Prevalence of Idiopathic Long QT Syndrome in Congenital Sensori-Neural Hearing Loss Students of Songkhla School for the Deaf

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Abstract

Objectives : To survey the prevalence of the long QT syndrome (LQTS), especially Jervell-Lange-Nielsen syndrome (JLNS), in Thai children (The first such study).

Background : LQTS is a rare inherited disease with a prevalence of 0.21 per cent in children with congenital deafness from other reports. These patients carry a high risk of recurrent syncope and fatal ventricular arrhythmia.

Study design : Cross-sectional survey from January 2000 to August 2000.

Method : A total of 276 children with congenital sensori-neural hearing loss were included. A questionnaire was employed and all children were examined by a pediatric cardiologist to rule out organic heart disease. EKGs were obtained and QTc intervals were blindly measured using standard methods in L2, V5 or any other leads with the longest QTc interval by three pediatric cardiologists. If QTc interval is prolonged, additional EKG (up to 3) were done to confirm the finding. Schwartz criteria was used to identify index cases with LQTS after repeated EKGs, and exercise stress tests. Also, echo-cardiography were done in patients suspected of having LQTS.

Results : A total of 14 children needed a third EKG and more work ups due to persistent long QTc interval after 2 consecutive EKG studies with QTc intervals ranged from 456 msec to 466 msec, and Schwartz score from 1.5 to 2.5. There were 6 twins and no triplets in the study. Finally, two subjects (not twins or siblings) had persistent prolonged QTc intervals after 3 EKG studies. After the exercise stress test, both still had a prolonged QTc interval, not corrected to the normal QTc interval even at the exercise peak. There was no cardiac abnormality either structurally or functionally from the 2D echo-cardiogram and Doppler color flow study.

Conclusion : The possible prevalence of JLNS was 0.7 per cent (2/276). Both children were in the low-risk group for having LQTS.

Key word : Long QT Syndrome, Congenital Sensori-neural Hearing Loss Children, Jervell-Lange-Nielsen Syndrome

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The long QT syndromes (LQTSs) are inherited or acquired disorders of repolarization characterized by prolongation of corrected QT interval (QTc) above 460 to 480 milliseconds, relative bradycardia, and T-wave abnormalities[1]. The LQTSs are associated with recurrent attacks of syncope, malignant ventricular dysrhythmias, and sudden cardiac death. The syndrome may be familial or idiopathic, with or without congenital deafness. The uncommon autosomal recessive form of the LQTS with congenital deafness (Jervell-Lange-Nielsen syndrome), along with the more common autosomal dominant form with normal hearing (Romano-Ward syndrome), are associated with sudden cardiac death[2,3].

The Jervell-Lange-Nielsen syndrome (JLNS) is a relatively uncommon inherited form of LQTS with a prevalence of 1 in 1,600,000 in the general population and 0.21 per cent in the deaf population[4,5]. It was first described in 1957 by Jervell and Lange-Nielsen[3] in a Norwegian family in which 4 of the 6 children were affected by both LQT and congenital sensori-neural deafness but the parents appeared normal. Three of the affected children died suddenly at the ages of 9, 5 and 4 years. Clinically, patients with JLNS usually have longer QT intervals compared to individuals with Romano-Ward syndrome and the disease also has a more malignant course. The genes associated with JLNS are the KVLQT1 gene (K^+ channel genes) on chromosome 11p15.5, and minK on chromosome 21 q 22.

The QTc intervals remain prolonged with exercise in LQT1 patients in contrast to LQT 2 and LQT3 patients in whom the QTc intervals normalize with exercise. These facts help explain why up to 66 per cent of the LQT1 patients had cardiac events during exercise[6].

The prevalence of JLNS in Thailand has never been studied, especially in students of a school for the deaf. This study is the first to examine the prevalence of this syndrome in a high risk population in southern Thailand.

