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CASE REPORT

Conscious sedation in a female older adult with familial dysautonomia. A case report

Sedación consciente en una adulta mayor con disautonomía familiar. Reporte de caso

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Abstract

Introduction: Familial dysautonomia (FD) is a rare hereditary disorder that poses multiple challenges during peri operative management.
Case presentation: A 77 year old female with controlled hypertension and FD was scheduled for lower limb arteriography and angioplasty of the lower limbs at a tertiary care hospital in Medellín (Colombia) due to chronic occlusive arterial disease and intermittent claudication. The patient exhibited several classic signs of FD, including dysphagia, gastroesophageal reflux with recurrent aspiration, sleep apnea without non invasive ventilation, kyphoscoliosis, frequent acute adrenergic crises, and autonomic dysfunction characterized by orthostatic hypotension, supine hypertension, and marked bradycardia during carotid sinus massage and tilt table testing. Given the increased risk of aspiration and adrenergic crises associated with general anesthesia due to her conditions, the procedure was performed under conscious sedation using target controlled infusion (TCI) of propofol combined with continuous dexmedetomidine infusion. No anesthetic complications or dysautonomic crises occurred, and the patient was discharged after 48 hours of observation.
Conclusion: Conscious sedation with TCI of propofol and continuous dexmedetomidine infusion may be a safe intra operative analgesic strategy for FD patients, who, given the multisystemic nature of this disease are at high risk of perioperative complications, even during low-risk procedures.

Resumen

Introducción. La disautonomía familiar (DF) es un trastorno hereditario poco frecuente que plantea múltiples retos para el manejo perioperatorio.
Presentación del caso. Mujer de 77 años con hipertensión arterial controlada y DF programada para arteriografía y angioplastia de miembros inferiores en un hospital de cuarto nivel de atención de Medellín (Colombia) debido a enfermedad arterial oclusiva crónica y claudicación intermitente. La paciente presentaba varios signos clásicos de DF, incluyendo disfagia, reflujo gastroesofágico con broncoaspiración recurrente, apnea del sueño sin ventilación mecánica no invasiva, cifoescoliosis, crisis adrenérgicas frecuentes y disfunción autonómica caracterizada por hipotensión ortostática con hipertensión en decúbito y bradicardia significativa durante masaje del seno carotídeo y prueba de mesa basculante. Teniendo en cuenta los riesgos de usar anestesia general en esta paciente debido a sus características clínicas (broncoaspiración y crisis adrenérgica), el procedimiento se realizó bajo sedación consciente con infusión controlada por objetivo (TCI, por su sigla en inglés) de propofol y perfusión continua de dexmedetomidina. No se presentaron complicaciones anestésicas ni crisis disautonómicas. Tras 48 horas de observación, la paciente fue dada de alta.
Conclusión. La sedación consciente con TCI de propofol y perfusión continua de dexmedetomidina puede ser una alternativa segura de analgesia intraoperatoria en pacientes con DF, quienes, dada la naturaleza multisistémica de esta enfermedad, tienen un alto riesgo de complicaciones perioperatorias, incluso en procedimientos de bajo riesgo.

Introduction

Familial dysautonomia (FD), also known as Riley–Day syndrome or hereditary sensory and autonomic neuropathy type III, is an autosomal recessive disorder that occurs mainly among individuals of Ashkenazi Jewish descent, with carrier rates ranging from 1:32 to 1:18.[1-3] FD is associated with mutations in the *IKBKAP* gene (9q31), a human gene encoding for the I-κ-B kinase complex associated protein (IKAP), which is involved in neuronal development during embryogenesis, as well as in transcriptional regulation.[1,4] Its estimated incidence among Ashkenazi Jews is 1 case per 10 000 live births in the United States and 1 case per 3 700 live births in Israel.[1-3]

Although FD entails high morbidity and mortality,[3-6] survival has improved considering that the mortality rate prior to 1960 was 50% before reaching 5 years of age and, at present, a newborn with FD has a ~50% chance of reaching 40 years of age.[6]

