Pacemaker and arrhythmias in pediatric patients. An update

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Keypoints

It is highly technical to implant a cardioverter-defibrillator transvenously in pediatric patients due to their structural anomaly, small size and age. In this article we suggest some points to improve anesthetic management.

Abstract

Arrhythmias in children are the enemy of any medical emergency. Different mechanisms should be very dangerous in particular for its adaptation mechanisms. Tachyarrhythmias (extrasistols, supraventricular tachycardia SVT, permanent junctional reciprocating tachycardia, atrial flutter, supraventricular tachycardias, ventricular tachycardias).

Bradyarrhythmias (atrioventricular blocks) and channelopathies are the most common forms of arrhythmias in pediatric population. Most of these changes requires a pharmacological treatment but in some cases requires the implantation of the pacemaker (PMK) or implantable cardioverter-defibrillator (ICD). The perioperative anesthetic management requires specific care.

Keywords: arrhythmias, pediatric anesthesia, implantable cardioverter- defibrillator

Introduction

A pacemaker or an implantable cardioverterdefibrillator (ICD) is recommended in pediatric patients patients with a positive ventricular stimulation in the electrophysiology study. However, it is sometimes highly technical to implant a cardioverter-defibrillator transvenously in these patients due to their structural anomaly and small size of these patients. These patients are usually very sick, have multiple comorbidities and have history of myocardial infarction, ventricular tachycardia and ventricular fibrillation. They may not be able to remain in supine position for a long period of time and it's important assure a good sedation. In this article, we suggest some points to improve anesthetic management of this young patients.¹⁻⁵

PACC

Arrhytmias in children

Tachyarrhythmias

Extrasystoles

Supraventricular ectopic beats are beats premature that originate from the atria and the junction atrioventricular. More detailed diagnosis, including cardiac examination, standard ECG, 24h ECG recording (Holter) and echocardiography Doppler, are necessary.

The ventricular ectopic beats originating from the ventricles and in the conduction system downstream of the bifurcation His bundle. They come in isolated form or repetitive monomorphic or polymorphic.

The ventricular ectopic beats are often diagnosed occasionally. They are usually idiopathic and sometime associated with congenital heart disease or acquired. It is important to exclude the presence of a structural cardiopatia or arrhythmic forms more complex. Supraventricular and ventricular ectopic beats, also in pairs and triplets, are generally a clinical arrhythmia climate irrelevant in which no therapy is indicated. Therefore, it is recommended in children and instrumental control (visit and ECG) every 3-6 months of age until a year.

Paroxysmal supraventricular tachycardia (paroxysmal SVT)

Paroxysmal supraventricular tachycardia (paroxysmal SVT) reentry arrhythmia is the most common. The atrioventricular reentry through an accessory pathway is the main mechanical cause.

Most striking healthy hearts, but there are also various structural heart disease (Ebstein's anomaly, the congenitally corrected transposition of the great vessels tricuspid atresia), neoplastic heart disease and (rhabdomyoma) and accumulation (Pompe disease or Danon). The trigger context can be neutral or characterized by fever or beta-stimulants (bronchodilators). The presentation can be as dramatic as confused with septic shock, aortic coarctation or other structural heart. The heart rate is usually > 220 b/min and can exceed 300 b/min. ECG, the common finding is the detection of narrow ORS. In most cases, the P wave is distinct from the ORS and identifiable between the end of the ORS and the ascending branch of the T wave, the high frequency, however, makes it difficult to detect.

Permanent junctional reciprocating tachycardia (PJRT)

Permanent junctional reciprocating tachycardia (PJRT) is a peculiar form supported by accessory pathway with retrograde slowly conducting with heart rate <200 b/min, the interval PR along with negative P in the inferior leads, and the character with incessant propensity to heart failure in just a weeks or months.