PATIENTS AND METHOD

This study was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University. After the consent forms were signed by the legal guardians, two hundred and seventy-six congenital sensori-neural hearing loss-students (140 girls and 136 boys, age 5-25 years, mean age 13 ± 4 years) from a total of 323 students at the Songkhla School for the Deaf, Hat Yai, Songkhla, Thailand were studied from January,2000 to August, 2000. The other students (24 girls and 23 boys, age 7-25 years, mean age 13 ± 5 years), who had other known causes of hearing loss or acquired causes of hearing loss, served as the control group. After obtaining their medical history from medical records, each subject was examined thoroughly and findings were recorded. None of the subjects at the school had known heart diseases, or

conduction disorders, and none were receiving medications that would affect repolarization.

All subjects had standard 12-lead electrocardiograms recorded with a paper speed of 25 mm per second and standardization of 1 mV as standard recording. Two cardiologists (S.S. and A.K.) read all EKGs blindly. The QT and QTc (calculated by Bazett's formula) intervals were evaluated in all lead II, V5, and other leads which had the clearest QT and RR interval to be measured. QT intervals were measured from the beginning of the QRS complex to the end of T-wave to baseline, excluding U-wave. Three consecutive QT and RR intervals were measured in the above mentioned leads and the averaged QTc intervals for lead II and V5 were calculated. If one or both of an average QTc interval was/were above 440 msec (0.44 second), a second standard 12-lead electrocardiogram was done, and so on for the third standard 12-lead electrocardiogram. To determine the interobserver variation, the authors had three pediatric cardiologists (S.S., A.K., and P.S.) interpret 30 EKGs blindly (half of the EKGs with a prolonged QTc interval and another half with a normal QTc interval) on the same EKG lead and beats.

