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Case Report

Review of Anesthetic Management of Myotonic Dystrophy and A Case Report of Sedation with Dexmedetomidine

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ABSTRACT

15 year-old male patient, with Steinert's Desease, was proposed for orthopedic surgery in left foot. He was sedated by continous perfusión of dexmedetomidine and an ultrasound-guided popliteal block was performed. The level of sedation achieved was adequate, without observing further adverse effects except of bradycardia with initial bolus. Dexmedetomidine was proved to be useful in this case; however, use of the drug should be carefully started at a low initial dose in patients with myotonic dystrophy. We also have reviewed the recent cases-report in patients with DM in past 15 years with a descriptive analysis.

Keywords: Dexmedetomidine; Sedative agent; Perioperative; Anesthesia; Surgery

ABBREVIATIONS

DM1: Myotonic Dystrophy type 1 or Steinert's Disease; BMI: Body Max Index; ICU: Intensive Care Unit; ASA: American Society of Anesthesiologists; ECG: Electrocardiogram

INTRODUCTION

Type 1 Myotonic Dystrophy (DM1), known as Steinert's Disease, is an autosomal dominant multisystemic disorder that affects the musculoskeletal, central nervous, gastrointestinal, endocrine, cardiac, and respiratory systems. DM1 has an incidence of 1 in every 8,000 births with a worldwide prevalence of 2-14: 100,000 [1,2].

It develops as a result of an expanded CTG triplet repeat of a non-coding DNA segment in the DMPK gene in chromosome 19q13.3. Although the gene is located on chromosome 19, there is no association with malignant hyperthermia [3,4].

Classic symptoms of DM1

DM 1 can be classified depending on the time of onset symptoms [5]. There is congenital, infantile and adult form. Their development and characteristics are different although some symptoms may be similar. Classification and symptoms summary are shown in Table 1.

CASE DESCRIPTION

15 year-old male patient, 65 kg, BMI 21, was programmed for surgery of plantar flexor tenotomies of the second to fifth toe of the left foot. He was previously diagnosed with congenital Myotonic Dystrophy type 1 (Steinert Syndrom) and had a brother with the same pathology.

A pre-anesthetic evaluation was performed prior to surgery where the latest reports from different medical specialists were collected. His periodic cardiology check-ups were normal. Neurologically, he presented moderate cognitive developmental delay and distal weakness in the hands and leg. The patient had a typical "myotonic facies" with a favorable airway. Obstructive sleep apnea syndrome was not suspected (but without recent polysomnography), no recent respiratory infections were present.

He was premedicated with bromazepam 0.5 mg orally 30 minutes prior to surgery and did not present anxiety during transfer to the operating room. tBasic ASA monitoring was used (EKG, non-invasive blood pressure, heart rate and oxygen saturation). A peripheral venous catheter was placed in the left hand, where continuous perfusion of dexmedetomidine was connected, prior bolus administration of 1 mcg/kg for 10 minutes and continuing

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throughout the procedure at 0.5 mcg/kg/min. During the initial bolus, a decrease in the heart rate from 65 bpmto 44 bpm was observed. We administered 0.1 mg/kg of atropine and decreased the initial bolus dose to 0.8 mcg/kg, resolving the bradycardia. Subsequently, we proceed to perform an ultrasound-guided popliteal block administering 8 ml of lidocaine 1% and 8 ml of levobupivacaine 0.5%. Oxygen therapy was administered throughout the procedure with nasal dispositive at 2 bpm. The patient did not suffer any desaturations or airway obstruction.

Table 1: Classification and symptoms of DM1.