FD affects the development and survival of sensory, sympathetic, and parasympathetic neurons, with progressive neuronal degeneration throughout life.[3] Its clinical manifestations include autonomic crises; gastrointestinal dysfunction (esophageal dysmotility, cyclic vomiting syndrome); aspiration; recurrent pneumonia; spinal deformities; labile body temperature; altered pain sensitivity; hypotonia; failure to thrive and delayed developmental milestones; corneal anesthesia; ataxia; and dysautonomic crises characterized by erythema, vomiting, sweating, and hypertension.[3,4,6,7] Furthermore, this condition differs from other hereditary sensory autonomic neuropathies due to the presence of profound autonomic dysfunction, orthostatic hypotension, and abnormal sweating.[4]

Given the multisystemic nature of FD and the sensory and autonomic alterations it involves, the use of anesthetics in these patients is complicated, as they often experience complications during anesthesia, as well as other intraoperative and postoperative complications.[4] Since it is a very rare disorder, the literature on the subject is mainly comprised of case reports and series that stress the difficulties encountered during the perioperative period.[4,6]

The following is the case of a 77-year-old female patient with FD who underwent arteriography and angioplasty of the lower limbs, and it focuses on the anesthetic management used during the intraoperative period.

Case presentation

A 77-year-old woman (62kg, body mass index: 21.2kg/m²) with FD and high blood pressure (treated with verapamil and enalapril) was scheduled for arteriography and angioplasty of the lower limbs in May 2023 at a quaternary care hospital in Medellín (Colombia) due to intermittent claudication secondary to chronic occlusive arterial disease. The patient had no signs of critical ischemia but her symptoms had worsened in the last few days. It should be noted that the patient reported taking acetylsalicylic acid without a documented medical indication.

The patient exhibited the following classic signs of FD: dysphagia, gastroesophageal reflux with recurrent aspiration; sleep apnea without the need for noninvasive ventilation; kyphoscoliosis; frequent acute adrenergic crises characterized by facial flushing and hypertension; small fiber neuropathy; hypoalgesia, with occasional skin lesions; hyperhidrosis; and autonomic dysfunction characterized by orthostatic hypotension, supine hypertension, and significant bradycardia (28bpm) during carotid sinus massage and tilt table testing at 60°.

Preoperative assessment and management: given her history of reflux and the fact that, due to the presence of FD, the procedure had to be performed without manipulating the

airway, an 8-hour fast for solids and a 2-hour fast for clear liquids was indicated, as well as the administration of a proton pump inhibitor (omeprazole 40mg orally) the night before and the morning of the procedure, in addition to metoclopramide (10mg intravenously) 30 minutes before the procedure.

During the intraoperative period, noninvasive monitoring of vital signs was performed using a 5-lead ECG, pulse oximetry, noninvasive blood pressure measurement (Figure 1), bispectral index (BIS) (Figure 2), and the Ramsay sedation scale to monitor the depth of anesthesia. Supplemental oxygen was administered via a nasal cannula at a flow rate of 3 liters per minute, and continuous spontaneous ventilation was maintained throughout the procedure. Given the risks of using general anesthesia in a patient with FD, such as aspiration and acute adrenal crisis, the procedure was performed under conscious sedation with target-controlled infusion (TCI) of propofol (0.5-1.2µg mL^{-1}) and continuous infusion of dexmedetomidine (0.2-0.35µg kg^{-1} h^{-1}) (Figure 3), the latter without an initial bolus and titrated to BIS 60-80 and Ramsay score 3-4. No anesthetic complications or dysautonomic crises were reported.

