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MAIN ARTICLE

Electrocardiogram screening of deaf children for long QT syndrome: are we following UK national guidelines?

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Abstract

Introduction: Jervell–Lange-Nielsen syndrome is characterised by congenital deafness and a long QT interval on electrocardiography.

Aim: (1) To survey UK national practice regarding electrocardiography screening of deaf children referred to cochlear implant centres, performed to evaluate for prolonged QT interval as recommended by national guidelines, and (2) to review local practice.

Methods: Data were collected via a questionnaire sent to all UK cochlear implant centres, and via review of the medical records of a local cochlear implant centre database.

Results: Eight (42 per cent) of the 19 cochlear implant centres surveyed performed electrocardiographic screening. Thirteen cases of long QT syndrome were reported in seven centres, with two related deaths. In our local cochlear implant centre, 14 (7.1 per cent) of 193 children had abnormal electrocardiograms; one definite long QT syndrome case and 13 borderline cases were identified.

Conclusion: Despite clear national guidelines for electrocardiographic screening of deaf children, there is wide variation in practice. Our local practice of performing investigations, including electrocardiography, during magnetic resonance imaging sedation has been very successful. Electrocardiograms should be reviewed by trained clinicians, and corrected QT intervals should be calculated manually.

Key words: Cochlear Implantation; Electrocardiography; Jervell–Lange Nielsen syndrome

Introduction

In the UK, the prevalence of confirmed permanent hearing impairment identified by universal neonatal hearing screening is approximately 1 in 1000 live births. This rises to 2 in every 1000 children aged nine to 16 years.[1,2] National guidelines have been developed by the British Association of Audiovestibular Physicians and the British Association of Paediatricians in Audiology, in order to guide the investigation of severe to profound permanent childhood hearing loss.[3] These guidelines have recently been updated to ensure a systematic approach to the evaluation of causes and associated conditions, and also to aid genetic counselling and to inform epidemiological research.

Investigations have been categorised into two levels. Level one investigations (Table I) should be performed on all children, while level two investigations should be considered when indicated from the history or clinical findings. One of the core investigations is electrocardiography (ECG), performed to evaluate for prolongation of the corrected QT interval, which is associated with Jervell–Lange-Nielsen syndrome. A corrected QT interval of more than 460 milliseconds in girls and 450 milliseconds in boys is considered abnormal; however, normal ranges for the corrected QT interval vary between hospitals.[3,4]

Jervell–Lange-Nielsen syndrome is a recessively inherited association between long QT interval and congenital deafness, and is characterised by a risk of syncope and sudden death due to a variety of polymorphic ventricular tachycardia. The population prevalence of Jervell–Lange-Nielsen syndrome is 1.6–6 per million births. This is thought to be an underestimate, because of the failure to make a diagnosis before sudden death.[5] The prevalence of this syndrome in deaf children has been found to average 0.21 per cent, with a range of 0–0.43 per cent.[6] Timely diagnosis in a child is likely to be life-saving, since long term studies have shown the untreated mortality to be in excess of 50 per cent.[5]

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TABLE I
LEVEL 1 AETIOLOGICAL INVESTIGATION FOR BILATERAL SEVERE TO PROFOUND PERMANENT HEARING LOSS IN CHILDREN: BAPA AND BAAP GUIDELINES[3]

1 Paediatric history
2 Clinical examination
3 Family audiograms (1st degree relatives)
4 Echocardiography
5 Ophthalmological assessment
6 Urine analysis*
7 Connexin 26 mutation testing
8 MRI of internal auditory meati or CT of petrous temporal bone

*For microscopic haematuria. BAPA = British Association of Paediatricians in Audiology; BAAP = British Association of Audiological Physicians; MRI = magnetic resonance imaging; CT = computed tomography

Previous studies of aetiological investigation of children with severe hearing loss have indicated a low compliance with ECG evaluation, despite recommendations.[7,8] The current study aimed (1) to survey UK practice regarding ECG screening of deaf children referred to cochlear implant centres, and (2) to review our local practice.

Methods

A questionnaire was sent to all paediatric cochlear implant centres to establish whether ECG screening was routinely performed, and if so who reviewed the ECGs, and also to identify cases of long QT syndrome and any related deaths. Non-respondents were followed up by telephone.

Locally, a retrospective review of medical notes was conducted for patients identified from the cochlear implant database, to establish the number of children with abnormal ECGs and to identify their outcome. In our cochlear implant centre, all deaf children had a blood test and an ECG performed during the sedation required for magnetic resonance imaging (MRI) scanning, as part of their initial assessment for cochlear implantation. All ECGs were read by a paediatrician with expertise in cardiology.

Results

Responses were obtained from all 19 paediatric cochlear implant centres, of which eight (42 per cent) routinely performed ECG screening of referred children. Where ECGs were performed, they were reported either by a paediatric cardiologist or a paediatrician with expertise in cardiology (three centres; 37.5 per cent), or by an ENT physician who made cardiology referrals where necessary (five centres, 62.5 per cent). Thirteen cases of long QT syndrome were reported from seven cochlear implant centres, with two known deaths.