	Congenital DM1	Childhood-onset DM1 (Symptoms of the adult form appear during the second decade)	Adult-onset DM1 (Classical form, first symptoms appear 15-35 years of age)
Facial abnormalities	Bilateral weakness "Myopathic facies" (open, tent-shaped mouth)	No "typical facies" weakness of facial and neck muscles	Cataracts "typical facies": Bifacial weakness, mild ptosis, progressive wasting of the muscles of mastication. Frontal balding.
Central nervous system: Mental retardation	Psychomotor impairment. Delay in speech and motor development	Mental handicap; difficulties in learning and speech	Psychosocial dysfunction and personality traits. Increased daytime sleepiness and obstructive sleep apnea
Endocrine dysfunction			Diabetes mellitus, hypogonadism, dysthyroidism
Gastrointestinal dysfunction: Dysphagia	Severe risk of aspiratorion	Could be present	Could be present, also constipation, gallstones, elevated G-GT
Squeletal muscles Weakness Myotonia	Talipes equinovarus other contractures could be present. Mild to severe. Hypotonic and inmobile at birth. Not present before 3-5 years of age	Early motor development normal or moderately delayed mild-moderate distal weakness. Present mild-moderate myotonia	Distal weakness mild to severe.
Cardiac dysfunction (arrhythmias, cardiomyopathy)	Often present but not symptomatic during childhood	Cardiac problems appear during the second decade	Always present: Arryhythmias: Atrioventricular block, atrial fibrillation,etc. Dilated cardiomyopathy Sudden cardiac death
Prognosis	Mortality rate of 50% in the neonatal period and 25% in the first year. Death before 30 years of age (mainly cardiac causes)	Variable	During fifth-sixth decade are more common: Chest infection by aspiration, respiratory failure, sudden cardiac death

The surgery went uneventful, we administered metamizole 0.4 mg/kg as an analgesic and dexamethasone 4 mg to prevent postoperative nausea and vomiting.

The level of sedation achieved was adequate, the patient was comfortable, easily awakable and cooperated. After the surgery, the dexmedetomidine infusion was withdrawn without observing further adverse effects. The patient was transferred to the Intermediate Care Unit without agitation or anxiety. The patient lived close to the hospital and had good family support; hence we decided to discharge him home and followed up with phone calls in the evening and the following morning. The pain was controlled by oral NSAIDs.

DISCUSSION

Case discussion

There is limited literature about the use of dexmedetomidine in patients with DM1. Yoshino et al. [6] described the case of a 53 year-old woman with DM1 for a total abdominal hysterectomy with regional anesthesia and dexmedetomidine as a sedative agent. Airway obstruction was observed after the initial bolus at 2 µg/kg, therefore authors conclude that dexmedetomidine should be carefully started at a low initial dose in patients with DM1. Gaszynski [7] report the anesthetic management using an opioid-free method of a patient with Steinert Syndrome under general anesthesia for laparoscopic cholecystectomy with a continuous infusion of dexmedetomidine as adjunct. Bolus dose was 0.6 µg/kg over 10 minutes followed by continuous infusion over 0.2 µ/kg/hour combined with propofol for maintenance of general anesthesia. In both cases the use of this drug was safe without adverse events reported. Our case is more similar to the one described by Yoshino et al. [6] regional anesthesia associated with dexmedetomidine as a sedative agent. We did not observe airway obstruction but bradycardia presented with initial bolus. This may suggest that dexmedetomidine should be carefully started at lower initial dose in patients with DM1.

It is important to clarify that none of the above mentioned patients, including the one described in our case report, suffered from arrhythmias or serious respiratory problems.

Dexmedetomidine reduces heart rate and blood pressure through central sympatholysis but at higher concentrations it causes peripheral vasoconstriction leading to hypertension. It does not often cause deep sedation and patients can be easily awakened. Therefore, it is not suitable for patients who do not tolerate these effects, for example pediatric cases or patients with cognitive developmental delay. Fortunately, in the present case, the patient cooperated. We should have special caution when administering dexmedetomidine to patients with pre-existing bradycardia. Data on the effects of dexmedetomidine in patients with a heart rate <60 are very scarce and special care should be taken. Bradycardia does not normally require treatment, but it generally responds to anticholinergic medications or to dose reduction, as in the case of our patient [8,9].