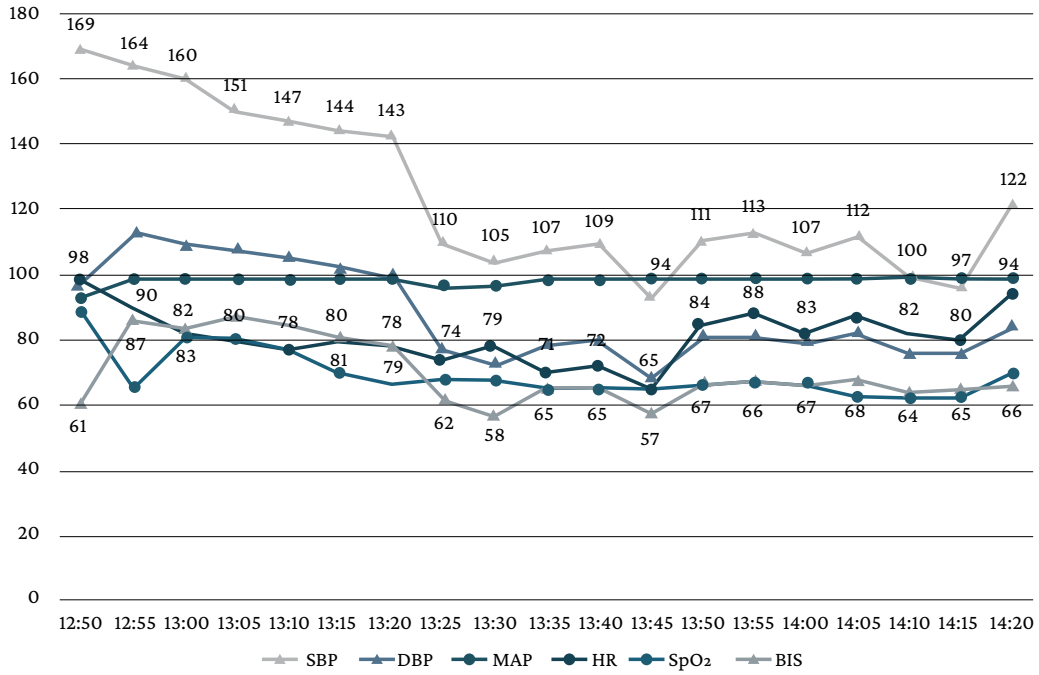

Figure 1. Intraoperative monitoring of vital signs.
SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; HR: heart rate; SpO_2: peripheral oxygen saturation; BIS: bispectral index.

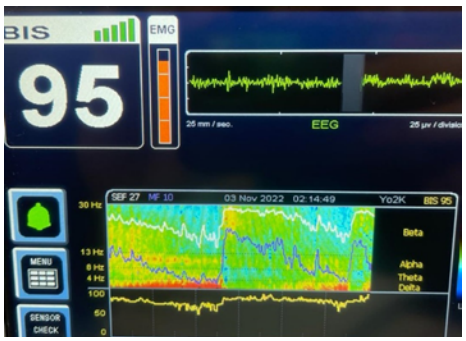

Figure 2. Monitoring of anesthetic depth with a bispectral index monitor.
BIS: bispectral index; EEG: electroencephalogram; Hz: Herzt.

