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86 - NONSYNDROMIC HEARING LOSS IN MORAVIAN PATIENTS: ONE FIFTH CARRYING BIALLELIC GJB2 GENE MUTATIONS, NO MUTATIONS IN SERPINB6, TMIE, COCH, ACTG1, KCNQ4 AND GJB3, VARIANTS WITH UNKNOWN PATHOGENICITY IN THE ESPN GENE

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GJB2 gene mutations are the most frequent cause of nonsyndromic hearing loss. There are many other genes less frequently causing this disorder. The aim of our study was to look for other genes mutated in Moravian population of patients with deafness. We have performed sequencing of *GJB2* coding region on ABI3130 and Δ(GJB6-D13S1830) detection using PCR and gel electrophoresis in 142 patients with nonsyndromic hearing loss. Biallelic pathogenic *GJB2* mutations were found in 31 patients (22%) thus explaining their hearing defect. In 9 patients (6%) only one pathogenic *GJB2* mutation was found. No patient carried Δ(GJB6-D13S1830). Sequencing of *SERPINB6, TMIE, COCH, ESPN, ACTG1, KCNQ4* and *GJB3 g*enes was performed on ABI3130 in 13, 13, 13, 30, 20, 14 and 30 patients without *GJB2* mutation, respectively. No pathogenic mutation was found in *SERPINB6, TMIE, COCH, ACTG1, KCNQ4* and *GJB3* genes. In *ESPN* gene, two variants with unknown pathogenicity were found in two unrelated patients: c.337C>T, p.Arg113Cys (Polyphen score 1.00) and c.1797_1808delCCCACCGCCGCC, p.Pro600_Pro603del. Both variants were inherited from parents without hearing loss. We cannot exclude big genomic deletion/duplication of *ESPN* gene on the other allele in the patients. There may also be bigenic mechanism of hearing loss pathogenesis. So far, however, we cannot conclude that these variants are causal in our patients. We are going to analyze *WHRN* gene encoding the whirlin protein, functionally associated with *ESPN* gene product espin.

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87 - ETIOLOGY OF CHILDHOOD SENSORINEURAL HEARING LOSS: THE IMPACT OF CONGENITAL CYTOMEGALOVIRUS INFECTION AND GJB2 GENE MUTATIONS

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Background: Childhood Sensorineural Hearing Loss (SNHL) is the most prevalent sensory disorder in developed countries. The main causes of deafness are viral infections, especially congenital Cytomegalovirus (cCMV), and genetic mutations, particularly GJB2 gene alterations. The early identification of these two factors in newborns allows for a prompt correction of hearing damage.

Aims: To estimate the impact of cCMV infection and GJB2 gene mutations in children with SNHL. Moreover, to describe deafness clinical aspects of children.

Methods: Ninety-six children with SNHL were analyzed for cCMV infection and for GJB2 gene mutations. Dried Blood Spot (DBS) specimens were used for CMV-DNA detection: CMV-DNA was extracted by thermal shock and amplified by nested PCR (CMV DBS-test). Blood samples were tested to investigate GJB2 gene alterations. Information regarding clinical characteristics of hearing loss (bilateral or unilateral deafness and severity of hearing damage) were retrieved for 94/96 children.

Results: cCMV infection and GJB2 gene mutations were identified in 17% and 44% of the patients respectively. In three cases both factors were present. 81% of CMV-positive children and 98% of children with GJB2 mutations had a bilateral hearing impairment ($p > 0.05$). Severe-profound hearing loss was in 88% and 85% of babies with cCMV infection and GJB2 mutations, respectively ($p > 0.05$).

Conclusions: cCMV infection and GJB2 mutations contribute here in more than half of SNHL. Hearing damage seems to be mainly bilateral and severe-profound in children with cCMV and with GJB2 mutations, but no statistically significant differences were found through these two factors. Because hearing loss at birth can adversely affect speech and language development, as well as social development, universal neonatal hearing screening associated with universal neonatal genetic and cCMV screening could be a feasible solution to early detect and correct hearing impairments.

88 - ATRIAL NATRIURETIC PEPTIDE REDUCES EXPRESSION OF THE A SUBUNIT OF THE EPITHELIAL SODIUM CHANNEL (ENAC) MRNA IN THE MOUSE STRIA VASCULARIS

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Atrial natriuretic peptide (ANP) has been demonstrated to be expressed extensively in the cochlea including the stria vascularis (StV). It was proposed that ANP may participate in the regulation of the water electrolyte balance. However, the functional significance of ANP in the cochlea is less understood and little is known about the exact mechanisms. Studies suggest that the epithelial sodium channel (ENaC) is important for regulating sodium transport across epithelia. ENaC may be involved in the clearance of endolymphatic Na^+ and maintenance of a K-rich and Na-poor composition in endolymph. Whether ANP has a regulatory effect on the Na^+ channel in the StV is still unknown. The objective of this study was to evaluate whether ANP affects the expression of the α subunit of the ENaC mRNA in the mouse StV using the real-time quantitative reverse transcription-polymerase chain reaction (RT-PCR) technique. The mouse StV tissues were incubated with 10^{-6}mol/L ANP for different times (2h, 6h, 12h, 24h and 48h), and thenharvested and α-ENaC mRNA was extracted for real time RT-PCR analysis of the mRNA expression of the α-ENaC. This study demonstrated the existence of α-ENaC in the mouse StV. Tissues treated with ANP (10^{-6}mol/L) showed a significant reduction in α-ENaC mRNA expression ($n=3$, $p<0.05$). A maximum effect was reached at 2h after treatment. Our results suggest that ANP may regulate cochlear ion transport and endolymph fluid balance in the inner ear via reducing expression of the α-ENaC mRNA in the mouse StV.

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