Case Report
pISSN 2383-9309 ▮ eISSN 2383-9317
J Dent Anesth Pain Med 2023;23(1):45-51 ▮ https://doi.org/10.17245/jdapm.2023.23.1.45

General anesthesia using propofol infusion for implantation of an implantable cardioverter defibrillator in a pediatric patient with Andersen-Tawil syndrome: a case report

Seyeon Park[1], Wonjae Heo[1], Sang-Wook Shin[1,2], Hye-Jin Kim[1], Yeong Min Yoo[1], Hee Young Kim[1,2]

[1]Department of Anesthesia and Pain Medicine, Pusan National University Yangsan Hospital, Yangsan, Republic of Korea
[2]Department of Anesthesia and Pain Medicine, School of Medicine, Pusan National University, Yangsan, Republic of Korea

Andersen-Tawil syndrome (ATS) is a rare genetic disease characterized by a triad of episodic flaccid muscle weakness, ventricular arrhythmias, and physical anomalies. ATS patients have various cardiac arrhythmias that can cause sudden death. Implantation of an implantable cardioverter-defibrillator (ICD) is required when life-threatening cardiac arrhythmias do not respond to medical treatment. An 11-year-old girl underwent surgery for an ICD implantation. For general anesthesia in ATS patients, anesthesiologists should focus on the potentially difficult airway, serious cardiac arrhythmias, such as ventricular tachycardia (VT), and delayed recovery from neuromuscular blockade. We followed the difficult airway algorithm, avoided drugs that can precipitate QT prolongation and fatal cardiac arrhythmias, and tried to maintain normoxia, normocarbia, normothermia, normoglycemia, and pain control for prevention of sympathetic stimulation. We report the successful application of general anesthesia for ICD implantation in a pediatric patient with ATS and recurrent VT.

Keywords: Andersen-Tawil Syndrome; Anesthesia; Implantable Cardioverter Defibrillator; Long QT Syndrome; Propofol.

INTRODUCTION

Andersen-Tawil syndrome (ATS) is a rare genetic disease with autosomal dominant transmission, caused by variants of KCNJ2. ATS is characterized by a triad of episodic flaccid muscle weakness, ventricular arrhythmias, and physical anomalies, including low-set ears, widely spaced eyes, small mandibles, fifth-digit clinodactyly, syndactyly, short stature, and scoliosis [1]. ATS-related symptoms vary widely and cardiac arrhythmias with varying severities, such as premature ventricular contraction (PVC), extrasystole, and ventricular tachycardia (VT), may occur. Serious cardiac arrhythmias can cause sudden death in ATS, and implantation of an implantable cardioverter-defibrillator (ICD) is required when cardiac arrhythmias that can be life-threatening, such as frequent VT, do not respond to medical treatment [2]. When general anesthesia is required in ATS patients, the clinical triad of these patients presents various challenges for anesthesiologists, including difficult airways, perioperative ventricular

Received: October 18, 2022 • Revised: December 4, 2022 • Accepted: December 11, 2022
Corresponding Author: Hee Young Kim, Postal address: Department of Anesthesia and Pain Medicine, School of Medicine, Pusan National University, 20, Geumo-ro, Beomeo-ri, Mulgeumeup, 50612, Yangsan, Republic of Korea
Tel: +82 55 360 2129 Fax: +82 55 360 2149 E-mail: yuvi1981@naver.com

