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Aminoglycoside antibiotics and hearing loss

Mutations in mitochondrial DNA (mtDNA) have been found to be associated with sensorineural hearing loss. As part of genetic screening program for hearing loss, we studied 40 patients with sensorineural deafness, whose cause might have been after aminoglycoside (ATB-AG), treatment. The affected and control subject's DNA fragments spanning the 12S rRNA gene or tRNASer(UCN) gene, that are associated with both aminoglycoside-induced and non-Syndromic hearing loss, were amplified and studied by PCR-RFLP. Three families have the homoplasmic 7444G> A mutation in the tRNAser (UCN) gene, the analysis of the mitochondrial genome in three family members did not detect any other pathology mutation. The clinical history shows one syndromic phenotype for matrilineal family. In the first family the muscle biopsy findings in the proband (III-5) and her mother (II-5), show in the electronic microscopy (EM) and in the light microscopy (LM) multiple mitochondrial abnormalities in the striated muscle. These findings have been correlated with the values from Citocromo Oxidase/Citrate Synthase ratio, which indicated poor activity of the Citocromo Oxidase. The matrilineal pedigree clinical feature, and the molecular, biochemical and morphological studies, might indicate that this is a novel syndromic presentation of the 7444G>A mutation in Córdoba - Argentina. In the fourth family, the report of the clinical, genetic, and molecular characterization in two of their members, revealed the variable phenotype of hearing impairment including audiometric configuration. Mutational analysis of the mtDNA in these pedigrees showed the presence of non syndromic homoplasmic 12S rRNA A827G mutation, which has been associated with hearing impairment. The A827G mutation is located at the A-site of mitochondrial 12S rRNA gene which is highly conserved in mammals. It is possible that the alteration of the tertiary or quaternary structure of this rRNA by the A827G mutation may lead to mitochondrial dysfunction, thereby playing a role in the pathogenesis of hearing loss and aminoglycoside hypersensitivity. Although the 827A> G mutation in the 12S rRNA, is associated with haplogroup B, its prevalence ≥ 2%, does not eliminate its participation and association to ototoxicity by ATB-AG. In addition, it is necessary to know more about the mechanism by which ATB-AG induces hearing loss, in the presence of the 7444 G>A mutation in the tRNAser (UNC).

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