We have reviewed the recent case reports of anesthesia in patients with DM in the past 15 years using PubMed as our search engine and related citations. Table 2 summarizes the cases with the type of surgery and type of anesthetics used. We have included reported complications and two pediatric cases [10-34].

Table 2: Review of reported cases of anesthesia in patients with Myotonic Dystrophy over the last 15 years.

Author	Anesthesia type	Surgery type	Complication
Mangla et al. [10] PMID: 31016049 2019	GA (Propofol+Rocuronium) Sugammadex	Robotic assisted laparoscopic total abdominal hysterectomy and bilateral salpingo-oophorectomy	Brief shivering episode after waking up
Gaszynski [7] PMID: 27631259 2016	GA-OFA (dexdor)	Laparoscopic cholecystectomy	none
Catena et al. [11] PMID: 17660741 2007	GA (TIVA-propofol/remifentanil and cisatracurium boluses Single lung ventilation for 4 hrs	Emergency thoracoscopy (VATS) for respiratory failure and sepsis secondary to a right parapneumonic empyema	none
Gupta et al. [12] PMID: 20640098 2009	General Anaesthesia (GA) with epidural anaesthesia	Exploratory laparotomy due to adnexal mass (suspected malignant ovarian tumor)	Respiratory distress and pneumonia. Ventilated for 390 days. 3 episodes of cardiac arrest. died of cardio-respiratory arrest on 391st day. She had dilated cardiomyopathy (DCMP). She had upper respiratory tract infection for 3 weeks before surgery for which she was on antibiotics
Bisinotto et al. [13] PMID: 20485964 2010	GA - TIVA propofol, remifentanil, and rocuronium	Video laparoscopic cholecystectomy	Respiratory failure and myotonia, which made tracheal intubation impossible. A laryngeal mask was used until full recovery of the respiratory function. The patient did not develop further complications.
Kim et al. [14] PMID: 31723621 2017	GA Neostigmine+Sugammadex	Emergency cesarean section	Respiratory failure. Tracheostomy.
Masamune et al. [15] PMID: 19462802 2009	GA propofol, remifentanil and vecuronium, combined with epidural anesthesia using ropivacaine	Laparoscopic cholecystectomy	None
Pinto et al. [16] PMID: 30301614 2018	GA (TIVA- propofol and laryngeañ mask) Supraclavicular nerve superior trunk block	Osteosynthesis of clavicle fracture	None
Joh et al. [17] PMID: 22949987 2012	GA-TIVA propofol and remifentanil Vecuronium bolus NINO 10 meses	Endoscopic third ventriculostomy for hydrocephalus	Extubated in ICU. No complication.
Mori et al. [18] PMID: 20715526 2010	Combined spinal-epidural anesthesia	Emergency cesarean section	None

Gandhi et al. [19] PMID: 21431056 2011	GA Desflurane+nitrous oxide Atracurium to neostigmine	Laparoscopic cholecystectomy	None
Shirasawa et al. [20] PMID: 24854518 2014	GA-tiopental+anectine Maintain with N2O, sevorane, rocuronium, propofol, fentanyl	Cesarean section	Atrial flutter MD diagnosed after cesarean section
Nakanishi et al. [21] PMID: 21077314 2010	GA TIVA (propofol+remifentanilo+ rocuronium) combined with epidural anesthesia	Laparotomy for uterine cancer	None
D Sivathondan [22] PMID: 16913352 2006	GA (propofol, fentanyl and atracurium with intermittent desflurane)	Hysterectomy	None
Subramaniam et al. [23] PMID: 27687340 2016	GA (fentanyl, propofol, vecuronium and sevoflurane)+epidural anesthesia	Pheochromocytoma resection	Extubated after 40 hours in ICU, required non-invasive ventilatory support (BiPAP) for a subsequent 2 days in ICU
Uno et al. [24] PMID: 29693947 2017	GA-TIVA Propofol+Rocuronium bolus Sugammadex TAP+thoracic epidural	Laparoscopic cholecystectomy	None
Furutani et al. [25] PMID: 19227172 2009	GA fentanyl+sevorane NINO	Emergency surgery for strangulation ileus	Left main bronchus collapsed with atelectasia. Several hours of mechanical ventilation in ICU.
Noguchi et al. [26] PMID: 30380223 2017	GA without muscle relaxant	Bilateral para-thyroidectomy	High flow nasal cannula therapy postoperatively due to increasing hypercarbia
Correia et al. [27] PMID: 26952230 2016	Continuous spinal anesthesia	Laparoscopic cholecystectomy	None
Owen et al. [28] PMID: 21485681 2011	GA	Emergency caesarean section	Re-intubation due to respiratory compromise, followed by a more gradual period of weaning from positive pressure ventilation

