ORIGINAL ARTICLE

The frequency of congenital long QT syndrome based on new formula in children with sensori-neural hearing loss

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Abstract

Introduction: Long QT syndrome (LQTS) is a repolarization cardiac disorder that can lead to syncope, cardiac arrest and sudden death in apparently healthy individuals. The congenital type can be accompanied with congenital sensory-neural deafness (Jervell-Lang-Nielsen syndrome). Although there are limited studies assessed the frequency of LQTS in these children in developed countries, regarding introducing the new formula, it is necessary to re-evaluate the frequency of this syndrome. **Materials and Methods:** This cross-sectional and descriptive study was done on 203 patients with congenital sensory-neural hearing loss (SNHL) that had cochlear implant surgery in Baqiyatallah cochlear implant center from 2008 to 2012. Corrected QT was calculated with this formula: QTC = QT + 1.75 (heart rate-60) Patients with QTC > 460 ms, were categorized in four groups: Long QT: QT > 460, Borderline: 440 < QTC ≤ 460, markedly long QT: QTC > 470 and very markedly: >500. Also, cardiac arrhythmias or arrest were evaluated in patients during cochlear implant surgery and in the postoperative recovery period. **Result:** Prevalence of LQTS in patients was 12.32% (25 patients). Prevalence of markedly long QT and very markedly long QT were 8.87% (18 patients) and 2.46% (5 patients) respectively. The prevalence of borderline group was 14.29% (29 patients). None of the patients during or after surgery were affected by cardiac arrhythmias or arrest. **Conclusion:** This study showed higher prevalence of LQTS in patients with SNHL than the normal population, and we suggest that all patients with congenital deafness should be screen for LQTS.

Keywords: Jervell-Lang-Nielsen Syndrome, Long QT syndrome, Sensory-neural hearing Loss

Introduction

Hearing loss is defined as a decrease in the ability to perceive sounds and considered among the most common congenital defects in newborns.[1] One per 750 babies born has a hearing loss.[2] In overall, there are about 125 million deaf persons in the world 100,000 people of whom live in Iran.[3] Studies have shown that 50% of deaf children have no known risk factor, and 20–30% of these infants are asymptomatic at birth.[4-7]

In studies, the incidence and prevalence of hearing impairments are as follows:

From each 1000 live births

- 1–2 infants suffer from bilateral moderate (30–50 dB), severe (50–70 dB), or quite severe (70 dB or more) sensory-neural hearing loss (SNHL)
- 0.5–1 infants have bilateral SNHL above 70 dB
- 1–2 infants have a milder or unilateral disorder.[8]

Usually patients with congenital SNHL, either hereditary or sporadic have no other disability (isolated defect).

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Nevertheless, there are over 70 recognized syndromes in which SNHL is associated with organ defects such as renal diseases, degenerative neurological disorders, mental retardation, metabolic abnormalities, etc.[9]

Among the most common and most important causes of hereditary congenital (or early) SNHL in humans, the following syndromes of Waardenburg syndrome, Pendred syndrome, Usher syndrome as well as more than 30 other genetic syndromes can be named.[10-12] In some of these symptoms such as Jevell and Lange-Nielson syndrome, which is an autosomal recessive disease associated with congenital cardiovascular heart disease (long QT), a clear association with certain heart disorders is seen. In addition to higher spontaneous mortality rate of deaf children concurrently with heart disease, the risks associated with general anesthesia in cochlear implants and other medical procedures indicate the importance of assessment of heart disorders in children with congenital SNHL. The long QT syndrome (LQTS) is an uncommon heart disease in the general population but a common one in genetic heart diseases. LQTS is seen in two congenital and acquired forms that the congenital type is a familial disorder, which can be associated with congenital SNHL and often undiagnosed.[13] Congenital LQTS belongs to cardiac repolarization abnormalities that may lead to syncope, cardiac arrest and sudden death in apparently healthy people.[14] These patients may also develop cardiac arrest during surgery under general anesthesia.[15]

