Phenotypic characteristics of p.E92K mutation in adults with cystic fibrosis (CF) in Russia

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The main reason for development of CF for the Chuvash – the fifth in population number (1.5 mln) nationality in Russia is of the “mild” p.E92K mutation (p.Glu92Lys, c.274G>A).

Objective: To identify the clinical and functional characteristics of the course of CF in the patients-carriers of p.E92K mutation.

Materials and Methods: Group 1: 26 adult CF patients homozygous or heterozygous for E92K, group 2: 103 adult patients homozygous for F508del. Age, gender, BMI, level of chloride in sweat, spirometry parameters, frequency of some complications (CF-related diabetes (CFRD), liver cirrhosis with portal hypertension (LCPH), distal intestinal obstruction syndrome (DICS)/meconium ileus (MI) in past medical history, cholelithiasis, urolithiasis, pulmonary hypertension (PH), asthma) were estimated. Results are described as mean±SD/median (IQR).

Results: The average age group 1 was: 25.5 (9.5) years, higher than in the group 2 – 23.6 (5.5) years (p = 0.007); age diagnosis of patients with E92K was: 13.3 (9.2), higher than among homozygous for F508del – 1.9 (4.5) years (p = 0.001). There was no significant difference in the level of chloride in sweat (101±30.5 mmol/l vs 103±32 mmol/l respectively) in the two groups. The spirometry parameters, BMI, the frequency of LCPH, DIO5/MI, cholelithiasis, urolithiasis, asthma and PH had no significant difference. CFRD had frequency in the group of the patients homozygous for F508del, and CFTR in p.E92K mutation was never once identified (p = 0.046).

Conclusion: p E92K mutation in patients-carriers is associated with late onset age, significant low frequency of CFRD, what is likely connected with the “mildness” of this mutation.

CFTR dele2,3 (21 kb) mutation in cystic fibrosis patients in Latvia

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Background: Cystic fibrosis (CF) is one of the most common severe autosomal recessive diseases in Latvia with frequency 1:3,300. It is classified as I class mutation causing a premature stop codon formation in exon 4. The phenotype is associated with early onset of disease and exocrine pancreatic insufficiency. So far only few cases with homozygous dele2,3 mutations have been described.

Methods: CFTR mutation screening was performed by standard molecular methods for 62 patients with clinical symptoms of CF.

Results: CFTR dele2,3 mutation was detected in 3 patients. The first was a girl with dF508/dele2,3 mutation who was diagnosed with CF at the age of 1 year due to poor weight gain, recurrent lung infections and positive sweat test. On therapy there was a symptom free period of several years. She died at the age of 13 years due to pulmonary and heart insufficiency. The second was a boy with P67L/dele2,3 mutation presented with meconium ileus and had died at the age of 3 months. The third patient, a girl, presented with meconium ileus and positive sweat test in first days of her life. The molecular testing revealed her to be homozygous for dele2,3 mutation. At the age of 1 year and 6 months, even having pancreatic enzyme replacement therapy, her height and weight is still below 3rd percentile.

Conclusion: CFTR dele2,3 (21 kb) mutation represents 3.2% of all CF alleles becoming the second most frequent severe CFTR mutation in Latvia. This mutation should be included in first step CF mutation screening together with dF508 mutation. The study confirms that dele2,3 mutation has severe phenotype – early presentation, exocrine pancreas insufficiency and recurrent lung infections.