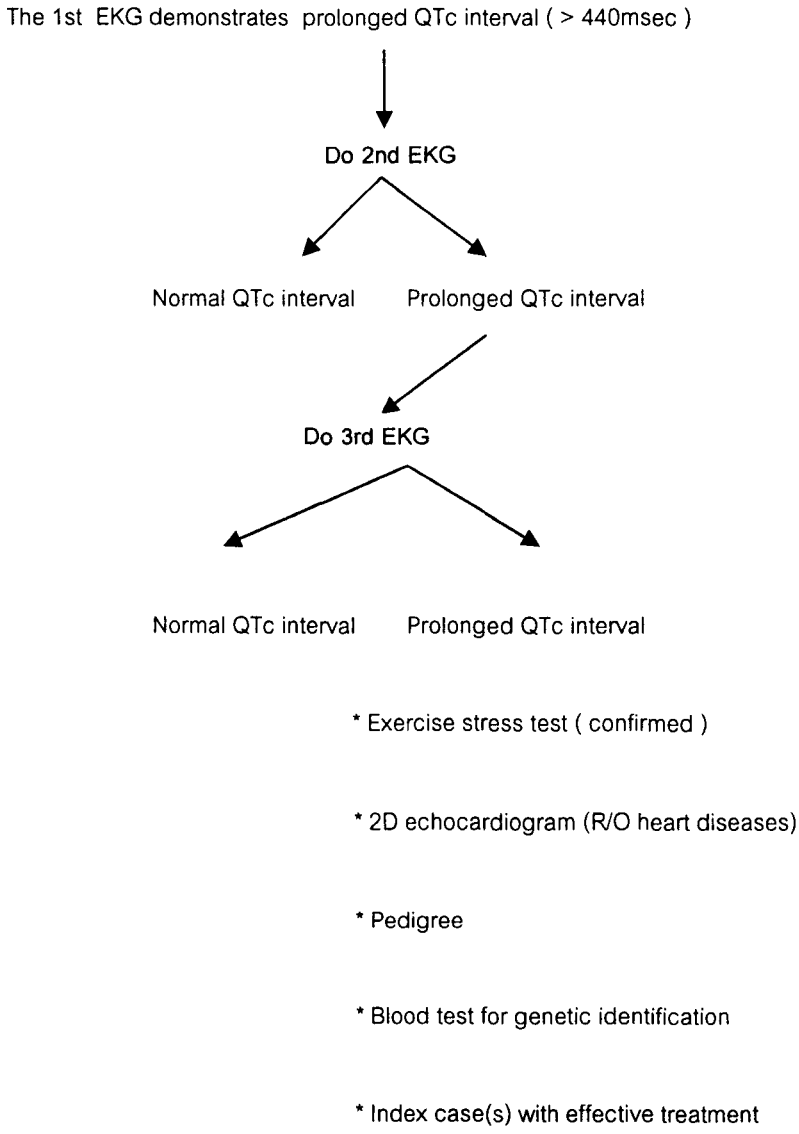

Fig. 1. Summary of the study design.

The students who had a prolonged QTc interval (> 440 msec) for all 3 EKG studies underwent 2D and M-mode echocardiography studies, an exercise stress test using a modified Bruce protocol on a treadmill and blood tests for chromosome study of LQT1, LQT2, LQT3, and minK. A summary diagram of the study design is shown in Fig. 1. To diagnose new cases of LQTS, the authors used the new diagnostic criteria of Schwartz[7].

Statistical analysis

The data were recorded using Microsoft Access and QTc interval was calculated using Microsoft Excel in Microsoft Office 97. The STATA statistical program was used to analyze the interobserver variation. Differences of QTc interval between the congenital sensori-neural hearing loss-students and acquired hearing loss-students were assessed by unpaired student *t*-test.

RESULTS

The students were divided into two groups according to their hearing loss. Group 1 was comprised of children with congenital sensori-neural hearing loss, and in group 2 hearing loss was caused by rubella, post mumps parotitis, severe otitis media or history of prematurity (Table 1).

Group 1 had 6 twins, all of whom had a normal QTc interval. Six students (not twins) had a sibling or siblings with congenital sensori-neural hearing loss, 5 with one sibling and one with two siblings. None of these students had a prolonged QTc interval. There were no signs of congenital heart disease detected by physical examination in the students of Group 1. Innocent heart murmur was found in 14 students and venous hum was found in 3 students. First-degree atrioventricular block (AV) block was found in 5 students in Group 1 and 2 students in Group 2, all had a normal QTc interval. In Group 2, there were 4 rubella embryopathy-children with patent ductus arteriosus (PDA). All of them had successful PDA closure either by surgery or PDA coiling.

QTc measured by two out of three investigators (S.S. and A.P.) had a good correlation (r = 0.86); one investigator (P.S.) consistently measured all QT intervals slightly longer than the others.

After the first EKG studies for both groups, forty-two students had a prolonged QTc interval with a mean QTc interval of 455 ± 286 msec (range 440-499 msec). Fourteen out of these 42 students still had a prolonged QTc interval after the 2nd EKG study. Finally, after the 3rd EKG study was done at a different time, only two students had a prolonged QTc interval. For Group 2, there were 8 students with prolonged QTc intervals. The summary of these findings is shown in Fig. 2.

Table 1. Details of the causes of hearing loss in the students.

Cause of hearing loss	Number	%
Group 1. Idiopathic congenital sensori-neural hearing loss	276	85.5
Group 2. The others		
Rubella embryopathy	40	12.4
History of prematurity	4	1.2
History of severe otitis media	2	0.6
Post-mumps parotitis	1	0.3
Total	323	100

These 2 students with persistently prolonged QTc underwent an exercise stress test and repeated measurement the QTc interval at baseline, peak of exercise, immediately after exercise at 2nd, 5th, and 10th minute as shown in Table 2. Both students had prolonged QTc intervals which did not shorten with exercise. Interestingly, case 1 had a normal QTc interval immediately before exercise and longer QTc interval at peak of exercise and 5 minutes after exercise. The reason for the shorter QTc interval at the 3rd minute after exercise remained unclear. Two-dimensional and M-mode echocardiographic studies of these two students, which showed normal cardiac structure and function, and normal pericardium and great vessels.

