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General anaesthesia in two patients with Limb-Girdle muscular dystrophy

Elizabeth Jane Baldeón-Chávez, José Ramón Ortiz-Gómez, Nerea Díez-Sánchez, Gabriel Cerdán-Rodríguez
Service of Anaesthesiology, Hospital Complex of Navarra B, Virgen del Camino Hospital, Pamplona, Spain

Abstract

We describe the perioperative management of two patients with Limb Girdle Muscular Dystrophy (LGMD) programmed for elective surgeries under general anesthesia. After preparation of the operating room according to a malignant hyperthermia (MH) prevention protocol, a total intravenous anaesthesia (target controlled infusion) of propofol and remifentanil were used uneventfully. Neuromuscular function was monitored and deep rocuronium induced neuromuscular blockades were antagonized with sugammadex in 5 and 6 min respectively. The key points in the management of general anaesthesia in LGMD are reviewed: MH susceptibility, excessive sensitivity to sedatives, airway complications, selection of anaesthesia techniques (regional *vs.* general), neuromuscular blockade assessment and reversal and recommended patient monitoring, including respiratory and cardiovascular.
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Introduction

Limb Girdle Muscular Dystrophy (LGMD) is a group of rare hereditary progressive myopathic disorders resulting from alterations in genes required for normal muscle function. It is characterized by autosomal dominant and recessive inheritance. The estimated prevalence ranges from 1:14,500 to 1:123,000 inhabitants. LGMD type 2A is the most common form of LGMD worldwide. Although strict recessive inheritance is assumed, patient carrying a single mutation in the calpain3 gene (calpainopathy) are often reported, as our first patient [1].

LGMD has a predominantly proximal distribution of weakness, which early in the course of the disease spares distal, facial and extraocular muscles. The age of onset varies from early childhood to adulthood. The severity of symptoms varies depending on the type of inheritance from one patient to another. Most childhood-onset cases have a pelvifemoral distribution of weakness. By comparison, adult-onset involves both shoulder and pelvic girdles with gradually increasing proximal limb weakness, thereby leading to restriction of mobility and eventually to wheelchair confinement [1].

The clinical and serum determination of creatine kinase establish the preliminary diagnosis, confirmed by muscle biopsy in combination with a genetic test [2].

Clinical report

We describe the anaesthetic management of two patients with LGMD in elective surgery under general anaesthesia. The preoperative evaluation included physical examination (both patients started to show weakness since childhood that increased progres-

sively until the necessity of wheelchair), airway, heart and lung examination, CBC, blood chemistry, X-ray chest and electrocardiogram. Written consent was obtained in both cases. The OR was prepared according to the Malignant Hyperthermia (MH) protocol. We monitored electrocardiogram, pulse-oximetry, capnography, noninvasive blood pressure, nasopharyngeal temperature, bispectral index, neuromuscular blockade (NMB) and ventilation.

Patient 1:

She was a 57 yr, 51 kg, 1.58 m, ASA III woman scheduled for total thyroidectomy. Her medical history included: LGMD type 2A, seizures treated with carbamazepine and controlled arterial hypertension. The preoperative tests were all within normal limits. Her daily medications consist of L-carnitine 1g/d, acetaminophen 1 g/d, amlodipine 5 mg/d and carbamazepine 200 mg/8 hr. We don't use premedication, and after prolonged pre-oxygenation, anaesthesia was induced with thiopental (275 mg) and fentanyl (150 μg). The lungs were ventilated with facemask and manual ventilation and NMB monitor was then calibrated according to international consensus guidelines using objective evoked electromyography of the *adductor pollicis* muscle. We administered rocuronium bromide (50 mg) after 4 min of calibration, when train-of-four (TOF) ratio (T4/T1) was stable (0,95-1,15) and first twitch of the TOF series (T1) was stable at > 0.90 of the baseline value. Deep NMB was achieved in 1,5 min (T1 = 0%) and then the patient was intubated and her lungs ventilated with O_2/Air (FiO_2 50%). The anaesthetic maintenance was performed with total intravenous anaesthesia (TIVA) target controlled infusion (TCI) of propofol and remifentanil. Three additional doses of 20 mg rocuronium were needed to maintain post-tetanic count (PTC) = 0. Morphine 5 mg was administered before extubation for postoperative pain control. Other drugs used were: pantoprazole 40 mg, dexamethasone 8 mg, acetaminophen 1g and ondansetron 4 mg.

The surgical intervention lasted for 120 minutes and sugammadex 3 $mg.kg^{-1}$ was administered, recovering a TOF ratio > 90% in 5 minutes. The patient started spontaneous ventilation and she was extubated after 11 minutes uneventfully. She was hemodynamically stable, with good pain control without temperature changes in the Post-anaesthesia Care Unit (PACU) for five hours. She was discharged from hospital 3 days after surgery without incidences.