Spontaneous resolution of tachycardia is not uncommon. Antiarrhythmic treatment is often effective. Radiofrequency ablation should be performed in older children or when rate is not controlled, especially in patients with persistent left ventricular dysfunction.⁶

Atrial flutter (AFL)

Atrial flutter (AFL) is an uncommon arrhythmia in newborns and infants. The low incidence of AFL in this age group makes it difficult to study. These previous studies were limited by small, non uniform patient populations. Atrial flutter remains a rare tachycardia in the newborn and young infant and usually presents in the newborn period with asymptomatic tachycardia. The diagnosis can be made from the surface ECG, which most frequently demonstrates 2:1 or variable atrioventricular conduction.⁷⁻¹⁵

Supraventricular tachycardias

Atrial ectopic tachycardia (AET) is a rare arrhythmia; however, it is the most common form of incessant supraventricular tachycardia (SVT) in children. Atrial ectopic tachycardia is believed to be secondary to increased automaticity of a non-sinus atrial focus or foci. This arrhythmia, which is also known as ectopic atrial tachycardia or automatic atrial tachycardia, has a high association with tachycardia induced cardiomyopathy. Atrial ectopic tachycardia is often refractory to drugs and is not usually responsive to direct current (DC) cardioversion. The diagnosis of atrial ectopic tachycardia is based on the presence of a narrow complex tachycardia (in the absence of aberrancy or preexisting bundle branch block) with visible P waves at an inappropriately rapid rate. The rates range from 120 to 300 beats per minute (bpm) and are typically higher than 200 bpm, although physiologic rates may be observed. Patients with atrial ectopic tachycardia may present with circulatory collapse similar to patients with cardiomyopathy. Immediate rate control is desired in these cases.

Three options are available for long-term treatment of patients with atrial ectopic tachycardia: medication to

suppress the arrhythmia or control the ventricular response, catheter ablation, or, uncommonly, surgery. The choice ablation is indicated only in a minority of cases and never for newborn.

Ventricular tachycardias

Ventricular tachycardia (VT) in children is different to that observed in the adult because ischemic heart disease is exceptionally rare in this age group. The arrhythmia sometimes presents with cardiac failure or loss of consciousness. Many cases of VT occur without any cardiac disease even after extensive investigations. Some are benign with a good prognosis. Amiodarone and betablockers are the best antiarrhythmic agents. Ablation techniques progress and the limited indications of surgery and implantable defibrillators have to be considered case by case. ¹⁶⁻¹⁷

Bradiarrhythmias

AV block

The congenital AV block is classified as first, second and third degree. Can be isolated or associated with congenital heart disease (25-50% of cases) and, in this case, more frequently at univentricular heart or the transposition congenitally corrected the great arteries In patients with congenital BAV (second degree and third degree) is recommended pacemaker implantation in the neonatal period when your heart rate setting is <55 b/min in the presence of structurally normal heart or <70 b/min in the presence of congenital heart disease. The pacemaker is also recommended in the presence of a wide QRS escape rhythm, especially if associated with ventricular extrasystoles complex or ventricular dysfunction. The pacemaker can be taken into account even in patients with syndrome long QT and BAV 2: 1 or BAV third degree.¹⁸⁻²⁰

Sinus node dysfunction

If the sinus node is not normal due to damage from surgery, drugs, congenital heart defects or other causes, the heartbeat may become slowly with blood pressure decrease. Atropine, beta-adrenergic agonists, adrenaline can be used and in extreme case temporary pacing external transthoracic or endocardial (accessible via the jugular or femoral vein) is necessary.

Sinus node dysfunction may lead to a bradycardia. Sinus node dysfunction can be treated with a permanent pacemaker.

Channelopathies in children

Channelopathies are uncommon in neonatal period except for the long QT syndrome. The identification of the molecular basis of several hereditary arrhythmia syndromes has been instrumental in this development.²¹⁻²³

Long QT syndrome

The long QT syndrome (QTc pediatric > 440 ms) is a genetic basis disease; this patients have high risk of ventricular arrhythmias and sudden cardiac death. In some children can observe the presence of BAV 2:1 functional (secondary to marked QT prolongation) and phenomena of alternation beat / beat T-wave (sign of electrical instability). It can lead to a characteristic polymorphic ventricular tachycardia known as torsades de pointes , leading to syncope, seizures, or sudden cardiac death. Therapy is primarily pharmacological but implantation of cardioverter defibrillators, and left cardiac sympathetic denervation are used in the treatment of these patients.

Catecholaminergic polymorphic ventricular tachycardia The catecholaminergic polymorphic ventricular tachycardia is associated with mutations of genes encoding proteins creating or interacting with the specialized ion channels in myocardial in a heart structurally intact. ECG baseline may present a marked bradycardia. Ventricular tachycardias occur during physical or emotional stress. It is reported in the literature only one case of catecholaminergic polymorphic ventricular tachycardia neonatal. Channelopathies predispose the patient to sudden cardiac death.