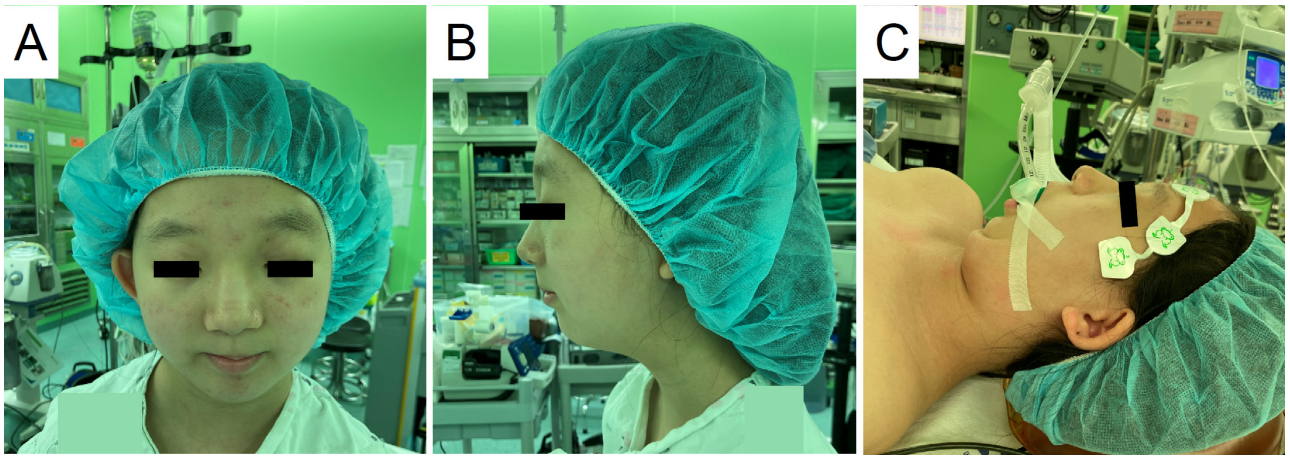

Fig. 1. Dysmorphic facial features of the patient. The patient has a small mandible (A), mild retrognathia, and short thyromental distance (B and C).

arrhythmias, and delayed recovery from neuromuscular blockade. We report the successful administration of general anesthesia during ICD implantation in a pediatric patient with ATS and recurrent VT.

CASE REPORT

Written informed consent was obtained from all parents. An 11-year-old girl (height 130.8 cm, weight 32.2 kg) experienced her first epileptic attack during light exercise. She had a recent history of periodic muscle weakness and micrognathia identified on physical examination. Her father and younger sister also had a similar appearance and a history of frequent PVCs. Basic exams, including 24-hour Holter monitoring and genetic testing, were performed. Finally, she was diagnosed with KCNJ2-mutation ATS. The results of 24-hour Holter monitoring showed sustained VT for 1 min, non-sustained VT (NSVT) that occurred 7 times, and isolated PVCs constituting 4% of all beats. Medical treatment was not effective in treating her critical arrhythmia despite the use of β-blockers, such as propranolol and nadolol, and antiarrhythmic drugs, such as flecainide and mexiletine. She had another four episodes of seizures or loss of consciousness caused by VT. A subsequent Holter monitor showed PVC bigeminy, sustained VT for 1 min, and frequent NSVT. We decided to implant an ICD due to symptomatic and recurrent VT.

We considered utilizing general anesthesia due to the patient's age and the advantages for dealing with unstable hemodynamic changes. We recognized difficult airway, ventricular arrhythmia, and the possibility of delayed recovery from neuromuscular blockade as anticipated risks related to ATS for general anesthesia. Endotracheal intubation was planned with reference to the difficult airway algorithm described in the 2022 American Society of Anesthesiologists guidelines [3] due to her small mandible, mild retrognathia, and short thyromental distance (Fig. 1). Before the induction of anesthesia, ID 5.0, 5.5, and 6.0, cuffed endotracheal tubes were secured, and pre-emptive preparations were made for the laryngeal mask airway, video laryngoscope (KoMAC video laryngoscope, KoMAC Co., Ltd., Korea), stylet, naso-pharyngeal airway, oropharyngeal airway, and fiberoptic bronchoscope. Several studies have reported that propofol infusion can reduce the frequency of ventricular ectopy [4-6]; therefore, we decided to use total intravenous anesthesia (TIVA) using 2% propofol and remifentanil.