Patient 2:

He was a 71 yr, 95 kg, 1.70 m, ASA IV man, scheduled for partial nephrectomy. His medical history included: LGMD, arterial hypertension, diabetes, nephrolithiasis, urinary incontinence and total cardiac blockade with permanent pacemaker. The physical examination showed difficult airway and global hypoventilation. Preoperative test were all within normal limits excepting ECG (pacemaker rhythm). His daily medication included L-carnitine 1g/d, acetaminophen 1g/d, diltiazem 180 mg/d, allopurinol 100 mg/12 hr, metformine 850 mg (1-0-0), valsartan/ hydrochlorothiazide 160/12.5 mg/d and tolterodine 4 mg/d. He received airway lidocaine spray and remifentanil infusion (0.03 $\mu g.kg^{-1}.min^{-1}$) for aware fiberoptic intubation. When endotracheal tube was placed, anaesthesia was induced with propofol (50 mg) and fentanyl (100 μg). The lungs were ventilated with a facemask while the neuromuscular monitoring was calibrated according to international consensus guidelines. After 10 min of calibration, we observed signal stabilization of TOF ratio (0.95-1.15) and T1 (> 0.92 of the baseline value). Then we administered rocuronium bromide (25 mg), with complete blockade in 2 minutes.

The anaesthetic maintenance was performed with TCI of propofol and remifentanil. Four additional doses of rocuronium (total, 75 mg) were needed to maintain PTC = 0. Morphine 4 mg was administered before extubation for postoperative pain control. Other drugs used were: ranitidine 50 mg, dexamethasone 8 mg, acetaminophen 1 g and mannitol 20 g IV.

The surgical intervention lasted for 145 minutes. A TOF ratio > 90% was obtained 6 min after sugammadex 2.5 $mg.kg^{-1}$ administration. The patient started spontaneous ventilation and he was extubated uneventfully in 9 minutes. There were no problems during the immediate postoperative period (Critical Care Unit). He was discharged from hospital 4 days after surgery without incidences.

Discussion

The anaesthetic considerations of LGMD are considered to be similar to other muscular dystrophies. However perioperative complications are not proportional to the severity of the disease, because they occur even in mildly affected patients [3]. Consequently, patients with LGMD should undergo careful preoperative consultation and evaluation.

There are several key points to consider in the LGMD anaesthesia management:

1. Clinicians must assume that these patients may be MH susceptible [4,5], even in patients with uneventful previous anaesthesia [6,7]. Despite of the association between MH and several neuromuscular syndromes, there are no physical findings that identify MH susceptible patients [6,8]. So, the operating room was prepared from the previous evening following the MH protocol of prevention [7] which included: avoid exposition to volatile anaesthetics and succinylcholine (the vaporizers were removed from anaesthesia machine to avoid unintended administration), new breathing bag, filters, respiratory circuit (washed with air (10 L/min) for at least 3 hr) and soda lime. The availability of an external pacemaker and the existence and enough quantity of dantrolene in the hospital pharmacy were also checked [2,6].
2. LGMD patients may be sensitive to sedative-hypnotics and opioids, which should be used judiciously. This aspect was revealed clearly in the second patient, who needed small sedation with remifentanil to perform fiberoptic intubation and only 50 mg of propofol for anaesthetic induction.
3. Airway management: these patients may show possible complication during induction of anaesthesia such as decreased laryngeal reflexes and prolonged gastric emptying time, accumulation of oral secretions and masseter spasm. It is important to be prepared for a difficult airway, especially in patients with potential airway problem, as in the second patient [9].
4. Regional anaesthetic techniques should be used whenever surgery allows because in order to avoid the risk of triggering agents, respiratory depression and enable the use of local anaesthetics for postoperative analgesia [10,13]. Regional anaesthesia was impossible in our patients. General anaesthesia in LGMD needs careful monitoring of respiratory and cardiovascular function, and prevention of metabolic alterations and MH in both intraoperative and PACU periods.
5. Concerning the management of NMB, the use of succinylcholine is contraindicated because of the potential risk of MH, rhabdomyolysis and hyperkalemia. The last are more likely to result in cardiac arrest and unsuccessful resuscitation. The use of no depolarizing muscle relaxants is usually accompanied by an increase in both maximal effect and duration of action. Traditionally, it was recommended the use of low doses (0.1 x ED_{95}) of benzylisoquinoline drugs such as atracurium (preferable regarding steroid derivatives for its more predictable recovery profile), and after evaluation of the neuromuscular function, the dose was progressively adjusted. Cholinesterase inhibitors have been the only option for NMB reversal before the development of sugammadex. It has changed the NMB management in patients with neuromuscular diseases. Even the shortage of references about what kind of anaesthesia used in these patients mainly by the profile of the LGMD complications during anaesthetic acts, Yamada et al. [14] and Mogi et al. [15] mentioned two successful cases of rocuronium reversal with sugammadex in patients with muscular dystrophies. We use large doses of rocuronium for two reasons: first, both surgeries needed deep neuromuscular blockade (PTC = 0), and second, we have previous experience with rocuronium – sugammadex in patients with neuromuscular diseases [16,17]. We observed a satisfactory recovery of deep rocuronium NMB with sugammadex, allowing early extubation in patients with respiratory muscle weakness.
6. General anaesthesia in LGMD needs careful monitoring of respiratory and also cardiovascular function, due to the high incidence of cardiac involvement [18]. Egi et al. [19] described the sudden apparition of a Wenckebach type of second degree AV block during the patient position change, that needed ephedrine and atropine administration to revert to sinus rhythm.

