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Perioperative Anaesthetic management for Cochlear implantation in a child with Jervell and Lange-Nielsen syndrome with pacemaker in situ : A case report and review of literature

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Abstract : Jervell and Lange-Nielsen syndrome (JLNS) is a rare syndrome characterized by congenital profound bilateral sensorineural hearing loss and long QTc interval in ECG, usually greater than 500 msec. These patients are prone to episodes of "torsade de pointes" (TdP) ventricular tachycardia which may deteriorate to ventricular fibrillation leading to syncope or sudden death. Management of such a case perioperatively is challenging for an anesthesiologist because of the risk of life threatening arrhythmias and sudden death. Many drugs prolong the QTc interval and are considered torsaedogenic. There are no definitive guidelines on anesthetic management as the knowledge regarding use of some drugs is meager and controversial. We describe here a trigger less anesthetic management strategy for a 3 yr old girl with Jervell and Lange-Nielsen syndrome with pacemaker in situ who successfully underwent cochlear implantation. More research is required for some drugs especially in adequately beta blocked patients before being labeled torsaedogenic.

Key words : Jervell and Lange-Nielsen syndrome ; congenital sensorineural deafness ; Cochlear implant ; Anesthesia.

Introduction

Lange-Nielsen syndrome has also been called cardio-auditory syndrome of Jervell and Lange-Nielsen (JLNS) and surdo cardiac syndrome. It is a rare congenital disorder determined by familial autosomal recessive transmission (1). In Scandinavian countries, JLNS has a high prevalence of 1in 200000 (2). In the international Long QT Syndrome (LQTS) literature, the prevalence of JLNS in the congenitally deaf ranges from 0.57% to 6.5% (3). It is characterized by profound bilateral sensorineural hearing loss and long QTc, usually greater than 500 msec (4). Prolongation of QTc interval may be associated with episodes of torsade de pointes (TdP) ventricular tachycardia which may deteriorate to ventricular fibrillation leading to syncope or sudden death (1). Arrhythmias are a result of mutations in cardiac ion channels leading to impaired ventricular repolarization (4). The gene responsible is KCNQ1 in 80% cases (JLN Type 1) or KCNE1 in 20% cases (JLN type 2) (5). Deafness is due to dysfunctional potassium channel function in the cochlea (4). About 50% of young JLNS patients experience cardiac events by 3 years of age (6). The presenting symptoms are bilateral profound sensorineural hearing loss with recurrent episodes of syncope, cardiac arrest or seizure like episodes precipitated by stress, pain, exercise, fright or physical activity. The clinical features are due to intermittent episodes of TdP arrhythmia which cause abrupt decrease in cerebral blood flow. Ventricular tachyarrhythmia is characterized by 'Twisting of the points' which describes the typical sinusoidal twisting of the QRS axis around the isoelectric line of the ECG. Most of the sudden deaths occur when TdP deteriorates to ventricular fibrillation but the mechanism of this conversion is not known (4).

The measured QT interval is corrected for heart rate using Bazette's formula : $QTc = QT/\sqrt{RR}$ interval. The QTc is considered prolonged if it is more than 440 msec measured in lead II (4). Amongst all variants of LQTS, JLNS is the most severe one with an early onset and where beta-blockers may not be as efficacious. Hence they require more aggressive therapy (6). If diagnosed early the mortality of symptomatic patients decreases from 21% in the untreated group to 1% in the treated group (7). JLN type 1 is also associated with microcytic hypochromic anemia (1, 8).

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Case Report

A 3-year-old female, weighing 15 kg and having profound bilateral sensorineural hearing loss was planned for cochlear implantation. The child was born at full term by cesarean section due to fetal distress. She had delayed motor and language milestones. There was a history of recurrent episodes of transient loss of consciousness suggestive of arrhythmic syncope on crying and recovering in about a minute. At 1.5 yrs of age she was detected to have bilateral sensorineural hearing loss. Based on clinical findings she was diagnosed to be a case of Jervell and Lange- Nielsen syndrome (JLNS). Her parents were asymptomatic with no hearing impairment. Genetic testing was not done, so the subtype of JLNS that the patient was suffering from was not known. She was started on high doses of Tab. Propranolol but remained symptomatic. She underwent pacemaker implantation in the upper chest at 2.5 yrs of age and was continued on Tab. Propranolol 160 mg three times daily (TDS). She had iron deficiency anemia at that time and was started on iron supplementation. The anesthesia administered at the time of pacemaker implantation was not known as the discharge summary only mentioned that there were no complications. The pacemaker was set up in synchronous AAIR for daily life. There was no syncopal attack post pacemaker implantation. She was followed up in the Arrhythmia clinic and referred for cochlear implantation. Her preoperative hemogram, serum electrolytes, renal function and liver function tests were within normal limits. ECG showed QT interval to be 492 ms and QTc interval to be 572 ms, which was prolonged. According to the diagnostic criteria of Schwartz (4), the score was calculated to be 5.5. Definite LQTS is defined by a score > 4 (4). After explaining the anesthetic risks of this condition to the parents, consent for anesthesia and surgery was taken.

