

Prevalence, Mutation Spectrum and Cardiac Phenotype of the Jervell and Lange-Nielsen Syndrome in Sweden

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Objectives: To explore the prevalence, mutation spectrum and cardiac phenotype of the uncommon Jervell and Lange Nielsen Syndrome (JLNS) in Sweden.

Methods: We performed a national inventory of clinical cases. Genotype and geographical origin was investigated. Clinical data, including information regarding timing between medical treatment and/or interventions and cardiac events, was collected from medical records and a personal interview.

Results: 19 cases in 13 Swedish JLNS families were identified. The mutation spectrum consisted of eight KCNQ1 mutations, whereof p.R518X in 12/24 alleles. Geographic clustering of four mutations (20/24 alleles) and similarities to Norway's mutation spectrum were seen. A high prevalence of heterozygous mutation-carriers in the Swedish population was suggested.

Three pediatric cases on β -blockers since birth were as yet asymptomatic. Seven out of 16 symptomatic cases had suffered an aborted cardiac arrest and four had died suddenly. Differences between the sexes were apparent, with regards to age at debut (earlier for males) and frequency of cardiac events in adulthood (higher for females). QTc prolongation was significantly longer in symptomatic cases (mean 605 ± 62 ms vs. 518 ± 50 ms, $p=0.016$).

Relation between cardiac events and medical interventions; β -blocker therapy, including data on type and dosage ($n=15$), left cardiac sympathetic denervation (LCSD, $n=3$) and implantation of a cardioverter-defibrillator (ICD, $n=6$) was described and efficacy discussed.

Conclusion: A JLNS prevalence $>1:200\ 000$ in preadolescent Swedish children was revealed, and Scandinavian founder effects could explain 83% of the Swedish mutation spectrum.

Due to the severe cardiac phenotype, the importance of optimal β -blocker therapy and compliance, and consideration of ICD implantation in case of therapy failure is stressed.