Many formulas have already been suggested to correct the effect of heart rate (HR) on QT interval. Among the most commonly used formulas, the formula introduced by Bazett in 1920 can be noted. The modified QT is calculated as follows:

$$QTC = QT/\sqrt{RR}$$

In this formula, QT and RR are measured in seconds. Recently, a joint committee of the America Heart Association and American College of Cardiology suggested a new formula that provides a better correction on the effect of HR on the QTC:

QTC = QT + 1.75 (HR-60)

Where HR is the heart rate per minute and QT is calculated in terms of milliseconds. As mentioned above, the QT interval in different leads varies and is specifically longer on v2 and v3 leads. Thus, the v2 and v3 leads are better used to calculate the QTC.[16]

The frequency of this syndrome in deaf children has been evaluated in a number of studies, particularly in developed countries; however, given new formulas provided for QT correction and consequently the possible changes in the prevalence of disease, the reassessment of disease incidence in deaf children appears to be necessary.

Materials and Methods

In a cross-sectional study, all children with a definitive diagnosis of congenital SNHL, who had been undergone cochlear implant surgery in Cochlear Implant Center of Baqiyatallah Hospital between 2008 and 2012, were studied. The patients information were entered in a checklist set with different factors, including the child's name, case number, age and sex of the child, information necessary to calculate the QTC consisting of HR, QT (in milliseconds) and QTC, type of anesthetic medicine used for cochlear implant surgery, arrhythmia or cardiac arrest during surgery and in the recovery period after surgery. The files of 203 patients were studied. Electrocardiograms (ECGs) from 12 cardiac leads were assessed by a cardiologist. The QT intervals in the ECGs were measured in milliseconds, and the QTC was calculated by the following formula:

QTC = QT + 1.75 (HR-60)

The ECGs of patients with QTC equal to or >440 ms were reviewed by a cardiologist and their QTCs were recalculated. The patients with 440 <QTC ≤ 460 were placed in the borderline group while the patients with QTC > 460 were included in the LQTS group. Also, the patients with QTC > 470 were classified in the markedly LQTS group.

All data were saved and stored after collecting in the SPSS database software, Version 16 (SPSS Inc., Chicago, Illinois). Then, using statistic frequency program, the LQTS prevalence was determined. Also, the mean age of children, percentage of patients by sex, average HR in patients, the incidence of markedly LQTS in patients with LQTS and other partial targets were examined. The studied subjects received no intervention. The patients' files were reviewed only by the research team and other information of the patients remained confidential.

Results

A number of 203 patients with SNHL were studied in the Cochlear Implant Center of Baqiyatallah Hospital. The mean age of the children in this study was 42.6 months. The youngest patient in the study was a 7 months old infant and the maximum age was related to an 89 months old child. Among the patients, 48.28% were females (98 subjects) while 51.72% were male (105 subjects). The average HR of patients was equal to 126.3 in this study (the highest and lowest HR beats in patients were 200 and 50, respectively). The average QT in patients was 312.4 ms; the minimum and maximum QT was 220 was 680 ms, respectively.

The prevalence of LQTS (QTC > 460) in patients was equal to 12.32% (25 patients). Among the children examined, 14.29% were in the borderline group (440 < QTC ≤ 460) ($n = 29$). Also, 5 patients had QTC > 500 (2.46% of patients). From 25 patients with LQTS, 10 patients were female, and 15 patients were male.

From 29 children suffering from borderline QTC, 16 patients were female, and 13 were male [Figure 1].

Among the patients, 8.87% (n = 18) had markedly LQTS (QTC > 470). Also, 5 patients had QTC > 500. None of the patients had experienced cardiac complications during or after the surgery. As shown in Figure 2, the anesthetic drugs used in patients with LQTS, Nesdonal, Isoflurane and N_2O had been used more frequently (in 8 patients out of 25 patients with LQTS).