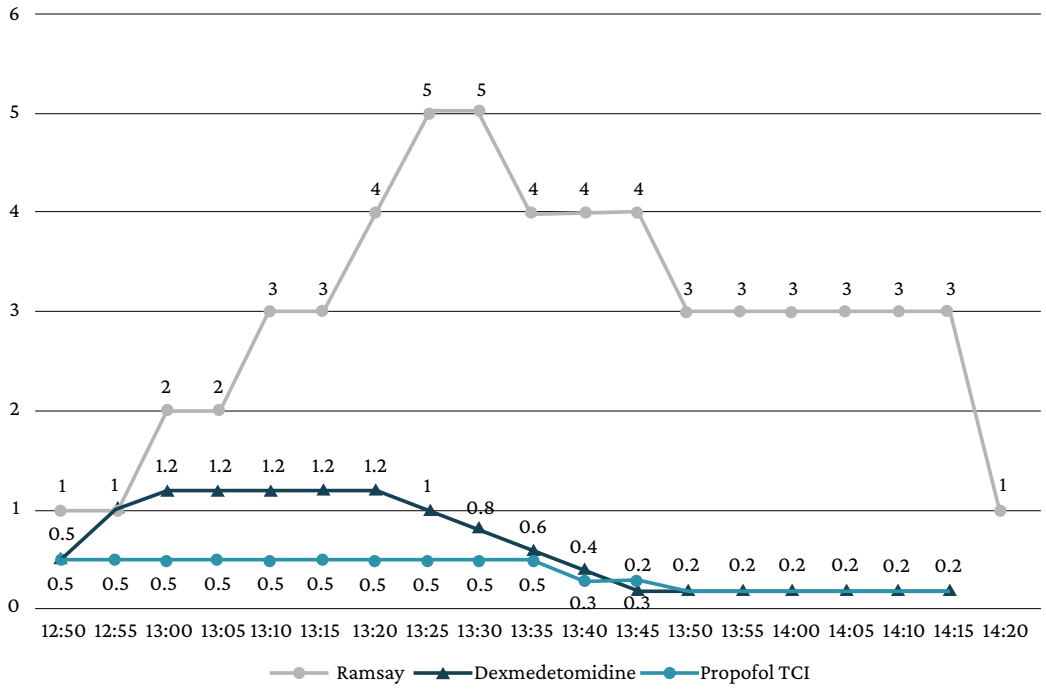

Figure 3. Monitoring of anesthetic depth using the Ramsay scale and relationship to sedative dosage. TCI: target-controlled infusion.

Once the procedure was completed, sedation was gradually reduced and, after confirming that the patient was awake, she was transferred to the post-anesthesia care unit for continuous monitoring due to the risk of adrenergic crisis.

After 48 hours of observation, she was discharged with instructions to attend follow-up appointments with the cardiology department, although she did not attend any of them.

Discussion

FD is a disorder that poses a complex perioperative scenario due to autonomic instability, hemodynamic lability, and a high risk of respiratory complications.[3,4,6,7] In this regard, in a systematic review that included 18 case series or case reports of perioperative management of FD patients (179 patients undergoing 290 anesthetics), Weingarten & Sprung[4] found that intraoperative complications were mainly cardiovascular with hemodynamic variability (hypotension, hypertension, bradycardia, dysrhythmias, complete heart block, and cardiac arrest), and that postoperative complications included vomiting and pulmonary complications such as pneumonia, atelectasis, excessive secretions, and respiratory arrest. These complications are explained by the lack of feedback from arterial baroreceptors and generalized sensory loss in multiple organs described in the pathophysiology of the disease.[2]

In our case, the patient presented several clinical manifestations of FD that were considered high risk (Table 1), such as significant inducible bradycardia, orthostatic hypotension, adrenergic crises, aspiration, and restrictive kyphoscoliosis. Notwithstanding the above, due to the adoption of a strategy focused on conscious sedation with low effect-site concentration of propofol and titrated dexmedetomidine during the procedure (arteriography and angioplasty), no perioperative adverse events were reported.

Table 1. Common manifestations of familial dysautonomia, occurrence in the reported case, and implications for anesthesia.

System	Common manifestations	Occurrence in the patient	Implications for anesthesia
Cardiovascular	Orthostatic hypotension, hypertensive spikes, bradycardia	Yes	Close monitoring and titratable sympatholytic drugs
Respiratory	Bronchiectasis, sleep apnea, decreased response to hypoxia	Yes	No respiratory depressants and airway management
Gastrointestinal	Reflux and delayed emptying	Yes	Reduction of aspiration risk (fasting + drugs + ultrasound)
Nervous	Adrenergic crises triggered by stress	Yes	Prophylaxis with dexmedetomidine

Source: Elaborated based on Weingarten *et al.*,[4] Axelrod *et al.*,[5] Ngai *et al.*,[6] González-Duarte *et al.*,[7] and Abulhasan *et al.*[8]

Dexmedetomidine is a central α2 agonist that reduces sympathetic discharge, attenuates catecholamine release, and, unlike benzodiazepines, mitigates autonomic crises without compromising spontaneous ventilation. Its usefulness has been confirmed both in intra-hospital adrenergic crises and during the perioperative period in adults and infants with FD.[8-10] The hemodynamic control observed in our patient is consistent with the heart rate stability and the absence of paroxysmal hypertension described in recent case series and studies that have used dexmedetomidine-based regimens.[9,11]

Although dexmedetomidine has beneficial effects in the anesthetic setting, including sedation, analgesia, anxiolysis, and reduced requirements for opioids and inhaled anesthetics, Kato *et al.*,[11] in a double-blind, randomized placebo-controlled study involving 12 healthy men who received dexmedetomidine infusions, reported that the cardiovascular reflex index to temporal reductions in blood pressure was attenuated during dexmedetomidine sedation. Therefore, according to these authors, when transient hypotension is induced by postural changes, bleeding, and/or other stressors, administering this medication may lead to an additional and sustained reduction in blood pressure.