DISCUSSION

Jervell-Lange-Nielsen syndrome is an infrequently occurring disorder with a prolonged QT interval and congenital sensori-neural hearing loss. The main clinical features, besides the occurrence of syncope/cardiac arrest in young individuals especially in association with stressful events, are several unusual EKG characteristics, including prolongation of the QT interval, episodes of T-wave alternans, low heart rate in relation to age, sinus pause unrelated to sinus arrhythmias, and notched or biphasic T-waves[2,8,9].

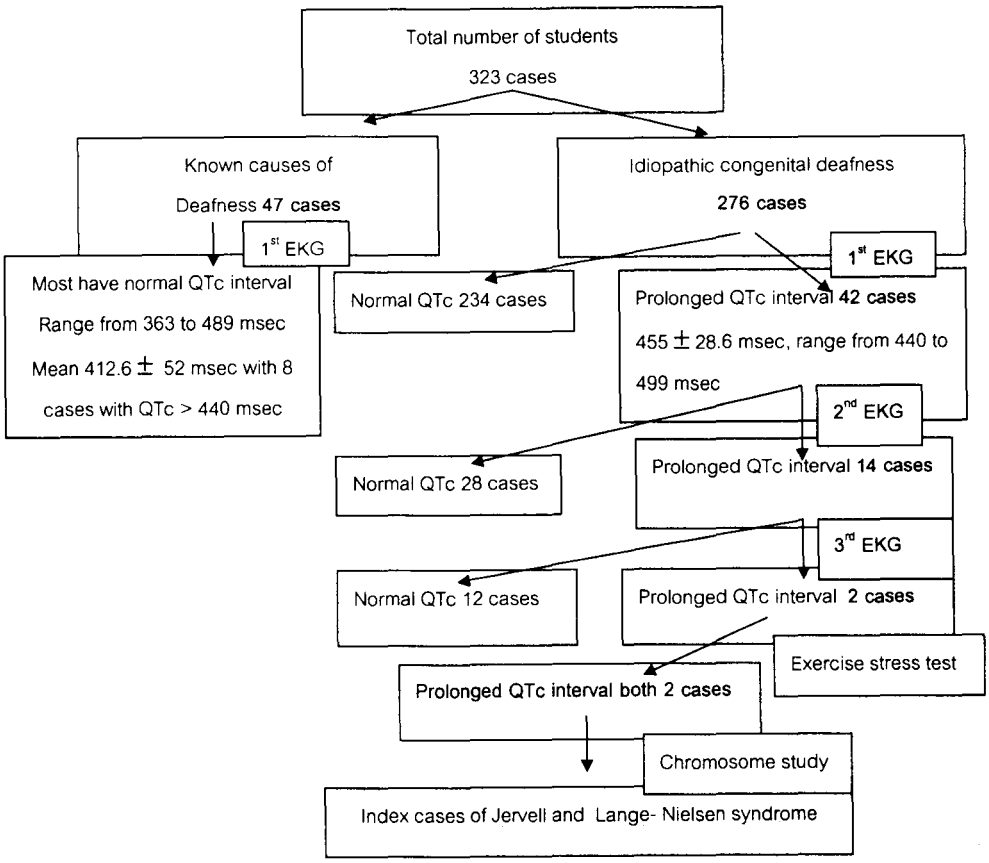

Fig. 2. Summary of the findings after EKG studies.

Table 2. QTc intervals measured before and after exercise.

