

Mutations in the Connexin 26 Gene among Bangladeshi with Nonsyndromic Hearing Impairment: A Pilot Project

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Introduction:

Mutations in the Connexin 26 (Cx26) gene are the most common known cause of hereditary hearing impairment (HHI). The frequency of this association and the specific mutations vary between different ethnic groups: 35delG being the most prevalent in Caucasians, 167delT in Ashkenazi Jews, and 235delC in Japanese populations. Overall carrier rates of in predominately Caucasians populations are estimated at approximately 3%, with 35delG accounting for over 85% of these mutations.

The hearing impaired population in Bangladesh has not previously been characterized, but is well suited for a study of Cx26 mutations for several reasons. The Bangladesh population gene pool is relatively isolated from neighboring populations because of religious and economic barriers and a cultural tolerance of consanguineous marriages contributes to a relatively isolated gene pool among affected individuals.

Hypothesis:

Mutations in Cx26 gene are involved in hereditary hearing loss among Bangladeshi with Nonsyndromic Hearing Impairment (NSHI) and the prevalence and type of these mutations will be dissimilar from our Midwestern population.

Methods:

After informed consent was obtained, persons with a history of bilateral hearing impairment underwent an otologic history, physical examination, air-conduction audiometry and phlebotomy for DNA isolation from peripheral lymphocytes. Cx26 coding region was amplified by PCR from DNA obtained from 57 patients from Cincinnati area referred to Center for Hearing and Deafness Research and 74 samples from Bangladesh. The amplified segments were then subjected to automatic sequencing and analyzed.

Results:

In our Midwest population, 17.5% (10/57) were homozygous for mutations in Cx26. All ten patients were Caucasian. The most common mutant allele is 35delG, allelic prevalence of 9.6% (11/114). Two novel mutation were identified that were not present in over 100 control chromosomes. 70% (7/10) of the Cx26-related deafness group had moderately-severe (>56 dB loss) or worse hearing thresholds, compared to only 44.7% (21/47) of the non-Cx26-related group. No disease causing Cx26 mutations were identified in Bangladesh population, although several polymorphisms were detected.

Conclusions & Significance:

The difference in prevalence of Cx26 mutations between our two study groups supports a founder effect hypothesis in Bangladesh. Alternatively, the differences in our study could be due to sampling error and therefore the results of this pilot study indicate the need for further study of the genetic factors of HHI in Bangladesh. Interestingly, our Midwestern population exhibits a lower Cx26 mutation rate than previously described and demonstrates novel deafness related sequence variants.