orphanaesthesia

Anaesthesia recommendations for

Brugada syndrome

Disease name: Brugada syndrome

ICD 10: I47.2

Synonyms: SUNDS - Sudden unexplained nocturnal death syndrome, Idiopathic ventricular fibrillation, Pokkuri (Japanese), Bangungut, Lai Tai (Philippines and Southeastern Asia)

Disease summary: Brugada syndrome is an arrhythmogenic cardiopathy defined both by the presence of ECG alterations at rest and by the occurrence of malignant tachyarrhythmias.

According to the electrocardiographic pattern in patients with Brugada syndrome, the type 1 or coved-type display concave elevation of ST segment ≥2 mm in the right precordial lead (V1-V3), followed by a negative T-wave recorded. The type 2 and 3, the saddle-back type, show a high initial augmentation of ST segment elevation of ≥0.5 mm, in one or more right precordial lead (V1-V3), followed by a convex ST segment and positive T-wave in V2.

Only the type 1 ECG pattern is definitive diagnostic of Brugada syndrome, the type 2 and 3 ECG patterns are suggestive but not diagnostic [53-54-55].

The prevalence of the disease ranges from 5–20 cases per 10,000 inhabitants worldwide and it is considered endemic in the South East Asia [56] where it is considered a major cause of sudden death among young males of Asian origin without cardiopathy background.

Although de novo mutations are possible, the syndrome shows an autosomal dominant inheritance with incomplete penetrance. Until now, over 500 mutations have been reported in 25 genes encoding for sodium, potassium or calcium channels, or proteins required for the function of such channels [57]. Thus far, only loss of function mutations in the gene encoding for cardiac sodium channel (SCN5A on chromosome 3p21-23) are certainly linked to the syndrome, but they are identified just in 25–30 % [57] of patients. Therefore, other ionic channel disturbances may have a role in the disease (e.g. calcium channel CACNA1c and CACNB2b alterations).

Clinical presentation includes syncope, typically occurring at rest or during sleep, and it is caused by fast polymorphic ventricular tachycardia; about 30 % of patients carrying the one of the SCN5A gene mutations, show Atrial Fibrillation (AF) with evidence of progressive cardiac conduction disease (PCCD) and prolonged atrioventricular and atrial-His conduction [57] and in some cases ventricular fibrillation may occur, leading to cardiac arrest and sudden death.

Average age of diagnosis is 40 years, and implantable cardioverter-defibrillator (ICD) is the only effective therapeutic option for symptomatic patients with spontaneous or pharmacologic-induced ECG pattern. Local anaesthetics (especially bupivacaine), as well as increased vagal tone, fever, inadequate analgesia and electrolyte imbalances, may trigger malignant arrhythmias in these patients.

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Typical surgery

Patients with a definitive diagnosis may turn to anaesthetists for insertion of an ICD just like unknown patients do for non-related surgery.

Type of anaesthesia

At present time, there is no definite recommendation neither for general nor for regional anaesthesia.

General anaesthesia can be performed safely, both as inhalational and as balanced with opiates. To date, the clinical effects of halogenated agents on the ECG and QTc interval are controversial. Several authors have reported variable patterns of QTc prolongation (or shortening) with almost every volatile anaesthetic available. This may raise safety concerns because of the patients' proarrhythmic condition. The body of evidence to recommend a specific agent is quite little and is based on seminal studies or case reports. However, in most of the cases, sevoflurane has been used with no intra-operative complications.

According to experimental animal models, propofol may affect cardiac calcium channel function, promoting the alterations of cardiac depolarisation underlying ST segment elevation in Brugada patients. While propofol boluses are considered safe, there are conflicting reports on the safety of propofol-based continuous infusions. Although some authors conducted propofol TIVA uneventfully, maintenance of general anaesthesia with propofol is recommended for the shortest period of time and with the lowest infusion rates as possible.

Propofol dose should not exceed 4 mg/kg/hour for long-term sedation. Arterial blood gases, serum lactate and creatine kinase should be monitored frequently if sedation is required for more than 48 hours [58].

