Abstract

Hearing loss is the most common sensory deficit and it affects 1 of 300 newborns. Genetic causes are responsible for 50-75% of cases. The most common cause of hereditary hearing loss (HHL) are mutations of *GJB2* gene, which account for 43 % of non-syndromic hearing loss (NSHL) in the Czech Republic. According to literature, the second most common genetic cause of HHL are mutations in *SLC26A4* gene. Bialelic mutations in this gene cause NSHL of type 4 (DFNB4) and Pendred syndrome (PS), which means a hearing loss associated with thyroid impairment. A typical symptom of both units is Enlarged Vestibular Aqueduct (EVA) and Mondini dysplasia (MD) on the HRCT of temporal bone.

Sequencing of *SLC26A4* gene was used to examine 315 patients with NSHL where bialelic mutations in *GJB2* gene were dismissed, out of that 30 familiar and 285 sporadic cases. At least one pathogenic mutation in *SLC26A4* gene was found in 6.9% patients and bialelic pathogenic mutations in 2.6% patients, however for familial cases it was 14.8% patients with at least one mutation, or 7.4% patients with both identified mutations. In the group of cochlear implant users with no *GJB2* mutations at least one pathogenic mutation was found in 13.0% and bialelic mutation in 7.6%. The *SLC26A4* mutations appear to represent the second most common cause of HHL in the population of the Czech Republic.

There were identified 20 pathogenic mutations in 40 alleles. There is no prevalent mutation of gene *SLC26A4* in the Czech population, the most frequent mutation is p.Val138Phe (17.5%), the others are p.Leu445Trp and p.Glu29Gln (10% each), the spectrum of mutations is broad a dispersed throughout the whole *SLC26A4* gene (14 out of 21 exons and 2 introns), which means that sequencing needs to cover the whole gene.

The most reliable diagnostic criterion appears to be bilateral EVA (72.2 % for at least 1 mutation and 50% for both) and fully developed thyroidal phenotype (53.4 % or 33.3 %).

Due to the elevated ratio of *SLC26A4* mutations in familial patients haplotypical analysis was introduced to examine siblings. Sequencing analysis of gene *SLC26A4* will follow, if there is a concord of STR markers in the DFNB4 locus of both siblings.

As a result of my study there was introduced routine diagnostics of the second most common cause of congenital non-syndromic hearing loss and there was set an algorithm for dispensarization of patients with *SLC26A4* mutations.