VOLUME-4, ISSUE-6

MITOCHONDRIAL MUTATION m.1555A>G IN MT-RNR1 AS A PREDICTIVE BIOMARKER OF AMINOGLYCOSIDE-INDUCED SENSORINEURAL HEARING LOSS IN CHILDREN

Madrimova A.G. Tashkent State Medical University, Tashkent, Uzbekistan

Keywords: MT-RNR1, m.1555A>G, aminoglycoside ototoxicity, mitochondrial mutation, hearing loss prevention, neonatal screening

Background. The mitochondrial mutation m.1555A>G in the MT-RNR1 gene (encoding 12S rRNA) structurally remodels the mitochondrial ribosome to resemble its bacterial counterpart, conferring extreme sensitivity to aminoglycoside antibiotics. Even a single standard therapeutic course of gentamicin or amikacin may trigger irreversible bilateral profound deafness in carriers. Given the widespread use of aminoglycosides in neonatal intensive care, identification of at-risk patients prior to drug exposure is of critical clinical importance.

Objective. To determine the prevalence of the mitochondrial variant m.1555A>G in MT-RNR1 among children with NSSNHL and perinatal complications, and to assess its clinical significance as a predictive biomarker of drug-induced hearing impairment.

Materials and Methods. Sixty children with bilateral NSSNHL and documented perinatal pathology (hypoxic-ischemic encephalopathy, hyperbilirubinemia, prematurity) were examined. Molecular genetic analysis of the MT-RNR1 m.1555A>G variant was performed using allele-specific Real-Time PCR. Clinical and audiological data were analyzed in relation to history of aminoglycoside exposure.

Results. The m.1555A>G variant was detected in 5.0% (3/60) of children with perinatal-associated NSSNHL. All carriers had a documented history of aminoglycoside therapy in the neonatal period and presented with severe-to-profound bilateral hearing loss. The mutation was absent in children without prior aminoglycoside exposure, supporting a direct gene-drug interaction as the mechanism of cochlear damage.

Conclusion. The mitochondrial variant m.1555A>G in MT-RNR1 represents a clinically actionable predictive biomarker of aminoglycoside-induced irreversible hearing loss. Pre-treatment genotyping of neonates with perinatal complications is strongly recommended prior to initiation of aminoglycoside therapy. Integration of MT-RNR1 screening into neonatal protocols would enable timely substitution of ototoxic agents and prevention of permanent hearing impairment in genetically susceptible infants.