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REVIEW ARTICLE

Perioperative management of hereditary arrhythmogenic syndromes

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Editor's key points

- Patients with inherited cardiac channel disorders are at high risk of severe perioperative arrhythmias.
- Agents used for treatment or to be avoided vary in the various syndromes and their subtypes.
- Understanding of the potential autonomic actions of anaesthetic agents on the different conditions is required.
- Preoperative optimization and preparation of the appropriate emergency drugs is essential.

Summary. Patients with inherited cardiac channel disorders are at high risk of perioperative lethal arrhythmias. Preoperative control of symptoms and a multidisciplinary approach are required for a well-planned management. Good haemodynamic monitoring, adequate anaesthesia and analgesia, perioperative maintenance of normocarbia, normothermia, and normovolaemia are important. In congenital long QT syndrome, torsades de pointes should be prevented with magnesium sulphate infusion and avoidance of drugs such as droperidol, succinylcholine, ketamine, and ondansetron. Propofol and epidural anaesthesia represent safe choices, while caution is needed with volatile agents. In Brugada syndrome, β-blockers, α-agonists, and cholinergic drugs should be avoided, while isoproterenol reverses the ECG changes. Propofol, thiopental, and volatiles have been used uneventfully. In congenital sick sinus syndrome, severe bradycardia resistant to atropine may require isoproterenol or epinephrine. Anaesthetics with vagolytic properties are preferable, while propofol and vecuronium should be given with caution due to risk of inducing bradyarrhythmias. Neuraxial anaesthesia should produce the least autonomic imbalance. Arrhythmogenic right ventricular dysplasia/cardiomyopathy induces ventricular tachyarrhythmias, which should be treated with β-blockers. Generally, β-adrenergic stimulation and catecholamine release should be avoided. Halothane and pancuronium are contraindicated, while large doses of local anaesthetics and epinephrine should be avoided in neuraxial blocks. In catecholaminergic polymorphic ventricular tachycardia, β-blocker treatment should be continued perioperatively. Catecholamine release and β-agonists, such as isoproterenol, should be avoided. Propofol and remifentanil are probably safe, while halothane and pancuronium are contraindicated. Regional anaesthesia, without epinephrine, is relatively safe. In suspicious cardiac deaths, postmortem examination and familial screening are recommended.

Keywords: anaesthesia; arrhythmogenic right ventricular dysplasia; Brugada syndrome; channelopathies; congenital long QT syndrome; congenital sick sinus syndrome; polymorphic catecholaminergic ventricular tachycardia

Hereditary arrhythmias comprise a heterogeneous group of cardiac channel disorders occurring in patients with apparently normal hearts.[1] Subtype 3 of congenital long QT syndrome (LQTS), Brugada syndrome, and congenital sick sinus syndrome (SSS) are associated with sodium channel dysfunction.[1] The cardiac ryanodine receptor-2/calcium release channel is involved in arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) and in catecholaminergic polymorphic ventricular tachycardia (CPVT).[1–3] The loss of function of L-type calcium channels is implicated in Brugada/short QT syndrome and potassium channel defects in subtypes of LQTS.[1] A phenotypic overlap and clinical combinations[1] of some channelopathies possibly indicate a relation or overlap between underlying genetic pathways and molecular mechanisms.

Inherited arrhythmogenic syndromes are underdiagnosed, as they may remain asymptomatic for a long time. Nevertheless, they represent the most common cause of sudden cardiac death in a young population.[1 3] Anaesthesia and surgery may unmask these syndromes, which usually present as life-threatening arrhythmias in patients with an unremarkable medical history.[4] A retrospective analysis of 1700 sudden cardiac deaths showed that 50 of them had occurred perioperatively, in young patients without a history of cardiac disease.[4] In the case of death due to a hereditary channelopathy, further investigation and familial genetic screening should be performed.[5]

The specific anaesthetic implications and prompt therapeutic interventions required in these cases make the perioperative management of these patients a challenge for the anaesthetist. This review analyses the clinical profile of hereditary arrhythmogenic syndromes and focuses on the anaesthetic management and perioperative care of patients with a diagnosed or suspected hereditary arrhythmia.

We conducted a PubMed® literature search for all types of published articles combining the free text and MeSH thesaurus terms: 'congenital long QT syndrome', 'Brugada syndrome', 'congenital sick sinus syndrome', 'arrhythmogenic right ventricular dysplasia', 'catecholaminergic polymorphic ventricular tachycardia', 'hereditary arrhythmias', 'inherited cardiac channelopathies', and 'inherited cardiac arrhythmias', with 'anaesthetic management', 'perioperative management', 'anaesthesia', 'general anaesthesia', 'epidural anaesthesia', or 'neuraxial anaesthesia'. A total of 248 articles, published up to November 2011, were retrieved; 114 of which were found to be relevant. There were no randomized prospective studies and the articles were mostly case reports, case series, and retrospective studies. Additional relevant studies were also sought by manual searching of the bibliographies found in the electronically identified articles. We also used articles that provided information on genetics, clinical features, diagnostic, and therapeutic approach of the syndromes. In total, 146 articles were found suitable to be included in the present review.