Immediately after the patient arrived to the operating room, vital signs were checked. Initial heart rate was 122 beats per minute (bpm), blood pressure was 86/40 mmHg, and oxygen saturation was 99%. Sinus tachycardia, ventricular bigeminy, prolonged QT interval, and

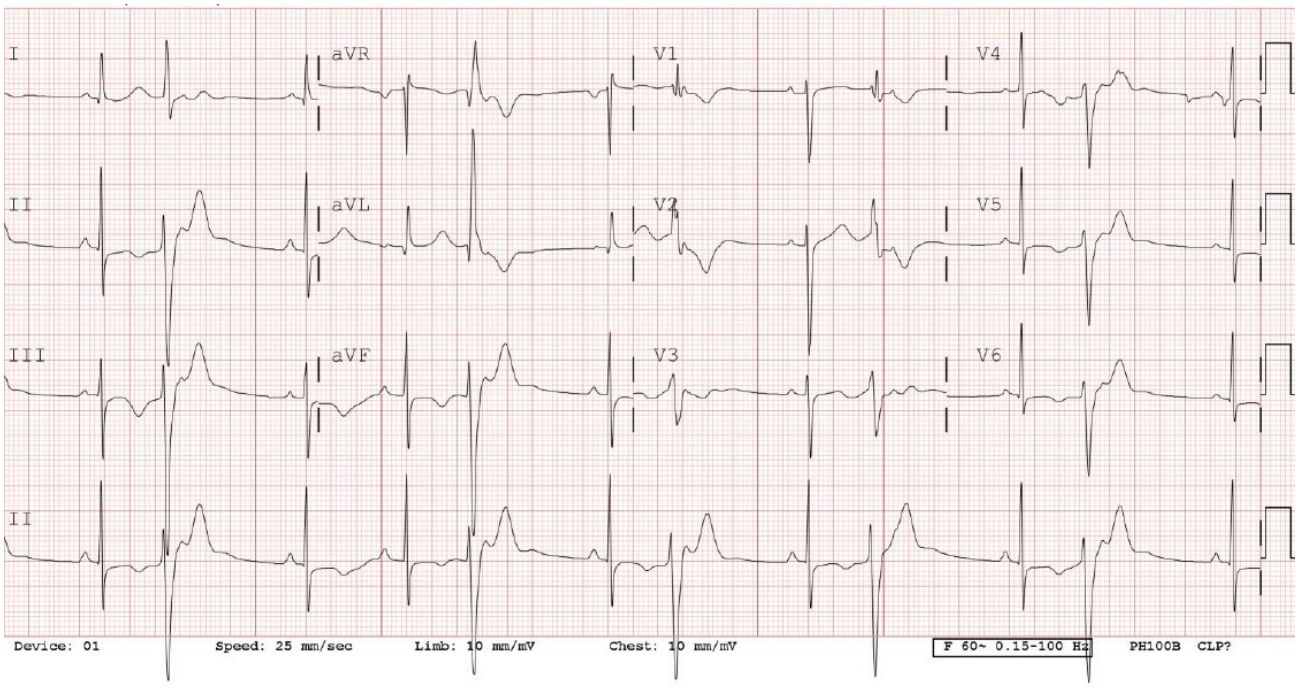

Fig. 2. Preoperative ECG. It showed ventricular bigeminy, prolonged QT interval (QTc 499ms). ECG, electrocardiogram; QTc, corrected QT interval.