Finally, a specific consideration: we use thiopental instead of propofol for anaesthetic induction in the first patient (and then a TCI-TIVA of propofol-remifentanil), due to her previous history of seizures.

In conclusion, we have effectively used sugammadex in two LGMD patients to reverse deep rocuronium NMB. We suggest that neuromuscular monitoring is essential in these patients. The prevention or complications such as MH should be considered in these patients. LGMD is a rare disease, and there are few references concerning the use of general anaesthesia, so more information is required to establish definitive anaesthetic management strategies.

Konflikt interesów / Conflict of interest
Brak/None

Correspondence address:
Elizabeth Jane Baldeón-Chávez
Service of Anesthesiology, Hospital Complex of Navarra B,
Virgen del Camino Hospital, Pamplona, SPAIN
Irunlarrea St. 3. Pamplona; 31008 Navarra, Spain.
☎ (+ 34) 848 422 100
F (+34) 848 422 303
elizabal@gmail.com

References

1. Darras BT. Limb-Girdle muscular dystrophy: UpToDate; 2013. Available from: http://www.uptodate.com /contents/limb-girdle-muscular-dystrophy.
2. Gallardo E, Saenz A, Illa I. Limb-girdle muscular dystrophy 2A. Handbook of clinical neurology 2011;101:97-110.
3. Cornelio F, Di Donato S, Testa D, Mora M, Gori G, Peluchetti D, et al. "Carnitine deficient" myopathy and cardiomyopathy with fatal outcome. Ital J Neurol Sci 1980;1:95-100.
4. Moro C, Dangelser G, Veyckemans F. Anesthetic management of a child with delta sarcoglycanopathy. Ann Fr Anesth Reanim 2007;26:359-62.
5. Richa FC. Anaesthetic management of a patient with limb-girdle muscular dystrophy for laparoscopic cholecystectomy. Eur J Anaesthesiol 2011; 28:72-3.
6. Ortiz Gomez JR. Anesthesia in malignant hyperthermia. Rev Esp Anestesiol Reanim 2008;55:165-74.
7. Ortiz-Gómez JR, Fornet-Ruiz I, Palacio-Abizanda FJ. Malignant hyperpyrexia. Rev Esp Anestesiol Reanim 2013;60:46-54.
8. Gurnaney H, Brown A, Litman RS. Malignant hyperthermia and muscular dystrophies. Anesth Analg 2009;109:1043-8.
9. Stevens RD. Neuromuscular disorders and anesthesia. Curr Opin Anaesthesiol 2001;14:693-8.
10. Azzolini M, Cesari G, Matuella C, Scillieri G. Combined block of the cervical-brachial plexus in the surgery of the scapula-humeral girdle. Minerva Anestesiol 1984;50:7-11.
11. Pash MP, Balaton J, Eagle C. Anaesthetic management of a parturient with severe muscular dystrophy, lumbar lordosis and a difficult airway. Can J Anaesth 1996;43:959-63.
12. Allen T, Maguire S. Anaesthetic management of a woman with autosomal recessive limb-girdle muscular dystrophy for emergency caesarean section. Int J Obst Anest 2007;16:370-4.
13. Von Breunig F, Goetz AE, Heckel K. Severe muscular dystrophy and pregnancy: interdisciplinary challenge. Anaesthesist 2012;61:52-5.
14. Yamada M, Kimura T. Successful use of sugammadex in a muscular dystrophy patient. Masui 2011;60:1205-6.
15. Mogi K, Shiba S, Hirabayashi Y, Seo N. Use of sugammadex in a patient with limb girdle muscular dystrophy. Masui 2011;60:710-2.
16. Ortiz JR, Lopez LA, Adame MM. Use of rocuronium in Duchenne's disease. Rev Esp Anestesiol Reanim 1999;46:179-80.
17. Ortiz-Gómez JR, Palacio-Abizanda FJ, Fornet-Ruiz I. Rocuronium induced neuromuscular blockade reversion with sugammadex in a patient with Charcot-Marie-Tooth disease. Anest Ratow 2010;4:307-9.
18. Sveen ML, Thune JJ, Kober L, Vissing J. Cardiac involvement in patients with limb-girdle muscular dystrophy type 2 and Becker muscular dystrophy. Arch Neurol 2008;65:1196-201.
19. Egi M, Tokioka H, Chikai T, Fukushima T, Ishizu T, Tanaka T, et al. Propofol anesthesia for a patient with progressive muscular dystrophy. Masui 2002;51:196-8.