In FD, the glossopharyngeal and vagus nerves are involved, causing afferent baroreflex failure with uncontrolled swings in blood pressure[2,12] because sympathetic efferent activity is no longer coupled to the cardiac cycle.[12] Consequently, insufficient baroreceptor feedback causes orthostatic hypotension with paradoxical slowing of the heart rate,[12] as observed in our patient. Similarly, involvement of the glossopharyngeal nerve in FD causes blunted chemoreflex responses to hypoxia and loss of protective airway reflexes, including the gag reflex,[2] making respiratory involvement equally challenging.

Respiratory complications are almost universally present in patients with FD.[10] Impaired input from peripheral chemoreceptors —normally transmitted to the central nervous system via the glossopharyngeal (cranial nerve IX) and vagus (cranial nerve X) nerves— results in markedly blunted ventilatory responses to hypoxia.[13] Respiratory abnormalities are a prominent feature of FD, with patients exhibiting varying degrees of upper airway obstruction (83%), lower airway disease (85%), and restrictive lung disease (94%).[13] Furthermore, in these patients, reduced tone in the upper airway and intercostal muscles during sleep can cause sleep-related hypoventilation or obstructive sleep apnea, as reported in our patient.[10] Similarly, these individuals experience daytime hypoventilation due to chemoreflex failure, leading to impaired ventilatory drive and restrictive lung disease, mainly caused by abnormal proprioception and kyphoscoliosis, with the latter also occurring in our patient.[13] In view of the foregoing, avoiding airway manipulation in patients with FD is essential, as intubation not only precipitates autonomic instability, but ventilatory depression from intravenous agents can turn subclinical hypercapnia into acute respiratory failure.[14,15]

Our decision to maintain spontaneous ventilation under conscious sedation was based on the principles outlined above and on the fact that, according to the literature, pulmonary disorders in patients with FD are common as a result of frequent episodes of aspiration throughout their lives.[4] In addition, to reduce the risk of aspiration, 8 hours of fasting for solids and 2 hours for clear liquids were indicated, as well as the administration of omeprazole and metoclopramide. However, it should be noted that gastric emptying (gastric volume <1.5mL kg^{-1}) can be confirmed via gastric ultrasound, thus avoiding prolonged fasting as it could worsen hypotension.[16] In our patient, stimuli that could cause laryngospasm were minimized by avoiding intubation and neuromuscular relaxants, while the already limited cough reflex was preserved, thus reinforcing lung protection.

Various pharmacological strategies for treating patients with FD are currently under investigation, including the use of carbidopa to manage hyperdopaminergic crises and control vomiting/retching,[17,18] or splicing modulators to increase IKAP levels,[19] which demonstrates the progression of treatment strategies over time for the disease. However, none of these strategies substitutes for the need to reduce the risk of aspiration during anesthesia.[16] In our case, the absence of desaturation and clinical signs of aspiration confirms that the combination of conscious sedation and pharmacological measures is effective for minimally invasive endovascular procedures in FD patients.

Finally, our experience demonstrates the importance of tailoring the anesthetic plan to the needs of FD patients, as they are at high risk for perioperative complications due to the multisystemic nature of this disease.

Conclusion

Anesthetic management in FD patients is challenging due to, among other reasons, autonomic lability and the high risk of aspiration. As observed in the present case, conscious sedation with propofol TCI and continuous dexmedetomidine infusion may be a safe alternative for intraoperative analgesia in patients with FD, who, given the multisystemic nature of this disease, are at high risk for perioperative complications, even during low-risk procedures. The findings of this case report support the adoption of conscious sedation protocols and advanced monitoring in low-stress endovascular procedures in FD patients.

Ethical considerations

This case report was prepared after the patient signed an informed consent form authorizing the use of her data.

Conflicts of interest

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