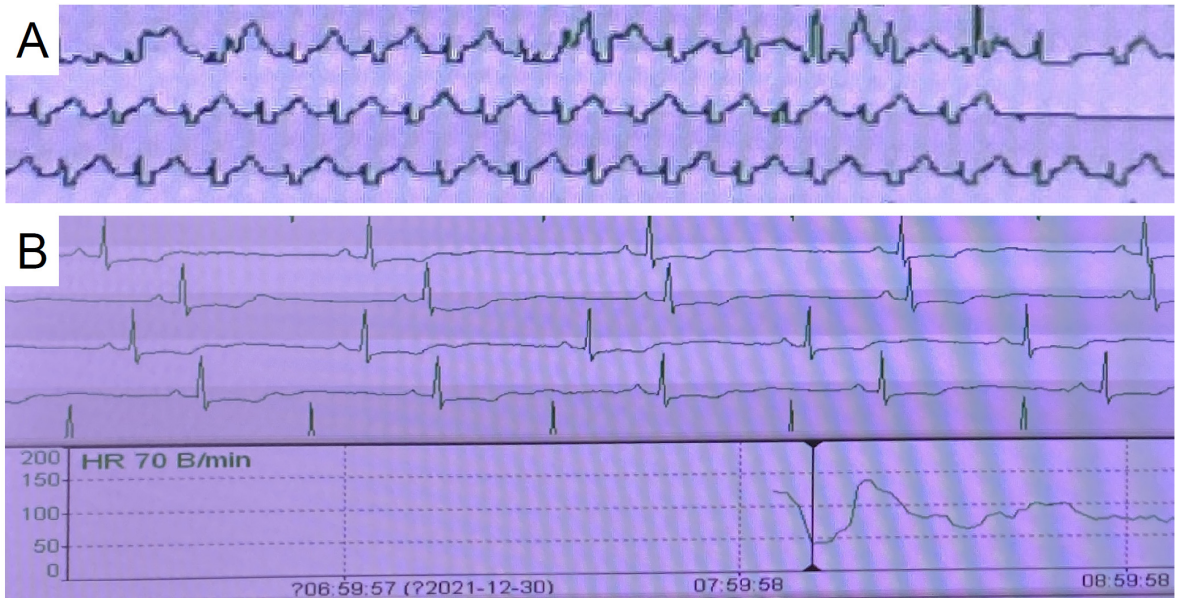

Fig. 3. (A) ECG immediately after the patient's arrival to the operating room. It showed sinus tachycardia, ventricular bigeminy, prolonged QT interval, and prominent U waves. (B) After applying total intravenous anesthesia using propofol and remifentanil, ECG showed sinus bradycardia (38-49 bpm) for a few minutes. bpm, beats per minute; ECG, electrocardiogram; TIVA, total intravenous anesthesia.

prominent U waves were observed on electrocardiography (ECG) (Fig. 2 and 3A). After applying TIVA, the ECG changed to sinus bradycardia (38-49 bpm) within a few minutes (Fig. 3B). Bradycardia was observed without any other intervention due to stable blood pressures. Intravenous rocuronium 20 mg was administered after confirmation of mask ventilation, without any problems. Successful endotracheal intubation was performed using a video laryngoscope with a size 2 blade, stylet, and ID 6.0 cuffed endotracheal tube. The

ECG then returned to its initial appearance after endotracheal intubation and titration of anesthetics without any other procedures. Anesthesia maintenance was performed with 4.35 mg/kg/hr of 2% propofol and 0.08 mcg/kg/min of remifentanil. There were no critical events, such as VT, during the operation. We used sugammadex (Bridion®, Merck and Co., USA) 150 mg (about 4 mg/kg) for emergence due to her recent transient muscle weakness, and we were unable to monitor neuromuscular transmission (NMT). The patient was transferred to the intensive care unit after successful extubation and discharged on postoperative day 6 without complications.

DISCUSSION

ATS is a rare genetic disorder with an incidence of 1/1,000,000 [7]. ATS is diagnosed at an early age, mainly in the 1st or 2nd decade since patients with ATS have symptoms such as muscle weakness, tachycardia, syncope, or dysmorphic physical characteristics [1]. The diagnostic criteria for ATS are presented in Table 1. However, each patient with ATS presented with different symptoms, even within a single family, and showed all possible combinations. The patient in this case had periodic paralysis, ventricular arrhythmias, wide-set eyes, a small mandible, and family members who met the inclusion criteria.

ATS is most often caused by mutations in the KCNJ2 gene or, rarely, by mutations in KCNJ5 [8]. KCNJ2 encodes the Kir2.1 inward rectifier potassium channel (IK1) proteins and is predominantly expressed in cardiac and skeletal muscles. IKI plays an important role in the stable resting membrane potential in excitable cells and in the late repolarization phase of the cardiac cycle [9]. Defects in the IK1 channel can result in muscle weakness, periodic paralysis, prolonged QT intervals, and cardiac arrhythmias in ATS patients. Since ATS is not a curable disease, medical treatment to control symptoms or an implantable device should be utilized. In ATS patients, β-blockers, such as propranolol, and antiarrhythmic drugs, such as flecainide, can be used to reduce the occurrence of VT. However, in patients who do not respond to antiarrhythmic drugs, ICD implantation should be considered, although its effectiveness in patients with is controversial [10].