Discussion

This study showed that the prevalence of LQTS among children with congenital SNHL is more than the normal population, which is actually due to the presence of Jervell and Lange-Nielsen syndrome (JLNS) in these patients. In one of the previous studies, the prevalence of LQTS was reported as 0.21% among children with congenital deafness; however, in our study, the prevalence of LQTS in these patients was as 12%. The reason for this higher incidence may be due to the lower age of our study population compared with other studies. The mean age of patients examined in this study was 42.6 months, which is lower than other studies done in this area, and at a lower age, HR rate is higher. In addition, in other studies performed at older ages, the LQTS patients might have been excluded from the study population due to sudden death in younger ages. Moreover, unlike other studies on LQTS, Bazett's formula was used in our study. Instead, the following formula was used, which was proven in recent studies to be capable of correcting the impact of HR on QTC more than the Bazett's formula.[16]

QTC = QT + 1.75 (HR-60)

For example, in a study by Sathyamurthy *et al.* on assessment of LQTS among 127 children with congenital deafness, their ECGs were examined, and the QTC was calculated by Bazett's formula. The results showed that 10 children with 460 < QTC < 500, and 37 children with borderline QTC.[17]

In Matin study on LQTS in children with sensori-neural hearing impairment, 799 patients were participated that ECGs were examined for all of them, and the QTC was calculated using the Bazett's formula. Further studies identified two patients with LQTS syndrome JLNS.[18]

Also, in a study by Ocal *et al.* 350 patients with hearing loss, aging from 6 to 19 years, were initially evaluated with ECG regarding LQTS that according to Bazett formula, 8 patients had QTC > 440 ms. Further diagnostic evaluations, including repeated ECG (3 times), exercise test, echocardiography and Holter monitoring were performed for them. Finally, two girls aged 14 and 15 were diagnosed with LQTS.[19]

In our study, due to lack of repeated access to the patients, their ECG records available were only studied. However, in some studies, genetic analysis was conducted regarding LQTS and the patients' genotypes were studied regarding LQTS. For example, in a study, Schwartz *et al.* evaluated the prevalence of congenital LQTS in infants looked healthy. In this study, 59,644 infants aging from 15 to 25 days were participated, and their ECGs were analyzed, and their QTCs were calculated. In infants with QTC > 450, the ECG was repeated, and genetic analysis was also conducted, in which 7 LQTS genes were investigated. Among infants whose genotypes were studied, mutations in 12 out of 28 cases with QTC > 470 were found. Also, 4 cases of 14 infants with QTC between 461 and 470 had mutations associated with LQTS, and one baby despite clinical diagnosis of LQTS and QTC = 482, had a negative genotype. The genotypes of newborns' families were also evaluated with positive genotype that 51% of them had mutations responsible for the disease. Finally, 17 infants were diagnosed with LQTS patients indicating an incidence of 1 in 2534 healthy babies.[20]

In our study, among 25 patients with LQTS, 10 patients were female, and 15 were male. From 29 children suffering from borderline QTC, 16 patients were female, and 13 were male,