Short QT syndrome

Congenital or familial short QT syndrome is a genetically heterogeneous cardiac channelopathy without structural heart disease that has a dominant autosomal or sporadic pattern of transmission affecting the electric system of the heart. Patients present palpitations due to episodes of paroxysmal atrialfibrillation and syncope and/or sudden cardiac death due to polymorphic ventricular tachycardia and ventricular fibrillation. Electrocardiographic (ECG) findings include extremely short QTc intervals (QTc interval \leq 330 ms) not significantly modified with heart rate changes and T waves of great voltage.Electrophysiologic studies are characterized by significant shortening of atrial and ventricular refractory periods and arrhythmias induced by programmed stimulation.

The treatment in the case of ventricular fibrillation is with DC shock and subsequent oral therapy drugs. There may be an indication of defibrillator implant.

Brugada syndrome

Brugada syndrome is hereditary arrhythmia associated with the characteristic peaked ST-segment elevation in the V1-V3 (type1) and leads and sudden cardiac death. The mean age of sudden cardiac death is 40 years; pediatric cases reported remain rare. Genetic testing and a greater awareness of the disease can result in many more children diagnosed with Brugada syndrome.²⁴⁻²⁵

Anesthesia

Clinical/Care pathways

The assistance of the patient should be monitored in a single structure (if possible) to accompany the young patient from the early stages of need of medical intervention. The parents of the young patient should be accompanied themselves in this way. All this to improve compliance of the small patient. for parents of child care are sad and often traumatic A good cllinical care management will guide him throughout his life quietly. ²⁶

Surgery: diagnosis and preparation

The diagnosis of arrhythmogenic events that require the installation of PMK and ICD occurs during normal routine control or at birth.

The focus in the early years of life is fundamental. The possibility that events can be lead to the diagnosis of symptomatic events arrhythmogenic primitive that in most cases require pharmacological intervention targeted and in conditions of hemodynamic stability allow careful reassessment at a distance; under conditions of hemodynamic instability and cardiac arrest require observational period in PICU.

When the arrhythmia does not respond to the treatments or the combination of multiple drugs are insufficient need an implant.

Premedication

When the child will have to undergo surgery facility pacemaker or ICD is important a good premedication can often start the evening before surgery.

The event surgery for the child is not "forgotten". The psychological structure of the child could record it as an event unrelated to hospital but rather with possible unexplained fears that might occur in the years ahead. They were of the opinion that preterm infant have the anatomical and functional ability to perceive pain.

The drugs listed in this first phase are represented by benzodiazepines, especially midazolam which is the most recommended drug for its rapid onset and a halflife of 2-4 hours. Often the lack of a venous access, from the first day of the surgery, it can be administered orally or nasal (good alternative to oral midazolam as premedication in the pediatric population)

In a recent study it was seen that intranasal dexmedetomidine premedication is more effective than oral midazolam to reduce preoperative anxiety in pediatric patients. a careful hemodynamic evaluation should be present in order to prevent known side effects. ²⁷⁻³⁰

Sedation

Sedation is required during the procedures to allay the anxiety, pain, and movement. The resulting physiological and behavioral responses can lead to long-lasting negative effects on the developing nociception system.

Definitions AAP (American Academy of Pediatrics) are: 1. conscious sedation - a state controlled medically depressed consciousness that allows protective reflexes to maintain; preserves the patient's ability to maintain a patent airway; and allows an adequate response by the patient to physical or verbal commands;

2. deep sedation - a state controlled medically depressed consciousness or unconsciousness from which the patient is not easily aroused. It may be accompanied by a loss of protective reflexes. This includes the ability to maintain a patent airway independently or allows the patient to responding specifically to physical stimuli or verbal commands.

3. general anesthesia - a controlled state of unconsciousness medically accompanied by a loss of protective reflexes, including the ability to maintain a patent airway independently or allows the patient to respond specifically to physical stimulation or verbal commands.

The preoperative assessment of the American Society of Anesthesiologists (ASA) has to be done previously. Informed consent must be obtained and documented prior to the procedure. The risk in individual patients must be weighed against the risk of delaying an emergent procedure.

Equipment and emergency drugs

The initial procedures which have appropriate, reliable monitoring and the need for an environment in which there is someone prepared to check list before starting any sedation for a procedure in a child.