In our local cochlear implant centre, 193 children were referred for cochlear implants over four years, 111 boys and 82 girls. These children had severe to profound deafness, defined as hearing only sounds louder than 90 dB HL at frequencies of 2 and 4 kHz. There were 190 children with congenital deafness and three with acquired hearing loss. A total of 135 (70 per cent) children underwent cochlear implantation, at a median age of three years (range, eight months to 16 years). Forty-seven (43 per cent) of 108 children tested had mutations of the connexin 26 gene.

In our local cohort, 14 (7.1 per cent) children had an abnormal corrected QT interval. Amongst these 14, one definite case of long QT syndrome and 13 borderline cases were identified. There were no deaths. A retrospective review of medical records showed that two of these 14 children were symptomatic, with recurrent 'fainting' episodes. One of these two children was diagnosed and treated for long QT syndrome, with nadolol. The other child's symptoms were attributed to a febrile illness, and subsequent ECGs and a 24-hour ECG strip recording were normal. All 13 borderline cases had a corrected QT interval of more than 450 milliseconds on screening; however, repeated ECGs at intervals of between one and three years were normal.

Discussion

Jervell–Lange-Nielsen syndrome is caused by homozygous or compound heterozygous mutations of the *KVLQT1* gene on chromosome 11 and the *KCNE1* gene (also called *ISK*) on chromosome 22. Most mutations reported in Jervell–Lange-Nielsen syndrome are nonsense or frameshift mutations which cause premature truncation of the encoded protein, which alters the function of potassium channels or prevents the assembly of normal channels. This leads to disruption of the flow of potassium ions in the inner ear and cardiac muscle, leading to hearing loss and irregular cardiac rhythm.[5,9,10] Any history of syncope or seizures precipitated by a 'fight, flight or fright' response in a deaf child should therefore raise suspicion of Jervell–Lange-Nielsen syndrome.

Genetic screening for Jervell–Lange-Nielsen syndrome is possible, particularly where there is a known mutation in families. Genetic testing of profoundly deaf children is already undertaken in the UK. In the present cohort, the incidence of connexin 26 gene mutation was comparable to other studies showing it accounts for 30–60 per cent of non-syndromic sensorineural hearing loss in the UK.[11] However, current testing techniques are too unsophisticated and costly to recommend routine genetic testing for Jervell–Lange-Nielsen syndrome at present.

Although Jervell–Lange-Nielsen syndrome is rare, the ECG is a simple, inexpensive and non-invasive investigation which can be the first indicator of serious underlying pathology. Our study found wide variation in UK practice, despite clear national guidelines for ECG screening in deaf children. In one centre, ECG screening was implemented following the deaths of two children related to long QT syndrome. In most cochlear implant centres, difficulties arise in organising the test, obtaining a good quality recording

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and finding the expertise to read the ECGs. Our local practice of performing investigations, including ECG and genetic blood tests, at the same time as MRI under sedation has been very successful.

Timely evaluation of the ECG is critical. Our findings suggest that most ECGs are currently reviewed by ENT clinicians. We recommend that ECGs should be reviewed by an experienced clinician who is familiar with long QT syndrome. We also recommend that the corrected QT interval should be calculated manually, as computer-generated diagnostic interpretations have an accuracy of only 50 per cent overall.[12] In our case of Jervell–Lange-Nielsen syndrome, the diagnosis was delayed for three years. In retrospect, a pre-operative ECG taken at the time of this patient's cochlear implantation showed a prolonged QT interval of 500 to 550 milliseconds. The diagnosis was confirmed and appropriate treatment initiated when the child became symptomatic and their original and current ECGs were reviewed by a paediatrician with cardiology expertise.

- **Jervell–Lange-Nielsen syndrome is a rare, recessively inherited association between long QT interval and congenital deafness**
- **This UK study found low levels of electrocardiogram evaluation of deaf children referred to cochlear implant centres, despite clear national guidelines**
- **Electrocardiograms should be reviewed by appropriately trained clinicians, and the QT interval should be calculated manually**

Children with Jervell–Lange-Nielsen syndrome undergoing cochlear implantation may face additional risks related to anaesthesia and surgery. An early diagnosis will improve operative safety. Special peri-operative precautions should be taken, including careful anaesthetic consideration, effective pain control, and minimising other triggers precipitated by emotion, exertion or loud noise.[5,13] A review of the literature identified four reports of cochlear implantation in a total of seven children with Jervell–Lange-Nielsen syndrome. Two of the cases were not diagnosed prior to surgery, but all the children had successful cochlear implantation.[13]

Conclusion

We conclude that timely diagnosis and management of Jervell–Lange-Nielsen syndrome in a deaf child is likely to be life-saving. Electrocardiogram screening, as recommended by national guidelines, should be performed for all deaf child with this diagnosis in mind, and a high index of clinical suspicion should be maintained especially in patients with a history of syncope. Electrocardiograms should be reviewed by appropriately trained clinicians, and the corrected QT interval must be calculated manually.

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