The development of a Brugada-like ECG has been reported in the late phases of Propofol Infusion Syndrome (PRIS). Accordingly, it remains unclear whether PRIS and Brugada syndrome share a common pathophysiology. Propofol-based general anaesthesia should be performed carefully with coexisting sepsis, impaired microcirculation, increased endogenous or exogenous cathecolamine levels.

Therefore, general anaesthesia with propofol induction and sevoflurane maintenance is safe even in patients with high risk of Brugada syndrome [59].

Regional anaesthesia and neuroaxial blockade may be performed with caution. Since local anaesthetics affect myocardial sodium channels, their use may precipitate ECG alterations and cardiac arrhythmias.

On balance, the doses of local anaesthetic commonly used in neuro-axial anaesthesia and in peripheral nerve blocks, are associated with low plasma levels and their use is probably safe but the first option should be a short-acting drug (preferably lidocaine), and if long-acting anaesthetics are administered, ropivacaine or levobupivacaine are to be preferred [55].

Local anaesthetics with slow dissociation properties (e.g. bupivacaine) should be avoided as long as several complications have been reported, mainly when performing epidural infusions. Lidocaine is considered safe when combined with adrenaline and used in low dose. Rapid absorption into the systemic circulation and the use of large amounts of local anaesthetics should be avoided.

Whenever feasible, ultrasound-guided peripheral nerve blocks should be preferred over neuroaxial/central blockade. When needed, longer-lasting analgesia could be produced by repeated boluses through a continuous nerve catheter.

Necessary additional pre-operative testing (beside standard care)

Despite being very characteristic (ST segment elevation ≥ 2 mm, coved-type with no isoelectric tract and with negative T-wave from V1 to V3 precordial leads), Brugada-like ECG is not an exclusive feature of the syndrome, and other primary heart diseases underlying this pattern should be ruled out (e.g. ischaemic heart disease, myopericarditis, pulmonary embolism, aortic dissecting aneurysm, hyperkalaemia or hypercalcaemia, dystrophinopathies, left bundle brach block). Once these conditions have been excluded, all patients with diagnostic type 1 ECG pattern and/or personal history of syncope, dizziness, vertigo, nocturnal agonal respiration or seizures of unknown origin should be referred to a cardiologist for risk stratification.

As soon as a patient with Brugada syndrome is identified pre-operatively, first-degree relatives should be screened for the disease and integral genetic testing or type 1 Brugada syndrome testing (SCN5A) should be considered in the case of individuals with a strong clinical suspicion based on the medical history, family history and observed ECG phenotype. Genetic testing was not indicated in the context of an isolated type 2 or type 3 Brugada pattern on the ECG tracing [60].

In case a patient already has an ICD, the model should be noted, and further intra-operative management of the device should be performed under the supervision of a cardiologist/ electrophysiologist and the ICD should be turned off before surgery.

If no programmer is available, a magnet should be place above ICD pocket.

If the patient needs an urgency/emergency surgery, if there are no additional reasons, surgery should not be delayed for the only reason that patient is affected from Brugada syndrome [56].

Treatment with beta-blockers should be continued only if the benefits clearly outweigh the risk of severe intraoperative bradycardia, which can be exacerbated by interactions with anaesthetic agents.

Asymptomatic patients with an uncertain ECG pattern (ST segment elevation < 2 mm, either coved or saddle-back type) are at lower risk of arrhythmias, therefore any further particular cardiological/arrhytmologic assessment in not necessary and the patient can be subjected to the intervention only with proper precautions in elective surgery [56].

However, they should be asked if sudden death at a young age already occurred in their families and should subsequently be referred to a cardiologist.

Isoproterenol, as a first choice, and quinidine may be used in patients with ICD and multiple shocks [61], in cases with contraindication to ICD implantation and in children as a bridge to ICD or as an alternative to it. Careful monitoring of QTc should be performed, and QT-prolonging drugs should be avoided.

Particular preparation for airway management

Not reported.

Particular preparation for transfusion or administration of blood products

Not reported. Promptly correct calcaemia or kaliaemia imbalances following repeated transfusion, as they may provide a substrate for arrhythmia triggering.