Emergency drugs atropine, adrenaline, hydrocortisone, flumazenil, naloxone should be available.

- 1. Appropriate endotracheal tube size
- 2. Laryngoscope
- 3. Laryngeal masks

- 4. FOB
- 5. Aspirator with probes of appropriate caliber
- 6. Facemask
- 7. Guedel airway
- 8. Source of oxygen
- 9. Emergency drugs
- 10. Presence of nursing staff support

Defibrillator must be available for immediate use during the perioperative period.

Peripheral venous access, premedication, induction and maintenance

It's indicate to conduct the patient in the operating room and use sevoflurane 3-6% and 100% oxygen and decrease to 2-3% for maintenance until the finding of blood vessel A standard non-invasive monitoring should be used: ECG, BP, pulse oximetry, respiratory rate, and capnography. It can also be used a neurological BIS monitoring for easy to use for sedation.

Halogenated volatile anesthetics (Halothane, Enfluorane, Isoflurane, Desflurane and Sevoflurane) prolong the QTc interval, even if data is controversial for some of them. Sevoflurane produced significant arrhythmias in a pediatric patient with congenital long QT syndrome and catecholaminergic polymorphic ventricular tachycardi; the clinical significance of these findings in patients with Long QT syndrome is unclear, but it is recommended to avoid these agents.³¹

In most cases the procedures are performed with the patient under general anesthesia. Alternatively, patients can receive total intravenous anesthesia. However, many procedures can be performed with mild sedation and without sedation in patients aged > 10 years without sedation, but general anesthesia and sedation were usually required in patients aged ≤ 10 years.

The toxicity of drugs for sedation should be considered. Most drugs in anesthesia have a liver metabolism and it's known as hepatic enzyme systems is mature in infants and premature babies as well as GFR decreased in infants and reach adult levels of a year old. Watersoluble drugs often have large volumes of distribution for most water vs fat.

Opioids

A single intravenous dose of fentanyl 1-4 µg/kg has rapid onset (<30 s) with a peak at 2-3 min and brief clinical duration (20-60 min). The initial i.v boluses of $0.5-2 \mu g/kg$ may be given over 2-5 min titrated to effect, followed by infusion of 0.2-2 µg/kg/h for maintenance of analgesia. As sedation does not occur at low doses (1-2 µg/kg), the concurrent administration of midazolam is required. The combination of fentanyl and midazolam minimize hemodynamic or respiratory compromise. Remifentanil is an ultra-short-acting opioid agent that has an onset of action of about 1 min and an elimination half-life of less than 10 min. It is given as an infusion of 0.05- 0.10 µg/kg/min in combination with midazolam. In case of invasive procedures, before cessation of the remifentanil infusion, a longer acting analgesic may be administered to ensure analgesia when the patient awakens from sedation. 32-33

Ketamine

Ketamine is characterized by profound analgesia, sedation, amnesia, and immobilization. Upper airway muscular tone and protective airway reflexes are maintained and spontaneous respiration is preserved although when administered i.v (dose is 1-1.5 mg/kg), it must be given over 1 min to prevent transient respiratory depression. Unpleasant emergence reactions are uncommon in children and teenagers and are typically mild.. It is an ideal sedative in patients with bronchospasm, hypovolemia, and shock.

Ketamine was used in premedication in children with undiagnosed Long QT syndrome (LQTs) but it is not recommended in patients with LQTs because its sympathomimetic properties can favor incidents of torsade de point.³⁴

Propofol

Propofol can be given to children in these settings with good efficacy, apparent safety, and rapid recovery. Use

of an analgesic is imperative in addition to propofol for painful procedures. Propofol has a wide array of benefits, including anticonvulsant activity, antiemesis, and ability to reduce intracranial hypertension. Propofol infusion syndrome seems an unlikely concern for procedural sedation. Propofol rapidly reverses sevofluraneinduced QTc prolongation in healthy patients and therefore may be beneficial. ³⁵

Dexmedetomidine

Dexmedetomidine is a highly selective alpha-2 adrenoreceptor agonist with sedative, anxiolytic, and mild analgesic properties with no depressant effect on respiratory drive. Although it does not have US FDA approval for use in children, its use has been well described in multiple settings. Although not approved for use in the pediatric population, an increasing number of reports describe its use in pediatric patients during the intraoperative period and in the intensive care unit It is administered as a loading dose of 0.5-1 μ g/kg over 10 minutes followed by an infusion of 0.2-1 μ g/kg/hr. Faster onset of action and time to recovery but its impact on the cardiovascular system secondary to its negative chronotropic and dromotropic effects must be considered.