Table 1. Diagnostic criteria for Andersen-Tawil syndrome[a]

An individual is diagnosed with Andersen–Tawil syndrome if this individual meets at least one of the sets of criteria A and B	
Set of criteria A	
Two of the following three criteria:	
1	Periodic paralysis
2	Ventricular arrhythmias (frequent premature ventricular contractions, bigeminy, ventricular tachycardia), prolongation of the rate-corrected QT or QU interval, and/or a prominent U wave
3	At least two of the following dysmorphic features: a Low-set ears b Wide-set eyes c Small mandible d Fifth-digit clinodactyly e Syndactyl
Set of criteria B	
1	One of the above three criteria
2	At least one family member who meets two of the above three criteria

[a]Modified from Venance et al. [19]

Implantation of an ICD requires defibrillation testing, and general endotracheal anesthesia has been reported as a safe method [11]. The anesthetic plan for general anesthesia of ATS patients should focus on the potential difficult airway, serious cardiac arrhythmias, such as VT, and muscle weakness, which could result in delayed recovery from neuromuscular blockade. ATS patients commonly have the potential for difficult airways, due to dysmorphic features, including low-set ears, hypertelorism, short palpebral fissures, broad foreheads, triangular faces, mild facial asymmetry, maxillary and mandibular hypoplasia, broad roots of the nose, micrognathia, and arched palates. Therefore, anesthesiologists should prepare various types and sizes of airway instruments, video laryngoscopes, and fiberoptic bronchoscopes. We also followed the difficult airway algorithm and performed successful intubation on the first attempt.

The choice of anesthetic for anesthesia induction, maintenance, and emergence is important since the

Table 2. Suggested perioperative medications in patients with LQTS [13]

Preferred agents	Need caution	Avoid
Sedation		
Midazolam 0.05-3 mg/kg iv		
Analgesia		
Lidocaine 1.5 mg/kg iv. Fentanyl 2 mg/kg iv Alfentanil 0.5-3 mg/kg/min Remifentanil 0.1-0.5 mg/kg/min iv Morphine 0.05-0.1 mg/kg iv	Buprenorphine 0.3 mg iv Methadone 0.1-0.3 mg/kg iv (do not exceed 200 mg/day)	Epinephrine Ketamine Sufentanil
IV anesthetic agents		
	Propofol 6 mg/kg/hr iv Etomidate 0.3 mg/kg iv Thiopental 2-6 mg/kg iv	
Volatile anesthetics		
Isoflurane 1-3% MAC inspired	Sevoflurane 0.5-3% MAC inspired Nitrous oxide 25-70% inspired	
Neuromuscular blockers and reversal agents		
Rocuronium 0.6-1.2 mg/kg iv Vecuronium 0.04-0.1 mg/kg iv for intubation 0.8-1.2 mg/kg/min for maintenance Cisatracurium 0.15-0.2 mg/kg/min for intubation 0.06-0.18 mg/kg/min for maintenance	Anticholinesterase-anticholinergic reversal agents	Succinylcholine Pancuronium Glycopyrrolate Atropine
Postoperative care and anti-emetics		
	Droperidol 0.625-1.25 mg iv Ondansetron 4 mg iv (do not exceed 16 mg) Metoclopramide 10-20 mg iv Dexamethasone 0.1 mg/kg iv	

iv, intravenous injection; LQTS, long QT syndrome; MAC, minimum alveolar concentration.

medications administered may further increase the corrected QT (QTc), and QT prolongation can lead to life-threatening persistent VT and sudden death. Smooth endotracheal intubation is required because it may prolong the QT interval by activating the sympathetic nervous system [12]. The preferred medications and those to be avoided during the perioperative period are listed in Table 2. Airey et al. reported that propofol infusion had an excellent effect on reducing the frequency of ventricular ectopy during general anesthesia in patients with ATS [4]. Studies have also shown that both propofol, and remifentanil neutralizes QTc prolongation caused by sevoflurane [5,6]. The precise mechanism of propofol is unclear, but it may be related to the overall central depression of autonomic function and K^+ currents. Non-depolarizing neuromuscular blockers such as rocuronium, vecuronium, and cisatracurium can be administered safely because they do not prolong the QTc [13]. In this case, sinus bradycardia occurred after propofol was infused, but the patient recovered spontaneously, and no serious arrhythmias occurred during the operation.

