GENETIC CHARACTERISTIC OF NON-SYNDROMAL NEUROSENSORY CHILDREN’S HEARING LOSS IN UZBEK POPULATION

The paper studies clinical signs of hearing disorders caused by mutation in gene Cx26 in order to determine approaches to treatment and rehabilitation. The problem of primary prevention of such pathology as NSHL among children of Uzbek population is important thing in our region because of the high level of birth rate where we can see the marriages between two relatives who have blood relationship with each other (inbreeding). Factor of inbreeding comes as additional precondition to investigate influence of the different genetic factors to NSHL in children. Determining mutation in gene Cx26 should lead to recommendation on testing this gene in all family members. In each specific case, during the obligatory medical and genetic consultation, we need to discuss on prevention of repeated cases in this family and in the following generations.

Keywords: Congenital loss of hearing, medico-genetic counseling, inbreeding.

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Development of medical genetics has made possible to find out the principle of hereditary transfer to man the signs of external resemblance and health state, some diseases and answer to questions regarding to the possibilities of preventing of congenital diseases and influences of the congenital factors to the genesis of neurosensory hearing loss (NSHL) in children.

Development of human population is influenced among other factors by migration and isolation. Isolated populations with a low index of migration in some regions of Uzbekistan condition an increased level of blood relationship (Kazanseva, 1999; Ubaidullaev, 2002). The high level of birth rate in consanguineous marriages (inbreeding) in the country makes the issue of primary prevention of such pathology as NSHL among children, as well as respective genetic counseling, highly important.

The inbreeding factor comes as an additional precondition in order to investigate the influence of the different genetic factors of NSHL in children. Consanguineous marriages represent a common practice among the indigenous population of Uzbekistan (Ubaidullaev, 2002; Kazanseva, 1999). Thus, according to the studies, the prevalence of inbred marriages in separate regions in Uzbekistan is somewhere between 9.7 and 13.2% (Kazanseva, 1999). Genetic importance of inbreeding is in increasing amount of homozygote population, i.e. the seldom recessive genes in inbred environment can have a big influence than in panmixed population. The more rare this gene in population, the more the factor of inbreeding in NSHL disease manifestation (Dahl, 2006).

Complex factors including customs, high level of children’s birth rate and low migration rate contribute to increasing the number of endogamy marriages when a husband and wife are some relatives, even not so near. These processes lead to situation of inbred depression conditioned by increased frequency of homozygote people together with a decreased genetic variability was noted.

Kazanseva (1999), in her studies of kindred marriages’ influence on the health status of children, noted that inbreeding results the higher level of morbidity among posterities of in kindred marriages compared to children from unrelated marriages. According to the data of various authors, consanguineous marriages increase the number of prenatal and postnatal children’s mortality, increase the frequency of congenital diseases and abnormalities, lead to higher disease severity and prolong their duration, condition appearance of new clinical manifestations of the diseases (Kazanseva, 1999; Ubaidullaev, 2002).
The aim of our research work was to investigate the clinical condition of the hearing function in children with characteristically clinical signs of hearing disorders caused by mutation in gene Cx26 in order to determine subsequent treatment or rehabilitation tactics.

For the present time, investigations of the most authors are devoted to the problems of congenital predisposition to the different diseases. Having studied the problems of heredity and the role of blood relationship marriages in the development and duration of NSHL it was noted that in patients with heredity burden and especially in posterities of blood relationship marriages the disease has begun in the early periods of life, was rapidly progressing with having complications and not having the treatment effects.

The character of family accumulation for most diseases with congenital predisposition can be better explained with the additive effect of genetic and environmental factors, i.e. each disease represents its own genetic heterogenic pathology (Koehne, 2006).

During the investigation of congenital predisposition, two separate phases are clearly distinguished:

1. establishing the existing facts for congenital predisposition to any disease;
2. discovering the mechanisms of relationship between congenital and environmental factors in the development of the disease itself (Smith, 2000).

Review of the literature showed that the most important predisposing factor in the development of NSHL is heredity. However, many aspects of molecular genetics are still not clarified. There were absent the scientific works regarding to the study of the role of heredity in NSHL in children in the condition of panmixion and inbreeding.

Nowadays, the basic clinical criteria of changes in Cx26 are considered hearing disorders occurred from birth or before the child is able to speak (from birth to 3 years old), both with a recessive type of inheritance and predominance of significant hearing loss up to deafness (Smith, 2000; Dahl, 2006). In general, clinical manifestations can have a wide spectrum of signs: from deafness and severe neurosensory hearing loss (NSHL) down to hearing disorders with a more weak degree. The results of clinical and genetically works were noted a clear relationship between defined genotype and phenotype, i.e. between clinical signs (severity of hearing loss and the age of the beginning of the signs). It has been shown that phenotype depends on the changes on the gene level (Koehne, 2006; Dahl, 2006).

In Japan, in contrast to European countries and USA, the widely distributed mutation is inactivated mutation of 235 del C (Wiles, 2007). By the action character it conforms to mutation of 35 del G. Homozygote and compound heterozygote with the presence of mutations in most cases have very severe hearing disorders up to deafness. So that families of European and Asian background need to perform genetic screening in order to determine congenital hearing loss taking into account the data regarding the frequency of these mutations. According to the data of literature, combination of the presented deletion with other changes in gene Cx26 or other mutations can cause mild hearing disorders as well. This explains why in case of mild disorders the screening of the whole gene should be undertaken; checking for one single mutation according to the data of most investigations is not effective. The absence of hearing loss in relatives does not exclude congenital causes of hearing disorders. The presence of relatives with hearing disorders in most cases allows us to orientate correctly the relatives about the congenital character of the disease.

Testing methods allowed us to diagnose more accurately and earlier the reason for these hearing disorders. The absence of the connectional channels in the tissues of the inner ear due to the inactive mutations of the gene can cause these peripheral hearing disorders, so that in most cases of severe NSHL connected with gene Cx26 modifications cochlear implantation was indicated as remedy. Children with non-syndromal hearing loss with mutation in gene Cx26 were distinguished by the normal function of the brain and the perfect development of speech in the process of using indicated cochlear implant. While children with hearing loss with the absence of mutation in gene Cx26 belong to the more heterogenic disease group. The last ones can have the opposite influence to the development of speech. So, the molecular diagnosis is more important for the clinical diagnostic and for choosing methods of rehabilitation and treatment.
Severe non-syndromal NSHL is the direct indication for DNA-diagnostic of mutation of gene Cx26. For parents, who have children with moderate and mild degree of NSHL, DNA-diagnostics (genetic counseling) is recommended. In case of gene Cx26 mutation, testing of this gene is recommended for all family members. Consequently, during the obligatory medical and genetic consultation, we need to discuss the various prevention methods both for the family members and following generations.

References