However in pediatric patients with congenital heart disease (CHD) use of dexmedetomidine to treat junctional ectopic tachycardia (JET) is rereported.

Analgesia

Acetaminophen is the most commonly used .It has limited efficacy for mitigating procedural pain. It is available in oral, rectal, and intravenous (i.v) form. Paracetamol i.v is administrated in a dose of 10 mg/kg up to 4 times a day; for children weighing more than 10 kg (and less than 33 kg), 15 mg/kg, up to 4 times a day.

Ketorolac It is efficacious as a sole analgesic for minor procedures. However, in acute renal failure, [[]prolonged prothrombin time and hypersensitivity have been reported to occur with its usage. Dose of ketorolac is 0.5 mg/kg i.v, every 6 hours for less than 5 days. (NSAIDS, though are not preferred in neonates because of their increased risk of side-effects. Commonly used drugs are acetaminophen and ketorolac).

Conclusions

Percutaneus intervention (PCI) is usually performed under sedation, especially if respiratory distress or hemodynamic instability are present. Intubation is always preferable to laryngeal mask airway (LMA). Invasive monitoring may be necessary in certain situations. Thrombosis is an acute complication during PCI.

Tachyarrhythmias hemodynamically significant present before mapping are treated with cardioversion, while you avoid antiarrhythmics. Deep sedation may be required at the time of electrical cardioversion in some procedures.

High-frequency jet ventilation (HFJV) was used for atrial fibrillation in order to reduce the movements of the chest wall and the lung, with reduction of left atrial volume changes. HFJV not only reduces the time the procedure, but also leads to improved intravenous anesthesia outcome.TIVAdovrebbero be used for the maintenance with this technique.

Temporary pacemaker should be available as these patients may not respond to atropine. Bennett (35) et al. have reported the incidence of cardiac arrest and death during the procedure. Complications higher in patients with pulmonary hypertension.

General anesthesia is chosen mainly in critically ill patients, prolonged procedures, patients uncooperative and procedures that require transesophageal echocardiography.

Generally, FiO_2 is reduced to about 25% or less at the check SaO_2 in different chambers of the heart. FiO_2 higher during the procedure may change pulmonary vascular resistance measurements. The blood must be provided in such interventional procedures in which there is the possibility of uncontrolled bleeding.

References

- Stefanelli B et al. Implantable cardioverter defibrillator therapy of life-threatening arrhythmias in young patients. J Interv Card Electrophysiol, Vol.6, No.3, (July 2002), pp. 235-244, ISSN 1215-4326.
- Kettering K. et al. Long-term experience with subcutaneous ICD leads: a comparison among three different types of subcutaneous leads. Pacing Clin Electrophysiol, Vol.27, No.10, (October 2004), pp. 1355-1361, ISSN 1551-1244
- Cannon BC et al. Defibrillator leads in patients with limited venous access to the heart. Pacing Clin lectrophysiol, Vol. 29, No.2, (February 2006), pp. 181–187, ISSN 1649-2305
- Snyder CS et al. Minimally invasive implantation of a cardioverter-defibrillator in a small patient. J Thorac Cardiovasc Surg, Vol.133, No.2, (May 2007), pp. 1375–1376, ISSN 1746-7466
- G Vaksmann et al. Permanent junctional reciprocating tachycardia in children: a multicentre study on clinical profile and outcome. Heart. Jan 2006;92: 101-104
- 6. Rodriguez-Coronel A et al. Clinical forms of atrial flutter in infancy. J Pediatr 1968;73:69-76.
- Moller JH, Davachi F, Anderson RC. Atrial flutter in infancy. J Pediatr 1969;75:643-651.
- Rowland TW, Mathew R, Chameides L, Keane JF; Idiopathic atrial flutter in infancy. A review of eight cases. Pediatrics 1978;61:52-56.
- Peng C, Chen M, Hou CJ. Atrial flutter in the neonate and early infancy. Jpn Heart J 1998; 39:287-295.
- Mendelsohn A, Dick M, Serwer GA. Natural history of isolated atrial flutter in infancy. J Pediatr. 1991;119:386-391.
- Dunnigan A, Benson W, Benditt DG; Atrial flutter in infancy. Diagnosis, clinical features, and treatment. Pediatrics 1985;75:725-729.