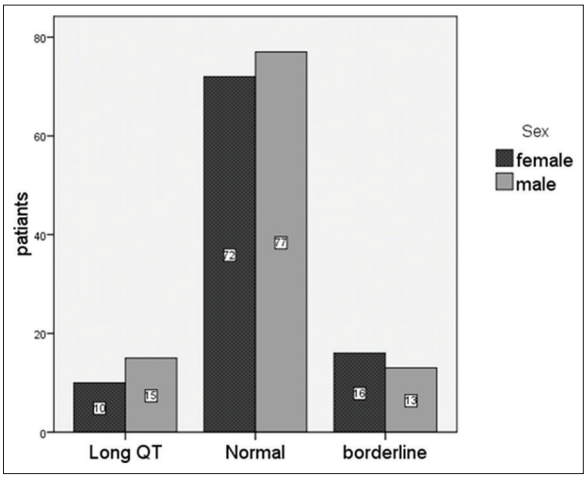

Figure 1: Patients with long QT and borderline QTC according to the gender

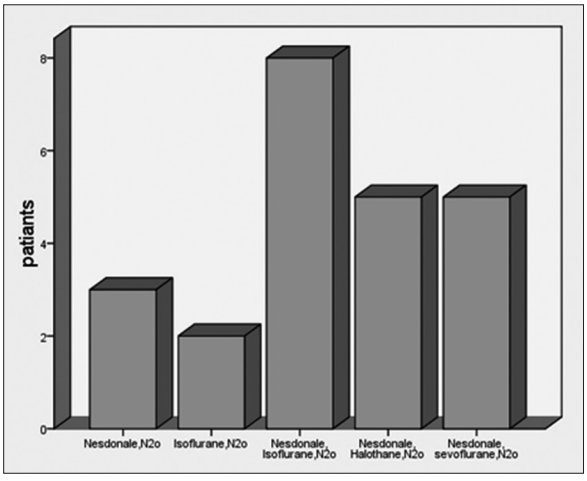

Figure 2: Anesthetics medications which were used in patients with long QT

which suggests the noninvolvement of gender in developing LQTS.

In addition, the types of anesthetic drugs used during surgery of cochlear implantation in patients with LQTS were extracted from the files existing in the hospital archive. Also, cardiac arrhythmias and cardiac arrest during surgery and in the recovery period after surgery were checked through anesthesia sheets in the files. Fortunately, none of the patients had intraoperative or postoperative cardiac complications.

The most anesthetic drugs used in patients were Nesdonale, Isoflurane, and N_2O. Unfortunately, cardiography during surgery or recovery period were not in the patients' records; as a result, it was not possible to examine the effects of anesthetic agents on QT. However, for an instance, Kweon *et al*. studied three 20-patient who undergone general anesthesia for laryngoscopy. In this study, 1 min before laryngoscopy, the first, second and third groups received saline, 0.5 μg/kg of remifentanil and 1 μg/kg of remifentanil, respectively. Significant prolongation of the QT interval immediately after intubation were seen ECGs of the first and second groups while no changes were seen in the third group compared to before intubation.[21]

Also, in a study by Lindgren 152 children who had undergone tonsils surgery and adenoidectomy were assessed. These children were anesthetized some by halothane and some by enflurane. Prolongation of the QT interval was significantly seen in the group anesthetized by enflurane. But no changes were seen in the halothane group.[22]

Conclusion

Given the higher prevalence of LQTS in patients with congenital SNHL in our study and the risk of cardiac arrest and sudden death in patients with LQTS with no previous symptoms, it is recommended that all patients diagnosed with congenital deafness will be screened for LQTS. Especially, in cochlear implant centers, the initial ECG should be taken from all patients candidates for cochlear implantation; since, cardiac arrest may occur during cochlear implant surgery, especially as some anesthetic drugs may cause prolongation of the QT duration. Thus, through early consultation with a pediatric cardiologist, the anesthetics used on the patient can be checked and ensured.

It is suggested to record the ECGs of patients with LQTS during anesthesia and surgery and the recovery period in a more complete and comprehensive study so that the exact value of QT and the effects of anesthetic drugs on QT can be compared. However, in our study, the ECGs of children during anesthesia and recovery period had not been recorded, and cardiac monitoring was done by the anesthesiologist during surgery and afterward, based on which the absence of arrhythmias or cardiac arrest had been was recorded in patients' medical records.

Given that the arrhythmias in these patients occur more often by auditory stimuli or sudden startling,[23] further investigations including repeated ECG and other provocative tests (exercise testing, etc.) are better to be done for patients with Borderline QTC. It is suggested to evaluate the genotypes of these patients with QTC > 460 regarding mutations associated with LQTS in the future. In addition, according the hereditary nature of LQTS and considering that the patients are sometimes without symptoms for years, it is better to screen their families regarding LQTS through taking ECGs.

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