If ATS patients have muscle weakness, anesthesiologists should take into consideration delayed recovery from neuromuscular blockade and use NMT monitoring, such as train-of-four, when neuromuscular blockers are administered. Unfortunately, we could not monitor the NMT because we accidentally did not attach the sensor. QT prolongation has also been reported with anticholinergic drugs, which are usually used in anticholinesterase-anticholinergic medication combinations [14]. Therefore,

in this case, approximately 4 mg/kg sugammadex was administered for the reversal of rocuronium. In addition, efforts should be made to maintain normoxia, normocarbia, normothermia, and normoglycemia and to control pain properly since amplified sympathetic activity can lead to QT prolongation [15].

Local anesthetics, including epinephrine, are used during dental surgeries. Epinephrine is a drug that should be avoided in patients with long QT syndrome. However, Theodotou et al. [16] and Wynn et al. [17] suggested that epinephrine could be used in patients with cardiac channelopathies. In addition, Oliveira et al. [18] recently conducted a study comparing arrhythmias caused by the use of two cartridges (3.6 mL) of 2% lidocaine (72 000 mcg of lidocaine) or two cartridges of 2% lidocaine with 1:100 000 epinephrine (36 μg of epinephrine) for mandibular nerve block in patients with Brugada syndrome and long-QT syndrome, and no prolongation of QT interval or life-threatening arrhythmic events were observed in either group. Therefore, they suggested that epinephrine at ideal doses (up to two cartridges) can be used relatively safely in patients with cardiac channelopathies whose symptoms are being controlled with medication and have no history of ICD insertion within the past three months. The amount of epinephrine used should be limited to the amount contained in one or two cartridges, and recent control of symptoms and status of treatment should be checked. If the patient has recently experienced symptoms, such as syncope, a referral to a cardiologist should be made prior to dental procedures.

In conclusion, various considerations, including a potentially difficult airway, drugs that can precipitate QT prolongation, fatal cardiac arrhythmias, and delayed recovery from neuromuscular blockade, are necessary when general anesthesia is required in patients with ATS. Anesthesiologists should also attempt to maintain normoxia, normocarbia, normothermia, normoglycemia, and pain control to prevent sympathetic stimulation.

AUTHOR ORCIDs

Seyeon Park: https://orcid.org/0000-0001-7183-1811
Wonjae Heo: https://orcid.org/0000-0001-5004-5133
Sang-Wook Shin: https://orcid.org/0000-0003-1355-7695
Hye-Jin Kim: https://orcid.org/0000-0003-1630-0422
Yeong Min Yoo: https://orcid.org/0000-0003-3536-0447
Hee Young Kim: https://orcid.org/0000-0001-7809-8739

AUTHOR CONTRIBUTIONS

Seyeon Park: Conceptualization, Data curation, Formal analysis, Visualization, Writing - original draft, Writing - review & editing
Wonjae Heo: Writing - original draft, Writing - review & editing
Sang-Wook Shin: Writing - original draft, Writing - review & editing
Hye-Jin Kim: Writing - original draft, Writing - review & editing
Yeong Min Yoo: Writing - original draft, Writing - review & editing
Hee Young Kim: Conceptualization, Data curation, Formal analysis, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing

DECLARATION OF INTERESTS: The authors have no conflicts of interest to declare.

FUNDING: This work was supported by a 2022 research grant from the Pusan National University Yangsan Hospital.

CONSENT: Informed consent was obtained from the patient and parents in this case report. This report was approved by the Institutional Review Board of the Pusan National University Yangsan Hospital (IRB No. 05-2022-216).