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transportation and mobilisation

Ventricular tachycardia in Brugada syndrome usually occurs during periods of bradycardia and increased vagal tone. Anaesthetists should be careful during intra-operative position changes to avoid unintentional parasympathetic stimulation and reflexes.

Interactions of chronic disease and anaesthesia medications

Not reported.

Anaesthetic procedure

Since they have resulted in Brugada ECG patterns, droperidol and phenothiazines are recommended neither as sedative premedication nor as antiemetic prophylaxis.

Benzodiazepines have been used uneventfully as pre-operative premedication.

The choice of induction agent is not critical. Thiopental sodium has been used as induction agent with no problems reported. Despite a few reports of adverse events (ST segment elevation), propofol boluses as well as etomidate [62] are probably safe.

To date, ketamine has been reported to develop Brugada-like ECG in case of acute intoxication with far higher plasma levels than those reached in clinical practice.

Although it has been used for neuromuscular blockade at intubation, succinylcholine raises concerns about the risk of bradycardia and hyperkalaemia and it is not recommended. Non-depolarizing agents have been used without any reported complication.

Volatile anaesthetics may be used for induction or maintenance of anaesthesia, both in O_2-air and in O_2-N_2O mixture. In the majority of clinical reports, sevoflurane was the most common chosen agent.

Among cardiovasoactive drugs, alpha-receptor agonists (e.g. norepinephrine, methoxamine, phenylephrine) have been reported to worsen ST segment elevation or unmasking Brugada ECG pattern in affected patients. Clonidine and dexmedetomidine have raised concerns as well, as they may induce bradycardia.

On the contrary, α-receptor antagonists and β-receptor agonists decrease the ST segment elevations. Also β1- and β2-receptor agonistic activity of isoproterenol and dobutamine reduce ST segment elevation suppressing arrhythmic events in patients with Brugada syndrome, so this drugs could be used to treat electrical storm.

Ephedrine as well was used to treat intra-operative hypotension without complications in Brugada patients.

Vasopressors with dual alpha and beta agonist action as dopamine have unpredictable effects [56].

Class IC sodium channel blockers (e.g. flecainide, propafenone) and class III amiodarone are contraindicated, as they precipitate cardiac arrhythmias.

Intra-operatively, factors known to affect autonomic tone such as light/too deep anaesthesia and inadequate analgesia should be minimised.

Careful monitoring that includes continuous ECG recording, bispectral index (BIS), temperature, degree of neuromuscular block and arterial blood pressure, is essential.

Furthermore, Analgesia Nociception Index (ANI), may be useful for the analgesic management to prevent haemodynamic instability [55].

Bradycardia as a result of increased surgical stimulation should be avoided. Fever and hyperthermia are known to worsen ECG manifestations of Brugada syndrome, and they should be prevented, both during the surgical procedure and post-operatively.

Position change intra-operatively is important to avoid unintentional parasympathetic stimulation and reflexes.

Hyperkalaemia, hypokalaemia, hypercalcaemia and metabolic acidosis may induce electrical instability. Therefore, electrolyte homoeostasis should be pursued.

Neuromuscular blockade (NMB) antagonisation is a matter of debate. Neostigmine and pyridostigmine may increase parasympathetic drive and induce bradycardia. Furthermore, while some authors have used neostigmine without complications, some others report accidents at awakening and recommend NMB to wear off spontaneously. To date, avoiding cholinergic agents seems to be prudent, even though likelihood of complications is reduced by simultaneous administration of atropine or glycopirrolate. When using steroidal non-depolarising agents to achieve NMB, i.v. sugammadex would be the reversal agent of choice. Up to 4 mg/Kg sugammadex have been used with no ECG alterations reported.

Opioid use has not been associated with complications, short or ultra-short acting opioids are to be preferred, since they are rapidly cleared, particularly fentanyl.

In the post-operative period, morphine is the drug of choice, but tramadol, intravenous lidocaine, ketorolac, diclofenac and paracetamol have not been reported to cause complications [55].