Congenital long QT syndrome

LQTS is a congenital (c-LQTS) or acquired disorder of cardiac ion channels characterized by heterogeneity of cellular repolarization and precipitation of tachyarrhythmias.[6 7] Jervell–Lange-Nielson and Romano-Ward syndromes were the first congenital LQT disorders described.[6 8] Six genotypes have been identified with six subgroups of c-LQTS (LQT1–LQT6), respectively.[8] The prevalence of c-LQTS is estimated to be <1:5000, even close to 1:2000–2500 in white infants.[9] The syndrome is characterized by autosomal-dominant transmission, while rarely the inheritance pattern may be autosomal-recessive, as in Jervell–Lange-Nielson syndrome.[6]

The subtypes of c-LQTS, as determined by genetic testing, are associated with different channel dysfunctions and variable clinical profiles. In c-LQT1 and c-LQT2, the potassium currents are affected, while c-LQT3 affects sodium channels.[1] Patients with c-LQT1 are prone to dysrhythmias after sympathetic activation such as exercise, while in patients with c-LQT2, dysrhythmias can be triggered by auditory stimuli, such as telephone ringing[10] or monitor alarm.[11] In contrast, patients with c-LQT3 are prone to cardiac events at rest or sleeping, due to polymorphic ventricular tachycardia (torsades des pointes) induced by bradyarrhythmias.[10]

The diagnosis of c-LQTS may be difficult, as 40% of genetically proven cases have no clinical symptoms when diagnosed and have a normal or borderline lengthened QT interval on their resting ECG.[8] As QT interval varies with heart rate, calculation of the corrected QT interval (QTc) is a more reliable marker. The ECG may be a useful diagnostic tool for c-LQT subcategory determination; in LQT1, T-waves are broad-based, with normal to high amplitude and indistinct onset; in LQT2, T-waves are usually bifid with low amplitude; while in LQT3, T-waves are peaked with late onset and ST segment is long.[12] A prolonged QTc (≥430 ms), suspicious clinical symptoms, and a family history of sudden death are specific characteristics of the syndrome. Affected individuals are at risk of developing torsades des pointes, which may be followed by ventricular fibrillation and sudden death.

Treatment of c-LQTS includes a permanent pacemaker and/or an implanted cardioverter-defibrillator (ICD) and left cardiac sympathetic denervation.[6 8 10] β-Blockers may be useful in patients with LQT1 and LQT2.[8 10] In patients with c-LQT3, sodium channel blockers are beneficial and β-blockade is contraindicated.[8 10] Left stellate ganglion block has been reported to shorten temporarily the QT interval in patients with Romano-Ward syndrome, and could possibly be considered in emergency cases.[13]

In patients with c-LQTS, reducing the risk of torsades des pointes is mandatory, as the haemodynamic compromise is severe, even though the episodes are usually short-lived and self-terminating. Magnesium sulphate (initial bolus dose of 30 mg kg^{-1}, followed by an infusion of 2–4 mg kg^{-1}) is the drug of choice for prevention and treatment of torsades des pointes.[6 14] Asynchronous defibrillation and cardiopulmonary resuscitation may be necessary if ventricular fibrillation occurs. A rapid and short-acting β-blocker, such as esmolol, should be considered in LQT1 and LQT2, while cardiac pacing may be beneficial in LQT3 patients.[12] Lidocaine 1.5 mg kg^{-1} i.v., with repeated doses of 0.5–0.75 mg kg^{-1} every 5 min up to a maximum dose of 3 mg kg^{-1}, may be useful.[15] Amiodarone should not be given as it prolongs the QT interval.[8]

Anaesthetic considerations

Since clinical and electrophysiological heterogeneity of c-LQTS render the effects of different drugs unpredictable, the available data are inconclusive.[7] Patients on β-blockers should continue their treatment perioperatively.[6] Preoperative preparation of the patient should be performed in a quiet and comfortable environment to avoid triggering torsades des pointes.[6] Midazolam and fentanyl have been used for anxiolysis without complications in adults[6 8] and children[16] with c-LQTS.

Several drugs that are commonly used perioperatively prolong the QT interval and should be avoided: droperidol, ondansetron, dolasetron, chlorpromazine, amiodarone, ephedrine, epinephrine, norepinephrine, dobutamine, dopamine, isoproterenol, phenylephrine, midodrine, diphenhydramine, oxytocin, and certain antibiotics. Among cardiovascular drugs, atropine, glycopyrronium, etilefrine, and metaraminol, have not been associated with QT prolongation and are not contraindicated in patients with c-LQT syndrome (www.QTdrugs.org, Arizona Center for Education and Research on Therapeutics). Perioperative infusion of magnesium sulphate (30 mg kg^{-1}) is recommended as a prophylaxis against torsades des pointes.[6] A defibrillator and transvenous pacing wires and leads should be ready for prompt use.[11 12]

Both general and neuraxial anaesthesia have been advocated in patients with c-LQTS (Table 1). Hypothermia should be avoided since it prolongs the QT interval, possibly