REFERENCES

1. Nguyen HL, Pieper GH, Wilders R. Andersen-Tawil syndrome: clinical and molecular aspects. Int J Cardiol 2013; 170: 1-16.
2. Yoon G, Oberoi S, Tristani-Firouzi M, Etheridge SP, Quitania L, Kramer JH, et al. Andersen-Tawil syndrome: prospective cohort analysis and expansion of the phenotype. Am J Med Genet A 2006; 140: 312-21.
3. Apfelbaum JL, Hagberg CA, Connis RT, Abdelmalak BB, Agarkar M, Dutton RP, et al. 2022 American society of

anesthesiologists practice guidelines for management of the difficult airway. Anesthesiology 2022; 136: 31-81.
4. Airey KJ, Etheridge SP, Tawil R, Tristani-Firouzi M. Resuscitated sudden cardiac death in Andersen-Tawil syndrome. Heart Rhythm 2009; 6: 1814-7.
5. Kleinsasser A, Loeckinger A, Lindner KH, Keller C, Boehler M, Puehringer F. Reversing sevoflurane-associated Q-Tc prolongation by changing to propofol. Anaesthesia 2001; 56: 248-50.
6. Kweon TD, Nam SB, Chang CH, Kim MS, Lee JS, Shin CS, et al. The effect of bolus administration of remifentanil on QTc interval during induction of sevoflurane anaesthesia. Anaesthesia 2008; 63: 347-51.
7. Schulze-Bahr E. Long QT syndromes: genetic basis. Card Electrophysiol Clin 2012; 4: 1-16.
8. Pérez-Riera AR, Barbosa-Barros R, Samesina N, Pastore CA, Scanavacca M, Daminello-Raimundo R, et al. Andersen-Tawil Syndrome: a comprehensive review. Cardiol Rev 2021; 29: 165-77.
9. Dhamoon AS, Jalife J. The inward rectifier current (IK1) controls cardiac excitability and is involved in arrhythmogenesis. Heart Rhythm 2005; 2: 316-24.
10. Airey K, Wilde A, Hofman N, Etheridge S, Ptacek L, Abuissa H, et al. Incidence of device therapy and complications in patients with andersen-tawil syndrome with ICDS. J Am Coll Cardiol 2011; 57: E1233.
11. Gold MR, Aasbo JD, El-Chami MF, Niebauer M, Herre J, Prutkin JM, et al. Subcutaneous implantable cardioverter-defibrillator post-approval study: clinical characteristics and perioperative results. Heart rhythm 2017; 14: 1456-63.
12. Michaloudis DG, Kanakoudis FS, Xatzikraniotis A, Bischiniotis TS. The effects of midazolam followed by administration of either vecuronium or atracurium on the QT interval in humans. Eur J Anaesthesiol 1995; 12: 577-83.
13. O'Hare M, Maldonado Y, Munro J, Ackerman MJ, Ramakrishna H, Sorajja D. Perioperative management of patients with congenital or acquired disorders of the QT interval. Br J Anaesth 2018; 120: 629-44.
14. Saarnivaara L, Simola M. Effects of four anticholinesterase-anticholinergic combinations and tracheal extubation on QTc interval of the ECG, heart rate and arterial pressure. Acta Anaesthesiol Scand 1998; 42: 460-3.
15. Booker PD, Whyte SD, Ladusans EJ. Long QT syndrome and anaesthesia. Br J Anaesth 2003; 90: 349-66.
16. Theodotou N, Cillo JE Jr. Brugada syndrome (sudden unexpected death syndrome): perioperative and anesthetic management in oral and maxillofacial surgery. J Oral Maxillofac Surg 2009; 67: 2021-5.
17. Wynn RL. Articaine 4% with 1:200,000 epinephrine: an acceptable option for patients with long QT syndrome. Gen Dent 2007; 55: 176-8.
18. Oliveira ACG, Neves ILI, Sacilotto L, Olivetti NQS, Santos-Paul MAD, Montano TCP, et al. Is it safe for patients with cardiac channelopathies to undergo routine dental care? Experience from a single-center study. J Am Heart Assoc 2019; 8: e012361.
19. Venance SL, Cannon SC, Fialho D, Fontaine B, Hanna MG, Ptacek LJ, et al. The primary periodic paralyses: diagnosis, pathogenesis and treatment. Brain 2006; 129: 8-17.