- Martin TC, Hernandez A; Atrial flutter in infancy. J Pediatr 1982;100:239-242.
- Till J, Wren C. Atrial flutter in the fetus and young infant. an association with accessory connections. Br Heart J. 1992;6:80-85.
- Casey A, McCrindle BW, Hamilton RM, Gow RM; Neonatal atrial flutter. Significant early morbidity and excellent long-term prognosis. Am Heart J 1997;133:302-306.
- Dagres N, Gutersohn A, Wieneke H, Sack S, Erbel R. A new hereditary form of ectopic atrial tachycardia with autosomal dominant inheritance. Int J Cardiol 2004;93:311-3.
- 16. Grolleau R et al. Ventricular tachycardia in children. Arch Mal Coeur Vaiss 1993;86(5 Suppl):789-9.
- Roworth AJ et al. Implantable automatic scanning pacemaker for termination of supraventricular tachycardia. Am J Cardiol 1982;49:753.
- Weng KP et al. The long-term outcome of children with isolated congenital complete atrioventricular block. Acta Paediatr Taiwan 2005;46:260-7.
- 19. Jaeggi ET et al. Prenatal diagnosis of complete atrioventricular block associated with structural heart disease: combined experience of two tertiary care centers and review of the literature. Ultrasound Obstet Gynecol 2005;26:16-21.
- 20. Friedman DM et al. Utility of cardiac monitoring in fetuses at risk for congenital heart block: the PR Interval and Dexamethasone Evaluation (PRIDE) prospective study. Circulation 2008;117:485-9.
- Arthur AM, Wilde MD Channelopathies in Children and Adults. Pacing and Clinical Electrophysiology Volume 31, Issue Supplement s1, pages S41– S45, February 2008.
- 22. Chockalingam P et al., The diagnostic and therapeutic aspects of loss-of-function cardiac sodium channelopathies in children. Heart Rhythm 2012;9:1986-9.

- Illikova V, Hlivak P, Hatala R. Cardiac channelopathies in pediatric patients -7-years single center experience. J Electrocardiol 2014 Dec
- Crosson JE, Nies M. Brugada syndrome in children. Expert Rev Cardiovasc Ther 2015;13:173-81.
- Joung B et al. Pediatric radiofrequency catheter ablation: sedation methods and success, complication and recurrence rates. Circ J 2006;70:278-84.
- 26. Lidow MS. Long-term effects of neonatal pain on nociceptive systems. Pain 2002;99:377-83.
- Walker SM et al. Long-term impact of neonatal intensive care and surgery on somatosensory perception in children born extremely preterm. Pain 2009;141:79-87.
- Linares Segovia B et al. Pre-anesthetic medication with intranasal dexmedetomidine and oral midazolam as an anxiolytic. A clinical trial An Pediatr 2014;8:226-3.
- Verma R et al. Premedication with midazolam nasal spray: an alternative to oral midazolam in children. Anesth Pain Med 2012;1:248-51
- McMillan CO et al. Premedication of children with oral midazolam. Canadian Journal of Anaesthesia 1992, Volume 39, Issue 6, pp 545-550.
- 31. Kenyon CA et al. Anesthesia for videoscopic left cardiac sympathetic denervation in children with congenital long QT syndrome and catecholaminergic polymorphic ventricular tachycardia. A case series. Paediatr Anaesth 2010;20:465–470
- Kennedy RM, Porter FL, Miller JP, Jaffe DM. Comparison of fentanyl/midazolam with ketamine/midazolam for pediatric orthopedic emergencies. Pediatrics 1998;102:956-6
- 33. Kaynar A, Kelsaka E, Karakaya D, Sungur M, Baris S, Demirkaya M, et al. Effects of different doses of remifentanil infusion on hemodynamics and recovery in children undergoing pediatric diagnostic cardiac catheterization. J Cardiothorac Vasc Anesth 2011;25:660-4

- Kim G et al. Ventilatory response during dissociative sedation in children-a pilot study. Acad Emerg Med 2003;10:140-5.
- Kleinsasser A et al. Reversing sevofluraneassociated Q-Tc prolongation by changing to propofol. Anaesthesia 2001;56:248–250.