Matsuzaki et al. [29] PMID: 24063143 2013	Combined spinal epidural	Cesarean section	Lower saturation for 4 days. No treatment needed.
Armendáriz-Buil et al. [30] PMID: 26786377 2015	Spinal anesthesia Bilateral TAP block+rectus muscle block	Hysterectomy and bilateral salpingectomy+oophorectomy with lymphadenectomy	Non-invasive ventilation in reanimation ward
Yoshino et al. [6] PMID: 19702215 2009	Combined spinal-epidural Dexdor sedation	Total abdominal hysterectomy	Airway obstruction with low dose of Dexdor
Baticón Escudero et al. [31] PMID: 18333395 2008	Incomplete axillary block + Sedation with ketamine continuous perfusion	Arthrodesis of the carpus	None
Koyama et al. [32] PMID: 32317885 2020	GA-TCI propofol and remifentanil+rocuronium bolus thoracic epidural	Laparoscopic cholecystectomy open	Increase in sputum production, difficult sputum expectoration and dyspnea with tachypnea BiPAP therapy was applied using NIP Nasal V® (Teijin Inc., Tokyo, Japan)
Araújo et al. [33] PMID: 19468609 2006	Subarachnoid block Sedation with propofol TCI Local infiltration with 0.5% ropivacaine	Hemorrhoidectomy	Intraoperatively, the patient developed myotonic crisis (10 minutes after being placed on the lithotomy position) that was controlled by sedation (the target concentration was increased to 1.5 microg. mL-1 and given a bolus of 40 mg)
Klompe et al. [34] PMID: 17239222 2007	GA (TIVA propofol, atracurium and sufentanil)	Implantation of a pulmonary allograft between right ventricle and pulmonary artery was indicated	None

RESULTS OF DESCRIPTIVE ANALYSIS

We found twenty-seven papers about anesthesia (general, regional or sedation) in patients with DM in the past 15 years. For the descriptive analysis qualitative variables were expressed in absolute frequencies and percentages. In Table 3 type of anesthesia is represented. Abdominal surgery was the most frequent (15 cases-55.5%) including laparoscopic (7 cases-25.9%) followed by c-section (5 cases-18.5%). The rest were single cases of neurosurgery, thoracic, orthopedics, etc.

Table 3: Type of anesthesia.

	Frequency	Percentage (%)
General anesthesia	13	48.1
General anesthesia+regional anesthesia	7	25.9
Regional anesthesia	4	14.8
Regional anesthesia+sedation	3	11.1

The complications are represented in Table 4. 14 of 28 cases did not suffer any complication (51.9%). The principal complication was respiratory (11 cases-40.7%), on 6 cases-54.4% of total respiratory complication needed mechanical ventilation after surgery and 5 cases-45.45% resolved with non-invasive ventilation or oxygen therapy. 8 (72.7%) of these cases of respiratory complication followed general anesthesia.

Table 4: Complications.