Anesthetic Management

The pacemaker was put on asynchronous mode-AAIR prior to surgery. Propranolol 200 mg was continued as per schedule. Antibiotics were given in the morning of surgery. Syrup Midazolam was given as premedication before bringing the child to the operation theatre. Her preoperative vitals were blood pressure of 100/60 mmHg, heart rate of 100/min and SpO2 of 100%. All standard monitors i.e. 5-lead ECG, SpO2, non invasive blood pressure, EtCO2 and temperature probe were attached. Neuromuscular monitoring was not done. A defibrillator and Magnesium sulphate were kept ready. Pediatric defibrillation pads were attached prophylactically, one on upper right side of the chest to the right of implanted pacemaker and the other to the apex of the heart. Two intravenous (IV) cannulas were placed. A 24G arterial cannula was placed in left radial artery for invasive blood pressure monitoring post induction.

A trigger less anesthetic management was planned with Total Intravenous Anesthesia (TIVA) using Target Controlled Infusion system (TCI). The patient was preoxygenated and induced with IV Fentanyl 2 μg/kg, Propofol 2 mg/kg and Vecuronium 0.1 mg/kg. Intubation was done with 5 mm internal diameter uncuffed endotracheal tube and connected to Penlon mechanical ventilator. Anesthesia was maintained with TIVA using TCI with Propofol 4 μg/ml as plasma target concentration. The Paedfusormodel of TCI was used for Propofol. Fentanyl was given as continuous infusion of 1 μg/kg/h using an infusion pump. Vecuronium 0.5 mg was given IV every 45 mins. No inhalational agents were used apart from oxygen and air. Dexamethasone 1.5 mg was given for postoperative nausea and vomiting (PONV) prophylaxis. Antibiotics i.e., Cefotaxime, Ampicillin-Cloxacillin, Metronidazole and Amikacin were given at the time of cochlear implantation for broad spectrum coverage to prevent infection leading to loss of the implant, acute otitis media and meningitis. The intraoperative heart rate was fixed at 100/min as the pacemaker was in the asynchronous mode-AAIR. Total anesthesia duration was 3 h and 45 min. The total blood loss was 100 ml. IV ringer acetate was used during the procedure. Intraoperative vitals were stable and the procedure was uneventful. Arterial blood gases and electrolytes were not checked intraoperatively. Local anesthetic infiltration was administered prior to skin incision with 3 ml of 1% Lignocaine without adrenaline. Reversal agents were not used at the end of surgery and patient's trachea was extubated once adequate tidal volume was attained. Patient was shifted to the post anesthesia care unit and given oxygen by facemask. All standard monitors i.e. SpO2, ECG and NIBP were attached. Hemoglobin, serum electrolytes levels and 12 lead ECG were advised. IV Paracetamol 15 mg/kg 6 hourly was given for postoperative analgesia and thereafter changed to syrup paracetamol. Postoperatively one dose of IV Propranolol was given. Patient was started orally after 6 h and oral Propranolol was resumed. Patient was then shifted to the ward after 6 h and further course in the hospital for 1 week was uneventful after which the patient was discharged home.

Discussion

Anesthesia in a case of JLNS is like walking a tightrope where both routinely used anesthetics and surgical stress can precipitate arrhythmias. We have to tread a path using anesthetics that offer optimum anesthesia with good surgical condition without precipitating any arrhythmias. Any drug that prolongs the QTc interval can precipitate TdP arrhythmia which may not respond to treatment and hence should be avoided. Torsaedogenic property of a drug can also be assessed by 'QT dispersion' (difference between the longest and the shortest QT interval) and the 'transmural dispersion of repolarization' (TDR) (time between the peak and the end of the T wave in a precordial lead) (9, 10). Currently there are no definitive guidelines on anesthetic management of congenital long QT syndrome (10). Effect of some drugs are summarized in Table 1.

Ventricular fibrillation and cardiac arrest has been reported following induction of anesthesia in a previously undiagnosed JLNS child (11). Therefore, systematic ECG and measurement of QTc in all deaf infants seems to be a safe precaution.

Hypothermia prolongs the QT interval, so core temperature needs to be monitored intraperatively. Magnesium sulphate is the treatment of choice of TdP arrhythmia, the initial bolus dose being 30 mg/kg given IV over 2-3 mins (which can be repeated every 15 mins if required) followed by infusion of 2-4 mg/min (4).

In a retrospective study of 114 anesthesia exposures in LQTS children by Nathan *et al*., 3 patients had adverse events during emergence from anesthesia including 1 patient who had TdP. All 3 were beta blocked patients who received volatile anesthetic during maintenance of anesthesia and received anticholinesterase-anticholinergic as well as antiemetic Ondansetron. One of the limitations of the study was that compliance to beta blocker therapy could not be ensured (17).

