLECULAR DIAGNOSIS IN ARGENTINEAN PATIENTS WITH CYSTIC FIBROSIS. CURRENT AND FUTURE CHALLENGES.

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INTRODUCTION: cystic fibrosis (CF) is an autosomal recessive disease caused by mutations in the transmembrane conductance regulator gene (CFTR). More than 2000 variants have been identified (www.genet.sickkids.on.ca/cftr). Since 2012 there are molecular pharmacological therapies for individuals affected of specific mutations. ***AIMS:*** 1) Molecular diagnoses. 2) Confirm the diagnosis in children and/or young adults with clinical compatibility 3) Establish the mutation's spectrum and frequency in the CFTR gene. ***PATIENTS:*** from Hospital de Niños/Córdoba (sections Neumonology and Gastroenterology); Assistance Program for CF; private Health institutions and centers of Córdoba and other provinces in Argentina. ***METHODS:*** 1) PCR/heteroduplex, multiple PCR, single strand conformational analysis, gel electrophoresis with denaturing gradient. 2) Oligonucleotides/PCR conditions were designed to perform complete sequencing, 27 exons/flanking sequences/deep intronic zones. The most frequent mutations in the CFTR gene worldwide were investigated. The complete genotype was determined. If stated an incomplete or unknown genotype, the full gene analysis was performed. ***RESULTS:*** Fifty mutations were identified, 10 with percentages greater than 1% (c.1521_1523delCTT, p.Phe508del: 51.63%; c.3909C>G, p.Asn1303Lys): 4.47%; c.1624G>T, p.Gly542*: 3.66%; c.3196 C>T, p.Arg1066Cys: 2.44%; c.2657+5G>A, 2789+5G>A: 2.03%; 2 mutations with 1.63% (c.3140-26A>G, 3272-26A>G and c.1657C>T, p.Arg553*) and 3 with 1.22% (c.1000C>T p.Arg334Trp; c.1766+1G>A, 1898+1G>A and c.3454G>C, p.Asp1152His). 142 patients with classic cystic fibrosis were defined through 2 positive sweat tests or by molecular analysis. In addition, 9 CFTR related disease by molecular diagnosis were detected. Total 151 patients. ***CONCLUSIONS:*** The recognition of 2 mutations in people with CFTR-related diseases (inconclusive or even normal sweat test values) confirmed the usefulness of genetic analyzes. Molecular diagnosis was essential to investigate the genotype of the patient due to the availability of molecular therapies, thus we developed conditions to carry out the full exome sequencing by Sanger. Challenges: -to establish the pathogenicity of a new genomic change (variants of uncertain significance), -to analyze and to understand results of next-generation massive technology (NGS), -to educate specialist physicians for young-adults, to evaluate the effectiveness of molecular treatments in patients. Grants: Assistance Program for CF, SECYT, PICT 2010, SLEIMPN.