	Frequency	Percentage (%)
None	13	48.1
Respiratory	11	40.7
Shivering	1	3.7
Miotony	1	3.7
Cardiac	1	3.7

Anesthesia and myotonic dystrophy (DM1)

Preoperative period: Preoperative evaluation of patients with DM should involve a multidisciplinary team including medical, neurology, cardiac, and anesthesiology specialties. Any preoperative weakness should be addressed and further evaluated. In patients with respiratory symptoms, we should consider pulmonary function testing. Patients may present with Cardiac rhythm management devices like pacemakers and defibrillators..

Patients suffering from DM are at higher risk of aspiration due to reduced gastric emptying and pharyngeal muscle dysfunction, preoperative administration of any sedatives should be avoided as it will further aggravate respiratory depression. Consideration should be given to preoperative prophylaxis with sodium citrate, metoclopramide, and H2 antagonists to prevent aspiration pneumonia.

Intraoperative period: Regional anesthesia with minimal sedation is the best option whenever possible. Spinal and epidural anesthesia have been reported to be successful and safe [18,27], either as a sole anesthetic or as a part of postoperative analgesia. As there are case reports of shivering and precipitation of myotonic crisis with uterine atony after epidural anesthesia for Cesarean section [35,36], patients should be closely monitored during spinal or epidural anesthesia. During general anesthesia, muscle relaxants should be avoided. If muscle relaxants need to be given, succinylcholine should be avoided and complete muscular block reversal should be ensured. Sugammadex is preferred to neostigmine as muscle reversal. The fear that neurostimulation during the peripheral nerve block might precipitate myotonia may not be an issue these days as nerve stimulator can be avoided due to ultrasound availability. We should not forget that patients with DM are very sensitive to opiates and anesthetic agents since they have a higher risk of respiratory depression and postoperative ileus.

Apart from standard ASA monitors, neuromuscular block and temperature monitors should be applied. Rapid sequence induction should be the chosen as these patients are at higher risk of aspiration due to pharyngeal muscle weakness. DM can be precipitated intraoperatively by hypothermia, shivering, surgical or mechanical stimulation and electrocautery [37,38]. Availability of temporary pacemakers and defibrillators should be ensured as well.

Postoperative period: Many cases of perioperative complications have been reported in patients with DM and most of them are respiratory [39] continuous pulse oximetry and ECG monitoring is necessary for longer period depending on type of the surgery, drugs administered, surgical time, etc. Furthermore, postoperative ventilation in patients with high risk of pulmonary complications should be considered. It is recommendable to restrict use of opioids and apply multimodal pain management after surgery. Pulmonary toilet with incentive spirometry, chest physiotherapy and cough assistant devices play an important role in the sooner recovery of these patients.

In our review of DM1 anesthetized cases, there is no data of association with malignant hyperthermia, so it seems safe to use inhalation agents. The only case that presented intraoperative myotonic crisis was an hemorrhoidectomy performed under subarachnoid anesthesia [33]. It was resolved by increasing sedation with propofol, so the causes of this complication could be the hypothermia in the operating room or surgical stress.

According to the descriptive analysis of our bibliographic search, respiratory complications are by far the most frequent in this type of patients and most of them occur in cases of general anesthesia, even without the use of muscle relaxants. They are of great importance since in half of the cases the patients required mechanical ventilatory support after surgery and consequent admission to the ICU. As previously mentioned, regional anesthesia, spinal or peripheral blocks, are probably safer options for these patients.

LIMITATIONS

In rare diseases like DM, most studies are based, like the present work, on reviews of clinical cases. There are no prospective randomized studies and it would be hard to develop them. Therefore, the sample of published cases is quite heterogeneous according to type of surgery, type of anesthesia, complications, characteristics and status of each patient, etc. So the possibility of establishing statistical relationships is difficult and not completely reliable.

CONCLUSION

Rare multisystemic diseases are an anesthetic challenge. The evaluation of the case starts during preoperative assessment and an anesthesia plan should be formulated to avoid complications. When it comes to reducing adverse events, both intraoperative and postoperaive care is important. The postanesthetic vigilance varies depending on patient state, type of surgery, type of anesthesia, etc. to minimize hospital stay.

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