Case number	Case 1	Case 2
Age (years	13	9
Sex	Female	Female
Mean QTc interval at 1st EKG (msec)	447	458
Mean QTc interval at 2nd EKG (msec)	462	446
Mean QTc interval at 3rd EKG (msec)	440	443
Immediately before exercise testing mean QTc interval (msec)	366	485
At peak of exercise, mean QTc interval (msec)	447	483
After exercise at 1st minute (msec)	415	465
After exercise at 3rd minute (msec)	380	476
After exercise at 5th minute (msec)	449	499
Schwartz score	2.5	1.5

The prevalence of JLNS has varied according to the investigators and study population, as shown in Table 3. In this study, after the 1st, 2ND, and 3rd EKG studies, only 42, 14 and 2 students respectively had a prolonged QT interval > 440 msec. As we know, the QT interval of LQTS may not be constantly pro-

Table 3. Other studies on the prevalence of JLNS.

Authors	Study population	Prevalence (%)
Ocal et al[10]	Deaf-mute school children	0.57 (2/350)
Hashiba[11]	Deaf population	0.3
Moss et al[12]	All LQTS patients (196 patients)	6
Komsuoglu et al[13]	Congenital deaf-mute population	1.2
Tuncer et al[14]	Deaf-mute school children	3.8
Present study	276 Deaf-mute school children	0.7 (2/276)

longed as shown in case 1 with a normal baseline QTc interval before exercise.

Linker et al[15], and Ambroggi et al[16], found large varieties of ST-T waveforms in LQTS, suggesting a high degree of dispersion of ventricular recovery time, which is an indicator for vulnerability to malignant ventricular arrhythmias. These variations in ST-T wave, however, are not related to the severity of symptoms, nor was it influenced by treatment with beta-blocking agents.

In this study, 2 cases of possible JLNS were identified (0.7%), which is comparable to previously reported prevalence of 0.3 per cent[11], and 1.2 per cent[14]. There were no family members with LQTS nor history of sudden cardiac death.

SUMMARY

Two deaf-mute students of Songkhla School for the Deaf were found with JLNS with Schwartz scores of 1.5 and 2.5. The prevalence of JLNS in Songkhla School for the Deaf was 0.7 per cent. As this is the first report from Thailand, we suggest further studies in all deaf-mute students of Schools for the Deaf throughout the Kingdom of Thailand to determine the prevalence and estimate the size of this health problem in Thailand.

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ความชุกของภาวะ Long QT ในเด็กนักเรียนโรงเรียนโสตศึกษา จังหวัดสงขลา

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ภาวะ idiopathic long QT syndrome พบได้น้อยในประชากรทั่วไป ภาวะ idiopathic long QT syndrome อาจพบร่วมกับ idiopathic congenital sensorineural hearing loss (Jervell–Lange–Nielsen syndrome) โดยพบ 2 รายจาก 1,000 ราย จากการศึกษาจากต่างประเทศ ผู้ป่วยจะมีความเสี่ยงต่อการเกิด จังหวะหัวใจเต้นผิดปกติ เป็นลมและถึงแก่กรรมในทันที ภาวะนี้ ยังไม่มีผู้ศึกษาในประเทศไทย คณะผู้วิจัยได้ทำการศึกษาความชุกของภาวะ Jervell–Lange–Nielsen syndrome (JLNS) ในเด็กนักเรียนโรงเรียนโสตศึกษา จังหวัดสงขลา โดยการตรวจร่างกาย ทำคลื่นไฟฟ้าหัวใจ (12 Lead EKG) วัด QT interval และคำนวณ corrected QT interval หากยังมี QT interval ที่ยาวกว่าปกติ จากการตรวจทั้ง 3 ครั้ง จะทำ exercise stress test และ 2D echocardiogram ให้การวินิจฉัย LQTS โดยใช้ Schwartz criteria ผลการศึกษา พบผู้ป่วยที่อาจเป็นภาวะ JLNS 2 รายจาก นักเรียน 276 ราย คิดเป็นความชุกร้อยละ 0.7 จึงควรมีการศึกษาเพิ่มเติมทั่วประเทศ เพื่อประเมินความชุก และขนาดของปัญหาของภาวะนี้ต่อไป

คำสำคัญ : ความชุก, เด็กหูหนวก, หัวใจเต้นผิดจังหวะ, ภาวะคิวทียาว, ประเทศไทย

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