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EARLY DETECTION AND PREVENTION OF NEONATAL SUDDEN DEATH USING ECG AND MASSIVE ULTRASEQUENCING GENETIC ANALYSIS

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1. Summary

Long QT syndrome (LQTS) is an arrhythmogenic disease characterized by the presence of a prolonged QT interval on the electrocardiogram. LQTS is associated with sudden cardiac death in the young, and is one of the most important causes of sudden infant death syndrome (SIDS), death of a child in the first year of life, with a normal autopsy. LQTS is genetic so other family members could be carriers of the same pathogenic genetic variants and be at risk of sudden death. Early identification of these individuals is essential to adopt protective therapies and prevent sudden death. Thus, in order to prevent SIDS, in recent years there has been an important impulse by some experts in the scientific community towards the implantation of a program of screening newborns with an electrocardiogram for the detection of this ECG abnormality. However, not all agree and there is great controversy as to the clinical value and cost effectiveness of this approach. In order to shed some light on this subject we propose a broad analysis by performing electrocardiographic screening of the newborn to identify abnormal prolongation of the QT interval. This will be done prospectively and consecutively. The identification of a prolongation of the QT interval will be followed by family evaluation and screening and a comprehensive genetic analysis in the patient and relatives in order to identify a potential causal variant associated with the disease. The results of this work will provide us with an answer as to the value of neonatal ECG screening in the detection of this lethal disease, and the prevalence of the genetic disease. Finally, this work will lay the foundations for implementing mandatory electrocardiographic screening in the newborn.

2. Results obtained

A total of 396 newborns were included in our study. At least one electrocardiogram (ECG) was performed during the first 48 hours of life in each newborn. Globally, 46.80% of those assessed were males. We identified 24 neonates (6.06%) showing QTc>450ms and <470ms. All they normalized the QTc value during first 6 months of follow-up. Eight additional cases (2.02%) showed a QTc>470ms, not normalized in any of them during follow-up. The mother of one of these cases suffered previous miscarriages, and 3 cases showed a family history of sudden arrhythmogenic death. At least one rare variant as potential cause of long QT syndrome was identified in 5 cases

(62.5%). Family assessment identified 36.6% of relatives clinically affected and carrying the same familial genetic alteration identified in the respective newborn. In conclusion, our study identified 2.02% of infants showing a malignant QT interval associated with high risk of sudden death. Clinical assessment and genetic analysis of relatives allows early identification of family members at risk. Implementation of ECG assessment in routine pediatric protocols is a simple, non-invasive, and low-cost approach which helps to prevention of sudden death in neonates and their relatives.

3. Relevance to possible future implications

Arrhythmogenic diseases leading to sudden cardiac death are usually due to deleterious genetic alterations, being therefore inheritable. This means that other family members may carry the same genetic defect and consequently be at risk of malignant arrhythmia. Unfortunately the first manifestation of the disease may be sudden death so apparently healthy individuals may suffer a lethal episode without prior symptom. Implementing use of the ECG in protocols of neonatal assessment can early identify individuals at risk, and adopt personalized therapeutic measures to reduce the risk of malignant arrhythmia and even sudden death.

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