High Diagnostic Yield with Massive Parallel Sequencing in Swedish Patients with Prelingual, Moderate to Profound Sensorineural Hearing Loss

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Background

Genetic pathological variants are the main cause of sensorineural hearing loss (SNHL) in children and young adult and the genetic variation in Sweden has not previously been studied.

Aim

To describe the genetic variation in a Swedish SNHL population examined with massive parallel sequencing (MPS), describe the process of implementation, and identify the patient groups who would most benefit from genetic testing in terms of diagnostic yield.

Method

A prospective cohort study of 96 patients with mild (21-40 dB), moderate (41-60 dB), severe (61-80 dB) and profound (>80 dB) SNHL at Lund and Örebro University Hospitals, two tertiary referral centers for audiology in Sweden. MPS (n=85) on DNA from venous blood was analyzed with a gene panel with 179-201 genes (HearSeq version 4.0, 6.0, 7.0). The variants were classified according to American College of Medical Genetics and Genomic criteria.

Result

Forty-five patients received a genetic diagnosis, with variants in 26 different genes. Prelingual onset (<2 years) dominated in the genetic verified cases (82%). In moderate to severe SNHL with prelingual onset, the diagnostic yield was 64%. In mild hearing loss the diagnostic yield was 8% (1/12). Fifteen had syndromic hearing loss and 30 had isolated hearing loss and in all but 4 cases autosomal recessive inheritance pattern, whereof 26 homozygotes.

Discussion

The genetic causes for SNHL are heterogenic, and genetic testing was particularly useful for cases with syndromic or prelingual moderate to severe SNHL in terms of diagnostic yield.