Table 1

Summary of some drugs affecting QT interval

Drug	Effect on QTc/TDR (If known)	Precautions / Comments
Volatile halogenated agents	Prolong QTc interval.	Not completely safe (4, 9).
Thiopental	Prolongs QTc interval.	Prevented by opioids and beta blockers (4, 9).
Propofol	No Effect on QTc interval or QTc dispersion, may reduce them and reverses QTc prolongation caused by sevoflurane. Some studies report QTc prolongation with propofol bolus (1.5 mg/kg) or as TCI (5μg/ml) but no significant effects on TDR were noted for 3-6 μg/ml TCI (4, 9).	Superior to Thiopental and Etomidate.[4,9]TIVA with Propofol should be used with caution,[5]especially in patients with JLN2 because it blocks the IKs channels. But the suppression was concentration dependent and the concentrations needed for IKs suppression are higher than what is presently used in the clinic (12).
Fentanyl	At 2 μg/kg does not increase QTc interval in non cardiac pathology patients and may even be protective during intubation. Decreased QTc interval in a patient with congenital LQTS.	Remifentanil infusion0.25μg/kg/min is the opioid of choice as it significantly decreases QTc duration, and also prevents post-intubation increase in QTc and is better than fentanyl (9).
Neuromuscular blocking agents	Only succinylcholine increases QTc duration.	Especially when used with thiopentone but not with methohexital or propofol (9).
Anticholinesterase-anticholinergic combinations	ProlongQTc interval. Impair the parasympathetic control of the heart rate which may cause unopposed cardiac sympathetic tone and hence increase the QTc interval (13).	Unopposed sympathetic tone can increase the QT interval which is supported by the in vitro prolongation of action potential duration by beta adrenergic stimulation (4).
Atropine and glycopyrrolate	Related to TdP and ventricular fibrillation (9).	But the statement is based on case reports on undiagnosed LQTS patients who were not on beta blocker therapy at the time of surgery (14, 15).
Sugammadex	Does not prolong QTc (9).	Used safely in LQTS (16).
Local anesthetics	No effect on QTc interval (9).	Avoid adrenaline additive to prevent QTc prolongation by adrenergic stimulation.
Droperidol, Ondansetron	Prolong QTc.	FDA black box warning.
Midazolam	No effect on QTc.	Beneficial as a premedication (4, 9).
Antibiotics	Macrolides, fluoroquinolones, pentamidine, amantadine, trimethoprim-sulfa, foscarnet and azole group of antifungals are considered torsaedogenic (10).	Up to date information on the safety of drugs in patients with a long QT can be found online at www.qtdrugs.com.
Inotropic agents and vasopressors	Dopamine, isoproterenol, dobutamine, epinephrine, norepinephrine, phenylephrine, ephedrine can also induce TdP (10).	Avoided.

Pacemaking function was reprogrammed to asynchronous mode as the patient was pacemaker dependent. Rate adaptive functions were suspended and bipolar electrocautery was used during the procedure according to ASA guidelines. Electromagnetic interference may continue to happen in spite of reprogramming pacemakers (18).

The arrhythmogenic potential of drugs is best evaluated by measuring the prolongation of TDR rather than simply measuring the QTc (19). But most data in the literature relate only to prolonging QTc. Moreover, as each long QT syndrome is caused by a different ion channel dysfunction, there could be genetic differences as well. Hence these recommendations may not be applicable to all patients with LQTS.

Long term Treatment of Long QT Syndrome

1. Beta blockers-They decrease mortality substantially but do not prevent cardiac events completely (4). Propranolol is the most widely used drug at a daily dose of 2-3 mg/kg. Nadolol also has been shown to be effective but Metoprolol is less effective (7).
2. Anti bradycardia pacing- Patients who develop severe bradycardia and patients who remain symptomatic despite adequate beta blockade require permanent pacing.
3. Implantable automatic cardioverter defibrillator (ICD)- Indications are (a) when syncope or TdP continue to occur despite beta blockade and pacing, (b) if the initial presentation was with a resuscitated cardiac arrest, or (c) if the QTc duration is more than 550-600 ms, where the risk of sudden death does not correlate with symptoms.
4. Left cervicothoracicsympathetic denervation (LCSD) for patients having syncopal attack despite full dose of beta blocker therapy, pacing and ICD therapy (4).

Conclusion

We were able to manage this case successfully with proper preoperative optimization because of the background knowledge of the Jervell and Lange Nielsen syndrome and about the drugs that may be torsaedogenic. All perioperative physicians should be aware of these drugs for safe management of these patients. Definitive recommendations on anesthetic management are not there in literature as the knowledge regarding use of some drugs is meagre, controversial and based on few contradictory case reports which may not be applicable to all patients with this syndrome. We suggest that more research is required for some drugs and on different variants of LQTS especially in adequately beta blocked patients before they are labeled as torsaedogenic and completely avoided.

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