Nausea and vomiting are concomitant with increased parasympathetic tone, and they should be prevented. Intravenous antiserotoninergic agents (ondansetron, granisetron) and dexamethasone are safe. Metoclopramide should be avoided because it may exert electrophysiological effects similar to those of class I antiarrhythmic agents [63].

It is recommended to avoid phenothiazine antipsychotics (trifluoperazine, thioridazine, perphenazine) [56].

Particular or additional monitoring

Standard monitoring should include: 5-lead ECG with continuous right precordial ST-tracing, pulse-oximetry and arterial cannulation. The last one allows the detection of a cardiac arrhythmia even in case of concomitant electrocautery disturbances. External defibrillation pads should be applied before starting anaesthesia. If already present, ICD should be turned off to prevent inappropriate discharge due to monopolar surgical diathermy. In pacemaker-dependent patients, the pacemaker/ICD should be switched to a non-sensing mode (VOO or DOO). Nonetheless, time spent in VOO or DOO should be limited to prevent a potential R-on-T phenomenon. The pacemaker/ICD should be turned on and reprogrammed soon after the end of the surgical procedure. The presence of a trained physician in the operating theatre is recommended. Defibrillation pads should remain on site until the time ICD is turned on again.

Body temperature monitoring is strongly recommended to avoid fever or hyperthermia. Furthermore, NMB monitoring is necessary for appropriate reversal or antagonisation at emergence from anaesthesia. To minimise autonomic imbalances due to inadequate anaesthesia and analgesia, some authors recommend BIS, Spectral Entropy and ANI monitoring [55] use to avoid an increase in parasympathetic tone associated to the condition of the deep anaesthesia or excessive analgesia.

Possible complications

ST segment elevation or increase, life-threatening arrhythmias such as rapid polymorphic VT and VF with cardiac arrest may develop as a consequence of bradycardia, hyperthermia, hyperkalaemia, neuro-mediated surgical reflexes, vomiting, interaction between the above mentioned drugs, or as a combination of them all. Notice that arrhythmias are more likely under these conditions, but they may occur even in their absence. Where persistent ST-segment elevation or worsening of an already elevated ST-segment are observed, low-rate isoproterenol (1-2 µg as an intra venous bolus, followed by continuous infusion of 0.15-2.0 µg/min) has been reported to be effective in restoring the previous ECG, in addiction to cardioversion and cardiopulmonary resuscitation [64].

Post-operative care

As for any other procedure, the degree of post-operative assistance and monitoring depends on the specific surgical procedure, on intra-operative complications and pre-operative conditions of the patient. ICU admission is not mandatory. However, post-operative monitoring of every patient (including those with an ICD) should include continuous ECG tracing for at least 24–36 hours. Thus, a short stay in a cardiology ward or a coronary care unit has been suggested by some authors.

Disease-related acute problems and effect on anaesthesia and recovery

Emergency situations caused by the illness have been described previously.

Ambulatory anaesthesia

Ambulatory anaesthesia is recommended only for low-risk surgery and in case potentially arrhythmogenic drugs have not been administered.

Obstetrical anaesthesia

Brugada syndrome is 8 times more frequent among young males than in females. Thus, few data about anaesthesia practice in the obstetrical field are available. Spontaneous delivery seems to be safe in patients with Brugada syndrome. Opioids may be used with confidence, both for intrathecal administration and for epidural infusion. Bupivacaine and ropivacaine should be avoided whenever possible. Nonetheless, subarachnoid use of 0,5 % bupivacaine for Caesarean section with no complications has been described. When large amounts of local anaesthetic are requested, due to the risk of systemic absorption, bupivacaine and ropivacaine epidural infusions should rather be avoided. In this case, lidocaine (with or without opioids) would be the drug of choice. While ergonovine alkaloids as uterotonic agents are not recommended, oxytocin use is considered safe. Intra-operative hypotension should be managed by i.v. fluid administration and ephedrine, although phenylephrine has been used without complications, too.

Children anaesthesia

All precautions taken in adults can be extrapolated to children. A particularly important measure is strict control of fever, which has been seen to be a clear inducer of arrhythmias [55].

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