Researchers identify the genotype of disorders causing cardiac sudden death syndrome

Researchers from the Hospital Virgen de las Nieves of the University of Granada have identified the most frequent mutations in the gene KCNH2 in patients with long QT syndrome.

Long Qt syndrome is a disorder of cardiac ionic channels that approximately affects one in every 2,500 people and may cause torsade de pointes episodes, which can trigger sudden death. This condition usually affects children and adolescents, and it is occasionally mistaken for convulsions, leading to a misdiagnosis of epilepsy.

So far, hundreds of mutations have been found in twelve genes of sodium and potassium channels. Thus, approximately 75% of the mutations in cases of LQTS are located in three genes: KCNQ1, the most frequent in other sectors of the population (potassium channel), KCNH2 (potassium channel) and SCN5A (sodium channel).

To carry out this study, researchers selected nine patients who met the diagnostic criteria for long QT syndrome, and four patients with ventricular fibrillation (cardiac arrest produced in the absence of any identifiable causes). These patients and their first-degree relatives were examined in the Arrhythmia Assessment Unit of the Hospital Virgen de las Nieves in Granada, Spain.

Genetic Study

Mutations were found in seven patients with long QT syndrome and in two patients with idiopathic ventricular fibrillation. Overall, 71.4% of mutations were in the gene KCNH2 and 28.6% were in SCN5A. No mutations were found in the gene KCNQ1. Only two mutations had been previously observed.

In fact, one of these mutations was studied in vitro, and their involvement in the etiology of the disease was definitely proved, which is a major contribution to this field of research (see picture). This test was conducted with the collaboration of the Department of Pharmacology of the Universidad Complutense of Madrid.

Of the 19 relatives studied, six were carriers of the mutation. Unlike previous studies, the study conducted in Granada proved that genetic testing had a high level of sensitivity for the diagnosis of patients with long QT syndrome, and that the most frequently mutated gene was KCNQ1. These results differ from the results obtained in studies with other populations, where the most frequently mutated gene was KCNQ1.

This study -published in the *Revista Española de Cardiología*- was conducted by **Juan Jiménez Jáimez, Luis Tercedor Sánchez, Miguel Álvarez López, Ricardo Sebastián Galdeano** (Hospital Virgen de las Nieves), **Esther Martínez Espín** and **José Antonio Lorente Acosta** (Department of Legal Medicine and

Toxicology of the University of Granada). Genetic analysis was performed at the Laboratory of Genetic Analysis Lorgen in Granada PTS.

"What it is important about this study is that it proves that genetic testing can help in diagnosing LQTS in patients without any phenotypic expression, that is, in patients with normal results in electrocardiogram and medical imaging tests" –researchers state. "This increases the chances of detecting relatives who may be carriers of the same disease but who obtain inconclusive results in other tests, which represents an important breakthrough, since these genetic diseases can be hereditary".

Although the results obtained are of great significance, the researchers warn about the fact that "this study is just an initial experience in our country, and it only describes the genotypic profile of a small sample of patients. A multicenter study will be necessary to obtain larger groups and draw conclusions that can be extrapolated to the general population" –researchers state.

Source : University of Granada