SUMMARY
Long QT & Hearing Loss Prospective Study Registry

Sponsor
MEDNAX Center for Research, Education and Quality

Steering Committee
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Study type – Prospective Descriptive Study Registry
Multicenter study - Number of sites – approximately 20
Study enrollment goal – 600
300 with sensorineural hearing loss
15 with sensorineural hearing loss and long QT (maximum 300)
Site enrollment goal – 15 with sensorineural hearing loss (maximum 300)

Purpose
The purpose of this study is to determine the true incidence of Long QT amongst a large cohort of patients with unilateral (right/left) or bilateral hearing loss sensorineural hearing loss (SNHL).

Background
The first family with LQTS, described by Jervell and Lange-Nielsen in 1957 consisted of 4 Norwegian children with sensory deafness and prolonged QT. The affected children had multiple syncopal episodes and 3 died suddenly (ages 4, 5, 9). In all cases the cardiac abnormality was autosomal recessive and quite rare. Although less common than the Romano-Ward version of LQT, the deafness-autosomal recessive Jervell Lange-Nielsen (JLN) carries an exceptionally high risk of sudden cardiac death. KVLQT1 protein has been shown to join with minK protein to form IKsr channels. The sub-protein minK disrupts the production of inner ear endolymph leading to deafness. Since then, however, there have been individuals identified with KVLQT1 mutations with normal hearing. Although initial teaching and discovery was commensurate with bilateral sensorineural hearing loss there is an increasing though unknown linkage between unilateral sensorineural hearing loss and ECG evidence of QT prolongation. The Jervell and Lange Nielson syndrome is an infrequent form of LQTS in which prolonged QT interval and congenital deafness exist together. In evaluating children with congenital deafness, either as part of a baseline screening or at the time of cochlear implant, definitive QT prolongation has been identified in 7-18% of patients. In a more recent study from Great Ormond Street comparing ECGs in 52 children (mean 8.4 years) with bilateral sensorineural hearing loss to 63 normal children (mean age 10 years) both QT interval and QT dispersion were significantly longer in those with hearing loss. In addition, 15% had episodes of dizziness, which in the past may have been wrongly ascribed to a primary audiologic problem. JLN patients also tend to suffer very early life-threatening events in that 90% will become symptomatic in a short-period of time and sudden death occurs in >25% despite optimal medical therapy. In a larger study of 350 children with congenital deafness (ages 6-19 years), 0.6% had QT prolongation but of
tremendous concern was that a large majority had very alarming sycnopal, life-threatening events.\textsuperscript{21} However, in neither the data from Turkey or the UK was genetic testing performed in those with abnormal ECG to provide genotype affirmation in those with a positive phenotype but more importantly no genetic testing was performed in those with a normal phenotype. It is estimated that 30\% of patients with gene positive LQT mutations have a QTc that overlaps normal children.\textsuperscript{5, 22} Recent data has shown that patients with SNHL have a 14 fold higher incidence of heterozygous LQT (KCNQ1 and SCN5A) but not JLNS compound heterozygous or homozygous genetic mutation. (\textit{AHA Abstract}) As genetic testing has become more frequent an increase understanding of genotype-phenotype correlation has been used both for specific genotype treatment and risk stratification.

\textbf{Study Population}

\textbf{Inclusion Criteria}

1. All newborns who demonstrate a refer in one or both ears on a routine newborn hearing screen
2. Documentation of informed consent. Informed consent will be obtained by the principal investigator and/or designated research staff for each subject before enrollment
3. Normal Term Newborns (\textgeq 37 weeks)
4. Ability to perform ABR (auditory brainstem response screen technology) screening test
5. No major anomalies
6. Subjects’ parents willing to provide follow-up data on their child. They will need to provide telephone contact number(s) for the follow-up procedures

\textbf{Exclusion Criteria}

1. Newborns with a syndromic cause of hearing loss
2. Parents unwilling to provide follow-up data
3. Major congenital anomalies (i.e., hypoxic ischemic encephalopathy (HIE), persistent pulmonary hypertension neonate (PPHN), etc.)
4. Major medical problem or conditions
5. Congenital cytomegalovirus (CMV)

\textbf{Outcome Measures}

Finding of a QT or QTC interval of \textgreater 450 msec in an infant with sensorineural hearing loss.

\textbf{Follow-up}

Follow-up will be completed on all enrolled subjects. The parent(s) will need to provide contact information including telephone number(s) and cellular phone number(s), in order for the study team to contact them to obtain the follow-up information on their child. This will be completed at the time informed consent and authorization is obtained.
References